FOURTH EDITION

Communicable Disease Control and Health Protection Handbook

Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere, Jim van Steenbergen

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Fourth Edition

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Foreword

Six years have passed since the third edition of the *Communicable Disease Control and Health Protection Handbook* was published. In many other areas of public health this may not seem a long time. However, when it comes to communicable disease control there is always an element of urgency, and each large international (or national) outbreak is an impetus for reflection on what went well and what could be done better next time. Therefore, our area of work is as much driven by the large events as it is by slow developments.

Since the last edition, the WHO has three times invoked formal declarations of public health emergencies of international concern (PHEIC) under the International Health Regulations (IHR 2005); in 2014 the polio declaration, the same year the Ebola declaration, and in 2016 the Zika virus declaration. Each of these emergencies has different characteristics and provides different lessons.

Two of the most tangible consequences of larger international outbreaks the last 10 years, are the new EU legislation on Cross-border Threats to Health (Decision 1082/2013) and the establishment of the new WHO Health Emergencies Programme. Both highlight the importance of increasing the core capacities of the countries to prepare for and respond to health threats, and the need for efficient international co-operation. These tasks cannot be performed by the health sector itself, but need an inter-sectoral and one-health approach. The new edition of the handbook, covers these areas.

However, the challenge does not only lie with the big outbreaks. We are also facing silent and slow, but no less threatening epidemics. Here I am of course referring to the growing problem of antimicrobial resistance, which can only be overcome by proper antibiotic stewardship and consequent infection prevention and control in hospitals. However, everyone needs to contribute, hence the one-health approach, to buy us the time needed for the introduction of new technologies and principles of fighting infections that may in the future save us from a situation similar to the one in the pre-antibiotic era.

The years since the previous edition of this book have also presented new challenges in the shape of increasing lack of trust in authorities, 'alternative facts', and social media filter bubbles, where rumours and myths are spreading. In the age of social media, vaccine sceptics are getting effective platforms for disseminating their messages. As public health professionals, we are, therefore, facing new tasks in debunking these myths. This is requiring new skill sets outside the traditional public health competencies, and as public health professionals, we will need to provide leadership, regardless of our specific position.

Public health professionals are facing numerous challenges. Many are working not only with communicable diseases, but in a broader public health setting, where some of the specific infectious diseases requiring public health actions are only rarely encountered. The practitioner in the field noting an infection case, or cluster of cases, therefore from time to time will need easy access to practical, authoritative and updated information to guide initial assessment and practical response.

In today's information age, we are not lacking sources of information – quite the contrary, but the format is not always relevant to the practical problem at hand. This is where the *Communicable Disease Control and Health Protection Handbook* has its niche. The format of the handbook is designed to provide the on-call public health officer with necessary information at a glance in the acute situation. It provides clear and practical guidance on what needs to be done and when to engage others. It is thus a good compliment to other sources of information, for example relevant national guidelines. At the same

time, the overview chapters are useful for setting the individual cases in a larger public health perspective.

As the Director of the European Centre for Disease Prevention and Control (ECDC), I especially appreciate the specific European dimensions of the book. The country chapters provide a useful overview of the public health systems in each of the EU countries and some more. This European dimension highlights that fighting communicable diseases is not only a national priority, but is a task requiring co-operation across the borders.

July 2018

Andrea Ammon
Director
European Centre for Disease Prevention and Control

Abbreviations

ACDP	Advisory Committee on Dangerous Pathogens
AIDS	Acquired immunodeficiency syndrome
AIH	Autoimmune hepatitis
AMR	Antimicrobial resistance
BBV	Blood-borne virus
BCG	Bacille Calmette–Guérin (vaccine against TB)
BSE	Bovine Spongiform Encephalopathy
CAP	Community acquired pneumonia
CCDC	Consultant in Communicable Disease Control (local public health doctor with executive responsibilities for CDC)
CCG	Clinical Commissioning Groups (health service purchaser)
CDC	Communicable disease control
CDI	*Clostridium difficile* infection
CFR	Case Fatality Rate
CHP	Consultant in Health Protection
CICN	Community infection control nurse
CJD	Creutzfeldt–Jakob Disease
CMV	Cytomegalovirus
CNS	Central nervous system
CRE	Carbapenem-resistant enterobacteriaceae
CSF	Cerebrospinal fluid
D	Diarrhoea
DEET	N,N-diethyl-*m*-toluamide
DNA	Deoxyribonucleic acid
DOT(S)	Directly observed therapy (supervised)
DPH	Director of Public Health
DTP	Diphtheria, tetanus and pertussis (whole-cell)
EBV	Epstein–Barr virus
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EHO	Environmental health officer
EIA	Enzyme immunoassay
EIEC	Enteroinvasive *Escherichia coli*
ELISA	Enzyme-linked immunosorbent assay
EM	Electron microscopy
EU	European Union
FSA	Food Standards Agency
FWE	Food, water and environment
GI	Gastrointestinal
GP	General Practitioner (Primary Care Physician)
GUM	Genitourinary medicine
HACCP	Hazard Analysis Critical Control Point
HAI	Hospital acquired infection
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCAI	Health-care associated infection
HCV	Hepatitis C virus
HCW	Health Care Worker
HDV	Delta Hepatitis
HEPA	High-Efficiency Particulate Air (Filters)
HEV	Hepatitis E virus
Hib	*Haemophilus influenzae* type b
HIV	Human Immunodeficiency Virus
HNIG	Human normal immunoglobulin
HP	Health Protection
HPT	Health Protection Team
HPV	Human papillomavirus
HSCT	Haemopoietic Stem Cell Transplantation
HSV	Herpes simplex virus
HUS	Haemolytic uraemic syndrome
ICD	Infection control doctor (hospital)
ICN	Infection control nurse
ICT	Infection control team (hospital)
IDU	Intravenous drug user
IFA(T)	Indirect immunofluorescent antibody (test)
IgG	Immunoglobulin class G
IgM	Immunoglobulin class M
IHR	International Health Regulations
IID	Infectious intestinal disease
IPV	Inactivated poliovirus vaccine
IU	International unit
IV	Intravenous

LA	Local Authority
LBRF	Louse-borne relapsing fever
LD	Legionnaires' disease
LGV	Lymphogranuloma venereum
MDR	Multi-drug resistant (usually referring to TB)
MERS	Middle-East respiratory syndrome
MLST	Multilocus sequence typing
MLVA	Multiple-locus variable number tandem repeat analysis
MMR	Measles, mumps and rubella vaccine
MRSA	Met(h)icillin resistant *Staphylococcus aureus*
MSM	Men who have sex with men
NAAT	Nucleic acid amplification test
NCSP	National Chlamydia Screening Programme
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPA	Nasopharyngeal aspirate
OPV	Oral poliovirus vaccine
Pa	Pertussis vaccine (acellular)
PBS	Primary biliary sclerosis
PCR	Polymerase Chain reaction
PEP	Post-exposure prophylaxis
PFGE	Pulsed-field gel electrophoresis
PHE	Public Health England
PPE	Personal protective equipment
PrEP	Pre-exposure prophylaxis
PSC	Primary sclerosing cholangitis
PT	Phage type
RAPD	Random amplified polymorphic DNA typing
RCGP	Royal College of General Practitioners
RNA	Ribonucleic acid
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcription polymerase chain reaction
SARS	Severe acute respiratory syndrome
SCID	Severe Combined Immunodeficiency
SOP	Standard Operating Protocol/ Procedure
Sp/spp	Species
STEC	Shiga-toxin producing *E. coli*
STI	Sexually transmitted infection
TB	Tuberculosis.
TBE	Tick-borne encephalitis
TBRF	Tick-borne relapsing fever
TSE	Transmissible spongiform encephalopathy
TTP	Thrombotic thrombocytopaenia purpura
TWAR	Taiwan Acute Respiratory Agent
UK	United Kingdom of Great Britain and Northern Ireland
UTI	Urinary tract infection
vCJD	Variant Creutzfeldt–Jakob Disease
VHF	Viral haemorrhagic fever
VRE	Vancomycin resistant *Enterococcus*
VZIG	Varicella-zoster immunoglobulin
WGS	Whole genome sequencing
WHO	World Health Organization (OMS)
WNV	West Nile Virus
XDR	Extensively drug resistant (usually referring to TB)

Vaccine abbreviations (used in Section 5)

BCG	Bacille Calmette–Guérin (vaccine against TB)
DTP	Diphtheria, tetanus and pertussis vaccine
HepA	Hepatitis A vaccine
HepB	Hepatitis B vaccine
HiB	Haemophilus influenzae type B vaccine
HPV	Human papilloma virus vaccine
IIV	Inactivated influenza vaccine
IPV	Inactivated polio vaccine
LAIV	Live attenuated influenza vaccine
MCV	Meningococcal conjugated vaccine (4-valent)
MenB	Neisseria meningitidis group B vaccine
MenC	Neisseria meningitidis group C vaccine
MMR	Measles, mumps and rubella vaccine
PCV	Pneumococcal conjugated vaccine
Rota	Rotavirus vaccine
RotaC	Rotavirus species C vaccine
TBE	Tick-borne encephalitis vaccine
VAR	Varicella zoster vaccine

Section 1
Introduction

1.1 How to use this book

This book is for those working in the field of communicable disease control (CDC) and health protection. It provides practical advice for specific situations and important background knowledge that underlies communicable disease control activities; therefore, it will be of interest to all these working in this broad field, including (but not exclusively) public health physicians, epidemiologists, public health nurses, other public health practitioners, infection control nurses, environmental health officers, microbiologists, general practitioners and policy makers at all levels, as well as students in medical, public health and related fields.

Since the publication of the third edition, there have been many important changes in CDC and health protection. The world has faced its first large multi-country epidemic of viral haemorrhagic fever and other new or re-emerging threats, such as Middle East Respiratory Syndrome (MERS) have been identified. There have been successes, such as new vaccine programmes, improvements in knowledge, new evidence reviews, updating of consensus guidelines and new laboratory tests, particularly in relation to molecular epidemiology. The combination of these with administrative changes in the European Union (EU) and in member countries like the UK has led to major revisions in the content of this Handbook.

The structure of the book is as follows:

Section 1 contains important background material. Chapters 1.2 and 1.3 run through the basic principles of transmission and control that underlie later chapters. Chapter 1.4 provides the basics of how action resulting from that knowledge can be communicated to those who need to know and Chapter 1.5 is aimed primarily at those who undertake on-call duties: in this chapter we assume that some may not practice in mainstream communicable disease control or health protection or may be in training and are undertaking health protection response duties for the first time.

Section 2 addresses topics in the way they often present to CDC staff in the field, that is, as syndrome-related topics rather than organism based, such as an outbreak of gastroenteritis of (as yet) undetermined cause, or a needlestick injury. In these chapters, we discuss the differential diagnosis (infectious and non-infectious), including how to decide the most likely cause based on relative incidence, clinical and epidemiological differences and laboratory tests. We also give general advice on prevention and control, including how to respond to a case or cluster when the organism responsible is not yet known.

Section 3 addresses communicable disease control in a more traditional way, by disease/organism. We have continued to make these chapters suitable for a pan-European audience, using EU-wide data and policies where these exist. We have used England and Wales (or the UK if appropriate) as an example in other instances: for differences relating to surveillance and control in other countries, the relevant country specific chapter in Section 5 should be consulted (e.g. those working in Germany should consult Chapter 5.14).

The chapters in Section 3 conform to a standard pattern, which we hope will make instant reference easier. Most chapters are ordered as follows:

1 A short introduction mentioning the syndrome(s) common synonyms and the main public health implications of the organism.

2 A box of *suggested on-call action*. This relates only to what needs to be done if cases are reported outside normal office hours. Further action may be needed during the next working day, which will be identified in 'response to a case'.

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

3 *Epidemiology* gives the relevant points on burden of disease; important differences by age/sex/season/year/risk group are given and important differences within Europe are noted.
4 Two sections deal with diagnosis of the infection: *clinical features* and *laboratory confirmation*. Both sections highlight the important points to practising CDC professionals. They are not meant as a substitute for clinical and microbiological textbooks.
5 *Transmission* details the main sources, reservoirs, vehicles and routes of spread of the organism. The main aim of this section is to give the investigator clues as to how a case or outbreak may have arisen to aid identification and control.
6 *Acquisition* deals with the incubation period, infectious period (if communicable), infective dose (if known) and any important factors affecting immunity or susceptibility.
7 The final five sections relate to control of infection. These are based on current available guidance and evidence: where this is unclear, they are often based on practice in the UK, our assessments of the evidence base, our understanding of good public health practice and the application of first principles. These sections are:

- actions likely to be effective in the *prevention* of infection,
- *surveillance* activities relevant to the organism,
- suggested public health actions to be taken in *response to a case,*
- suggested approach to an *investigation of a cluster* of cases of that organism, and suggested actions to help in *control of an outbreak*, including a *suggested case-definition* for use in an epidemiological study.

Diseases that are generally less of a public health issue in Europe are summarised in the tables at the end of Section 3. Some infections may also be mentioned in relevant chapters in Section 2 and in chapters in Section 3 covering related organisms (e.g. information on other diarrhoeagenic *Escherichia coli* is given in a table in the chapter on Shiga-toxin producing *E. coli* (STEC)): please check the index for these.

Section 4 refers to the organisation of CDC/Health Protection services and could be titled 'how to run a CDC service'. For the authors who have worked as Consultants in CDC, this is the textbook that we wished we'd had on appointment! It deals with the services that a CDC department is expected to provide, including the non-communicable disease functions that have been attached to the health protection role in some countries. Some of those chapters are UK focused, although this has been reduced and we try to draw out the general principles underlying each approach, so that most will be of equal use to European colleagues.

Section 5 gives a brief overview of structures for infectious disease notification and public health action internationally and in each EU/European Economic Area (EEA) country. The objective of this section is to allow an orientation on public health structures relevant for infectious disease control in various European countries and to offer a starting point for further information on individual countries. Lengthy descriptions have been avoided, but internet addresses for contact points in the countries and for further information, reports and data have been given.

Finally the appendix and two lists of useful websites detail further sources of information and advice for those undertaking CDC functions routinely or on-call. Please note that the information and suggestions given in this book are not meant to override existing national or international guidelines; please also note that the information is a snapshot of the situation at the time of writing and that further data or advice will become available after writing. It is always sensible to check your national country website for up-to-date guidelines to inform public health action: if there are no national guidelines, then the European Centre for Disease Prevention and Control (ECDC) may give EU-wide guidance and other national centre (e.g. Public Health England [PHE]) or other authoritative websites may have something that can be applied to your situation. For this reason, the lists of websites have been placed inside the front and back covers for easy reference.

We are indebted to a number of individuals who have helped us in preparing this book,

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1.2 Basic concepts in the epidemiology of infectious disease

Identification

Infections can be identified by their clinical features, epidemiology and the use of appropriate laboratory procedures.

Epidemiological triangle

The traditional model of infectious disease causation is the epidemiological triangle. It has three components: an external agent, a susceptible host and environmental factors that bring the host and the agent together.

The agent is the organism (virus, rickettsia, bacterium, fungus, prion, etc.) that produces the infection. Host factors influence an individual's exposure, susceptibility or response to a causative agent. Age, sex, socio-economic status, ethnicity and lifestyle factors such as smoking, sexual behaviour and diet are among the host factors that affect a person's likelihood of exposure, while age, genetic makeup, nutritional and immunological status, other disease states and psychological makeup influence susceptibility and response to an agent. Environmental factors are extrinsic factors that affect the agent and the opportunity for exposure. These include geology, climate, physical surroundings, biological factors (such as insect vectors), socio-economic factors such as crowding and sanitation and the availability of health services.

Natural history of disease

This refers to the progress of a disease in an individual over time without intervention. Following exposure to an infectious agent there is a period of subclinical or inapparent pathological changes, which ends with the onset of symptoms. This period is known as the *incubation period*. For a given infectious disease, the incubation period has a range and a median and mean value. For hepatitis A, the range is two to six weeks with a mean of three weeks. During the incubation period, pathological changes may be detectable with laboratory or other tests. Most screening programs attempt to identify the disease process during this early phase of its natural history, since early intervention may be more effective than treatment at a later stage. The onset of symptoms marks the transition from the subclinical to the clinical phase. Most diagnoses are made during this stage. In some

people the disease may never progress to a clinically apparent illness. In others the disease process may result in a wide spectrum of clinical illness, ranging from mild to severe or fatal.

Occurrence

Two rates are commonly used to describe the occurrence of infectious diseases:

$$\text{Incidence} = \frac{\text{New cases over a given time period}}{\text{Persons at risk}}$$

$$\text{Prevalence} = \frac{\text{Existing cases at a given point in time}}{\text{Persons at risk}}$$

The occurrence or amount of an infectious disease will vary with place and time. A persistent low or moderate level of disease in a specified geographic area is referred to as *endemic* and a higher persistent level is called *hyper-endemic*. A pattern with occasional cases occurring at irregular intervals is called *sporadic*. A number of cases related in time and space is referred to as a cluster. When the occurrence of an infection exceeds the expected level for a given time period, it is called *epidemic* or *outbreak*. When an epidemic spreads over a wide geographical area affecting several continents it is called *pandemic*. Epidemics vary in size and duration. An *epidemic curve,* a frequency histogram of the number of cases against time or date of onset (see Figures 4.2.1–4.2.3), should be plotted. If exposure to the infectious agent takes place over a relatively brief period, a *point source* outbreak might be suspected. Intermittent or continuous exposure broadens the peaks of the epidemic curve, and so an irregular pattern is observed. An outbreak that spreads from person to person is called a *propagated* outbreak. In theory, the epidemic curve of a propagated outbreak would have a series of peaks at intervals approximating to the incubation period. Usually, the epidemic wanes after a few generations because the number of susceptible people falls below a critical level, or effective control measures have been introduced. Some epidemic curves have both common source epidemic and propagated epidemic features because of secondary person-to-person spread. These are called *mixed epidemics*.

Reservoir

The reservoir of an infectious agent is any person, animal, arthropod, plant, soil or substance (or combination of these) in which the infectious agent normally lives and multiplies. The reservoir may be different from the *source* or *vehicle* of infection. This is the person, animal, object or substance from which an infectious agent actually passes to a host. Many of the common infectious diseases have human reservoirs which include clinical cases, those who are incubating the disease and convalescent carriers. *Colonisation* is the presence of a micro-organism in or on a host, with growth and multiplication, but without evidence of infection. Shedding of an organism from a colonised host may be intermittent. Infectious diseases that are transmissible from animals to humans are called *zoonoses*. The *portal of exit* is the path by which an agent leaves the source host, which usually corresponds with the site at which the agent is localised, for example respiratory tract, genitourinary system, gastrointestinal system, skin or blood. The *portal of entry* is the route by which an agent enters a susceptible host.

For any given infection, understanding the chain of infection allows appropriate control measure to be recommended.

Susceptibility and resistance

Various biological mechanisms present barriers to the invasion and multiplication of infectious agents and to damage by their toxic products. There may be inherent resistance in addition to immunity as a result of previous infection or immunisation.

Box 1.2.1 Terms used to describe the outcomes of exposure to an infectious agent

- *Infectivity*: the proportion of exposed persons who become infected, also known as the *attack rate*.
- *Pathogenicity*: the proportion of infected persons who develop clinical disease.
- *Virulence:* the proportion of persons with clinical disease who become severely ill or die (Case Fatality Rate)

Hepatitis A in children has low pathogenicity and low virulence (Box 1.2.1). Measles has high pathogenicity but low virulence, whereas rabies is both highly pathogenic and highly virulent. Nevertheless, it is difficult to draw a clear line. The case fatality rate (CFR) in measles is low in industrialised countries, but could still be several percent in children with pour nutrition and low access to health care.

The *infectious dose* is the number of organisms that are necessary to produce infection in the host. The infectious dose varies with the route of transmission and host susceptibility factors. Because of the clinical spectrum of disease, cases actually diagnosed by clinicians or in the laboratory often represent only the tip of the iceberg. Many additional cases may remain asymptomatic. People with subclinical disease may nevertheless be infectious and are called carriers.

Infectious period

This is the time during which an infectious agent may be transmitted directly or indirectly from an infected person to another person. Some diseases are more communicable during the incubation period than during the actual illness. In others such as tuberculosis, syphilis and *Salmonella* infection the infectious period may be lengthy and intermittent. This period may be shortened by (antibiotic-) treatment (though in some infections antibiotics may prolong carriage and hence the communicable period).

Mode of transmission

This is the mechanism by which an infectious agent is spread from a source or reservoir to a susceptible person. The mechanisms are detailed in Table 1.2.1.

Table 1.2.1 Modes of transmission of infectious agents

Types of transmission	Examples
Direct transmission Transmission by direct contact such as touching, biting, kissing, sexual intercourse or by droplet spread on to the mucous membranes of the eye, nose or mouth during sneezing, coughing, spitting or talking. Droplet spread is usually limited to a distance of 1 m or less.	**Direct route** Infections of the skin, mouth, and eye may be spread by touching an infected area on another person's body. Examples are scabies, head lice, ringworm, and impetigo. Sexually transmitted infections are also usually spread by the direct route. **Respiratory route** Sneezing, coughing, singing, and even talking may spread respiratory droplets from an infected person to someone close by. Examples are the common cold, influenza, whooping cough, and meningococcal infection. **Faecal-oral route** Gastrointestinal infections can spread when faeces are transferred directly to the mouth of a susceptible host.

(*Continued*)

Table 1.2.1 (*Continued*)

Types of transmission	Examples
Indirect transmission This may be *vehicle-borne* involving inanimate materials or objects (*fomites*) such as toys, soiled clothes, bedding, cooking or eating utensils, surgical instruments or dressings; or water, food, milk or biological products such as blood. The agent may or may not multiply or develop in or on the vehicle before transmission. It may be *vector-borne*. This in turn may be mechanical and includes simple carriage by a crawling or flying insect as a result of soiling of its feet or proboscis or by passage of organisms through its gastrointestinal tract. This does not require multiplication or development of the organism. It may be *biological* when some form of multiplication or development of the organism is required before the arthropod can transmit the infected form of the agent to human when biting.	**Faecal-oral route** Faeces contaminate food or objects like toys or toilet flush handles. Animal vectors such as cockroaches, flies and other pests may transfer faeces. Environmental surfaces may be contaminated. This is particularly important in viral gastroenteritis when vomiting occurs because the vomit contains large numbers of infectious viral particles. Examples of infections spread in this way are food poisoning and hepatitis A. **The blood-borne route** There is transfer of blood or body fluids via a contaminated item from an infected person to another person through a break in the skin such as through inoculation, injection or transfusion. **Respiratory route** Droplets from the mouth and nose may also contaminate hands, cups, toys or other items and spread infection to others who may use or touch those items.
Air-borne spread *Air-borne* spread is the dissemination of a microbial aerosol to a suitable port of entry, usually the respiratory tract. Microbial aerosols are suspensions of particles that may remain suspended in the air for long periods of time. Particles in the range 1–5 μm are easily drawn into the alveoli and may be retained there. Droplets and other larger particles that tend to settle out of the air are not considered air-borne. Microbial aerosols are either droplet nuclei or dust.	Examples are infection with *Legionella*, *Coxiella* and, in some circumstances, TB.

1.3 Basic concepts in the prevention of infection

The information in this chapter might be appropriate for professionals/organisations to provide to the general public. The chapter deals with preventive measures, and more information on community control measures could be found in other parts of this book, for example in Chapters 2.2 and 4.3. For specific information related to immunisations see Chapter 4.7 and the travel health Chapter 4.11.

Individual measures against infections

Hand hygiene

Handwashing with soap is among the most effective and inexpensive ways to prevent gastrointestinal and respiratory infections. This should always be done before and after meals, after visits to the toilet and after direct contact with wounds, blood, nasal discharge and other body fluids (own and others), after direct contact with animals and after spending time in crowded conditions – especially during seasons with much respiratory tract or gastrointestinal infections. Liquid, antibacterial

soap is preferable. Rings and jewellery should be removed before handwashing. It may be more practical to carry a small bottle of alcohol disinfectant than relying on finding a place for handwashing when outdoors.

Prevention of food-borne infection

Food handling

Proper hygiene knowledge is necessary to avoid food-borne infections.

- Minimise transportation time. If it is not possible to return home immediately from the store, use a cool box.
- Always check the 'best before' date to avoid buying food with high bacterial levels. It is important to note that food contaminated with pathogenic bacteria does not necessarily smell bad or look un-fresh. Many bacteria, such as *Yersinia enterocolitica*, *Listeria monocytogenes* and *Clostridium botulinum*, can grow well in low temperatures if stored in the refrigerator too long.
- When preparing large amounts of food it is important to chill the food as quickly as possible. The food could be chilled in small containers.
- Always wash your hands before, during and after preparing food to prevent contamination and cross-contamination. Never cook for others when you have diarrhoea or an infected wound on the hands.
- Rinse vegetables, fresh herbs, and fruit thoroughly before use.
- Cook meat thoroughly. This is especially important for chicken, which often contains *Campylobacter* or *Salmonella*.
- To avoid cross-contamination use different cutting boards for meat, vegetables, and prepared food. Plastic cutting boards can be washed in a dishwasher. Change dishcloths often or boil them in water. Let them dry thoroughly between use.
- When barbequing, never put the meat back on plates that were used for the raw meat.

Risky food

Handling food to be eaten without being heated requires proper hygiene measures to ensure that it does not contain pathogenic microbes. Some food is associated with a higher risk of infection:

- Unpasteurised milk and milk products should be avoided, especially for small children, as diarrhoeagenic *Escherichia coli*, *Salmonella* and *Campylobacter* are not uncommon, even in milk from healthy cows.
- Oysters and mussels filter large amounts of water, and micro-organisms (especially norovirus and hepatitis A virus) could be concentrated in the molluscs if they have been grown in contaminated water.
- Many large *Salmonella* outbreaks and in 2011 a large STEC outbreak in Germany have been caused by contaminated bean sprouts. The sprouts are best stored in refrigerator.
- Fresh vegetables and herbs should always be rinsed, regardless of what is stated on the package.
- Raw or soft-boiled eggs may contain *Salmonella*. Risk for infection is highest if eggs are used in products that are not heated properly (e.g. custard on cakes).
- Frozen raspberries have caused several international outbreaks of Norovirus and hepatitis A.

Measures against respiratory tract infections

Most respiratory tract infections have an airborne mode of transmission or are spread through droplets. An alternative important mode of transmission is through a direct contact between hands and mucous membranes. Especially during the flu season it is advisable to avoid crowded settings, avoid touching the face with the hands and wash the hands regularly. Covering the mouth when coughing and sneezing prevents spread to others. During peak flu season, working from home may be an option in some workplaces.

Other effective measure to avoid respiratory tract infections include stopping smoking, immunisation against respiratory tract pathogens as appropriate (depending on age and risk group) and using a face mask when being exposed for specific pathogens such as

Aspergillus (renovations of cellars and attics), hantavirus infection (environment soiled by urine from the bank vole).

Measures against sexually transmitted infections

Sexually transmitted infections (STIs) require close person-to-person contact for transmission. It should therefore be noted that most other infectious diseases (e.g. gastrointestinal and respiratory tract infections) also easily transmit during sexual contact. All forms of vaginal, oral and anal intercourse are associated with a risk of STI transmission even if condoms are used. It is therefore more appropriate to talk about 'safer sex' than 'safe sex'. Condoms should be used throughout intercourse. Even if they are generally durable, they may be torn by sharp nails or rupture during anal intercourse without lubrication. Lubrication should be water or silicon based, as oil-based lubricants such as Vaseline and skin creams may dissolve the condom.

Measures against blood-borne infections

Hepatitis B, hepatitis C and Human Immunodeficiency Virus (HIV) are the three major viral infections transmitted via blood.

Intravenous drug use

The most important risk factor for blood-borne infections outside medical care settings is intravenous drug use. The infection is mainly transmitted through the use of non-sterile needles and syringes. A lesser-known route of infection, even among drug addicts, is the transmission through the cup or saucer in which the drugs are dissolved before being drawn into the syringe. Viruses can be killed through boiling the syringes and needles (for several minutes), alternatively by cleaning them in chlorine. To affect the hepatitis B viruses, which are hardier than HIV, the needles and syringes must be in contact with chlorine for at least two minutes. Both these methods are effective, but not completely safe. The only safe way is never to share injection equipment. As a harm-reduction measure, most European countries organise needle-exchange and/or oral substitute programmes.

Tattoos

Becoming tattooed with a non-sterile needle carries the risk of blood-borne infection. It is therefore important to ensure that the tattoo is done by a reputable craftsman. In many countries there are associations of professional tattoo artists. If uncertain, it is advisable to consult the local public health/environmental health department. Tattooing abroad in countries with generally low levels of hygiene should be avoided as the prevalence of blood-infected persons may be high, and the regulation of tattoo artists is inadequate in many parts of the world.

Other blood exposure

Exposure to blood occasionally happens outside healthcare environments, for example in relation to accidents. The basic rule for all contact with blood is to consider it as infected. It is especially important to avoid getting blood splashes in the eyes, mouth, or nose. Blood on the skin should be immediately washed with soap and water. Blood spill, even minimal amounts, should be dried as soon as possible. Chlorine solution (one part bleach to nine parts water) effectively destroys the virus on blood-soaked surfaces or objects, but should not be used directly on skin or on textiles. Blood-stained clothes should be washed with pre-wash and then at the highest possible temperature. Plastic or latex gloves and disposable plastic aprons should be included in car and home first aid kits. A nozzle with a check valve for mouth-to-mouth resuscitation is a valuable part of a first aid kit.

The risk of blood contamination increases with cuts and puncture wounds. If the skin is

penetrated by contaminated needles, scalpels or similar, the risk of hepatitis B infection is about 30%, hepatitis C infection about 2% and HIV about 0.3%. The injured area should be bled and the area should be washed thoroughly with soap and water. After any exposure that might have a risk of blood contamination a doctor should be immediately contacted.

Protection against insect-borne infections

Protection against tick bites

The tick season usually lasts from early spring to autumn. The best protection against bites is to avoid the typical tick-infested terrains (damp and shaded terrain with half-high grass). In gardens, the number of ticks could be reduced by keeping the grass short and clearing away shady bushes and trees. Full dress, with trousers stacked in boots, is an effective protection. Furthermore, it is advisable to inspect the skin regularly, as the ticks often take some time before biting. Mosquito repellent has some effect even against ticks.

Ticks prefer to bite through thin skin. Most common areas in adults are the legs, while in children the bite is usually higher up on the body, often in the groins. Transfer of Tick-borne encephalitis (TBE) virus is instantaneous after the bite, while the risk of infection with *Borrelia* and *Ehrlichia* increases with the time the tick is attached. Ticks are best removed with tweezers (preferably special tick tweezers which can be bought in pharmacies in tick-infested regions). A gentle, twisting motion increases the chance that the entire tick is removed and reduces the risk of bacterial transmission. Margarine or cooking oil should not be used. The wound is washed with soap and water. Any remaining tick parts give rise to an inflammatory reaction and can be removed after a few days. These do not increase the risk of infection. Doctors should be contacted if an erythema occurs around the bite site.

Protection against mosquito bites

Personal protection against mosquito bites in risk areas include wearing covering clothes (long-sleeved shirts and long trousers) and regular application of mosquito repellents containing DEET (N,N-diethyl-*m*-toluamide), or alternatively other approved substances such as icaridin, lemon eucalyptus, or citronella in accordance with the manufacturers' instructions. This is especially important for protection against day-time bites of *Aedes* species (transmitting dengue, chikungunya, zika virus and yellow fever). The best effect against mosquito species that have a preference to bite indoors at night, as *Anopheles* species (transmitting malaria), is to sleep in screened, air-conditioned rooms, or otherwise using long-lasting insecticide treated bed nets (LLIN) impregnated with permethrin, deltamitrin or alpha-cypermethrin. Removing mosquito breeding sites in nearby outdoor or indoor premises is a more permanent measure.

Integrated vector management

In case of outbreaks of mosquito-borne infections (dengue, chikungunya, Zika virus) in areas with an abundance of competent vectors it is important to reduce mosquito vector density in a sustainable manner.

- Reduce outdoors and indoors breeding sites by draining or removing sources of stagnant water (e.g. flower pots, vases, used tyres, tree holes and rock pools), or, if that is not possible, treatment with larvicides. Open water containers should be well covered.
- Use physical barriers (window screens and mosquito nets) and air conditioning.
- Elimination of adult mosquitoes through aerial spraying could be considered.

Infection control precautions in care settings

The following infection control measures are general and may need to be adapted

depending on the specific type of care setting, for example community care settings (see also Chapter 4.3) and health care settings (see also Chapter 4.4).

Standard precautions

It is not always possible to identify persons who may spread infection to others, therefore standard precautions to prevent the spread of infection must be followed in health care settings at all times (Box 1.3.1). In addition, for persons with respiratory infections, droplet precautions may be recommended (Box 1.3.2) and in those with diarrhoea and/or vomiting enteric precautions should be followed (Box 1.3.3). These precautions are valid for any care setting.

Handwashing is the single most important part of infection control. Soiled hands should be washed with soap and water. If soap and water is not available, alcohol gel or rub can be used. Hands should be washed before contact with patients, after any activity that contaminates the hands (removal of protective clothing and gloves, using the toilet) and before handling food. Nails should be kept short, rings should not be worn, artificial nails should be avoided and cuts and abrasions should be covered with a waterproof dressing. Adequate handwashing facilities must be available in all patient areas. Liquid soap dispensers, paper hand towels and foot-operated waste bins should be provided.[1]

Box 1.3.1 Infection control standard precautions in health care (abbreviated)[2]

- Hand hygiene: handwashing 40–60 seconds with soap and water or use of an alcohol hand rub or gel. Cover wounds or skin lesions with waterproof dressings.
- Appropriate use of gloves, gowns, aprons and facial protection (eyes, nose and mouth).
- Prevention and management of needlestick injuries, injuries from other sharp instruments and blood splash incidents.
- Respiratory hygiene and cough etiquette.
- Safe disposal of contaminated waste.
- Managing spillages of blood and body fluids.
- Safe collection and transport of specimens.
- Decontaminating equipment including cleaning, disinfection and sterilisation.
- Maintaining a clean clinical environment.
- Safe management of used linen.
- Place patients with infections in appropriate accommodation.

Box 1.3.2 Droplet precautions when managing respiratory infections

- Wear a medical mask if working within approximately 1 m of the patient or upon entering the room/cubicle of a patient.
- When performing aerosol-generating procedures (chest physiotherapy, nebulisation) wear a particulate respirator, perform procedures in an adequately ventilated room and limit other persons in the room only to those required for the patient's care.

[1] World Health Organisation. Guidelines on hand hygiene in health Care. http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf.

[2] World Health Organisation. Infection control standard precautions in health care. http://www.who.int/csr/resources/publications/4EPR_AM2.pdf.

Box 1.3.3 Enteric precautions when managing diarrhoea and vomiting

- Patients should normally use a flush toilet for the disposal of excretions and soiled materials. Attendants should wear disposable plastic gloves and wash hands thoroughly.
- Faecal material on soiled clothing and bed linen should be flushed into the toilet bowl. Linen should then be washed in washing machine on a 'hot' cycle. Soaking in disinfectant before washing is not necessary.
- Use of disinfectants is important in schools, nursery schools and residential institutions. Toilet seats, flush handles, wash-hand basin taps and toilet door handles should be cleaned daily and after use with a bleach-based household cleaner, diluted according to manufacturer's instructions. Alcohol-based wipes may be used on seats and other hard surfaces. Bedpans and urinals should be emptied into the toilet bowl, washed with a disinfectant and rinsed.
- Patients and carers should be advised about personal hygiene and the hygienic preparation and serving of food. Children and adults in jobs likely to spread infection (e.g. food handlers) should stay away from work or school for 48 hours after the diarrhoea has stopped. In the NL, workers can resume work as soon as diarrhoea has stopped. Day care is not regarded as a job likely to spread infection. Most important criterium is if a worker can adequately comply to hygienic precautions.

1.4 Emergency risk communication

Emergency risk communication is increasingly seen as a fundamental part of preparedness and response to health threats, and is one of the eight core capacities of the International Health Regulations (IHR). When communicating during a crisis, the media should be considered as an ally in protecting the health of the public. They are one of the most powerful influences upon the public. Relationships with the media should be developed proactively; good routine relationships with the media will make dealing with them during emergency situations much easier.

Communicable disease issues arouse interest and anxiety in the public. The public have a right to be informed and the press is often the best route. Virtually all issues can be presented in a way that the public can understand. Professionals should not hide behind technical obfuscations. Do not expect to have any control over material that you provide, press releases can be selectively quoted and interviews can be edited. However, journalists are usually interested in accuracy.

Training

Anyone who is likely to deal with the media should undergo media training. This will help in understanding what the media needs. Journalists often have a similar agenda to public health workers, they wish to inform and educate the public. If they encounter a group of professionals who understand their needs, and are trying to help, then journalists are less likely to be antagonistic. Identify people within the organisation who are particularly good with the media – they may not be the most senior people.

Routine relationships

As for other aspects of preparedness, good emergency risk communication is best based on good relations with media cultured before the crisis. Develop regular contact with your local print and broadcast media. Be available to answer their questions, and treat your local reporters in a friendly way. If they trust you and rely on you as an authoritative source it will make things much easier if a story is breaking.

Local papers may be willing to publish a regular column; this is a powerful way of getting health advice across. Use opportunities

to publish in local papers, women's magazines, parents' magazines, and so on. This will probably have a greater influence on health than publishing in the peer-reviewed medical press. Have basic information packs available for journalists. These should describe the clinical features and importance of an infection and the salient epidemiological features and recent trends.

Communicating during a crisis

During outbreak or emergency situations it is important to maintain good relations with the press. Journalists have a job to do, they can become intrusive, but they will understand that you also have a job to do. Let the journalists know that they will be kept informed, that there will be regular briefings, daily or even twice daily. Ensure that the briefings do happen. Appoint a media spokesperson and ensure that all media briefings are done through that person. The outbreak control team should co-ordinate the local flow of information. Sometimes, several actors (at different levels) are involved, all with their own media contacts, it is then important to have co-ordinated messages and shared lines-to-take. If not, journalists will likely focus on the differences rather than on the main messages.

WHO has developed outbreak communication guidelines that could be used as a reference by anyone involved in outbreak communication. The main principles include the following:

- build, maintain and restore trust,
- announce early,
- aim at maximum transparency (taking into account privacy issues),
- understand the public, and
- plan in advance.

Messages

Decide beforehand what your key messages are; if possible discuss these with the journalist and discuss the questions that will be asked. Decide if there are any areas that you do not wish to be drawn into. Be honest, accurate and keep technical details to a minimum. Get the key message across first, then provide the reasoning behind it. Stress the facts and explain the context. Do not try to hide the truth or lie. If you are uncertain of the facts or some detail say so and offer to get the information. Do not be drawn into areas you feel you cannot or should not discuss, be firm and polite and say that you cannot discuss that issue. Try to avoid discussions of money and cost saving, stress public health action and your concern for safeguarding public health. Avoid being drawn into speculation or criticisms of other groups. Behave as if you were always 'on the record'. Make sure that you know if a broadcast is live or recorded. Always ask to see the article before it is published in order to correct factual mistakes – most serious journalists appreciate that. However, do not expect to be able to change the direction or angle of the article, attempts to do that will likely just upset the journalist.

Press releases

Keep the press release short (8–10 paragraphs), make sure you have considered the message and the audience for the release and consult a press officer. Get the most important message into the first paragraph and support it with a quote from a senior official. In the introduction, describe who, what, where, when, why/how. In the middle, expand the story with supporting detail, conclude by summarising and identifying the next steps.

Social media

As has been seen in the 2016 US election, social media is rapidly replacing traditional media when it comes to forming public opinions, and a strong presence in social media is imperative for any successful emergency risk communication. Compared

to traditional one-way communication, social media provides for monitoring debate and opinions in real time as well as engagement with key influencers. Social media also create new opportunities for interaction with users, and sensibly used messages could get through and multiplied in a very short time. However, the two-way communication inherent in social media also takes time and resources, and it is important for any organisation to have a clear social media strategy. For this purpose, ECDC has developed a toolkit on 'Social media strategy development: a guide to using social media for public health communication', available on the ECDC website.

Problems

The press might want access to cases or locations, such as outbreak rooms for atmospheric pictures or interviews. These requests should be considered very carefully. Considerations of confidentiality and the smooth running of an investigation must come first. However, on occasion such photo opportunities might, by raising public awareness of an issue, be beneficial. If things go wrong remember that they can do so in the best of relationships. Developing good relations with the media takes time and effort. If errors of fact appear in an article, or you feel you have been misrepresented, contact the journalist and discuss them; if necessary talk to the editor.

1.5 Health protection on-call

During office hours, health protection activity is usually undertaken by individuals who are highly expert in their field and who have access to a full range of supporting services. Outside office hours, duties may be covered by more generalist staff and/or key support services, such as laboratories and environmental health teams, may also offer a much reduced service.

Requirements for on-call staff

Undertaking health protection on-call should present few problems for those adequately trained in public health, as the skills applied are the same as those used in everyday public health practice, that is:

- defining the problem,
- collecting the necessary information,
- undertaking a risk assessment,
- identifying good practice,
- implementing the response,
- evaluating the outcome.

In addition to these generic public health skills, basic specialist health protection knowledge and experience is needed for safe out-of-hours health protection practice. A suggested list of the competences required is given in Box 1.5.1. These competencies need to be maintained by incorporating them into the continuous professional development plan for each individual, for example by attending an on-call updating course and participating in simulations and exercises.

Access to knowledge on-call is important and is available from

- this handbook: on-call actions and underlying theory are given for all the most common pathogens,
- a local on-call pack, detailing local policies, procedures, plans and contact details,
- national guidance documents (see Appendix),
- websites, including those of the national communicable disease control or health protection organisation (see lists inside book covers),
- local, regional and national specialist on-call, for example the local acute hospital will usually have a consultant medical microbiologist on-call and the national health protection organisation will usually provide access to a communicable disease epidemiologist.

Box 1.5.1 Suggested competences required to undertake consultant-level health protection on-call duties

1 Familiarity with the principles and practice of being on-call, including
- professional obligations,
- legal issues,
- professional responsibility to ensure appropriate public health action taken in response to all incidents.

2 Ability to perform a risk assessment of a problem, decide whether public health action is necessary and decide appropriately whether action is required out of hours.

3 Ability to effectively exercise the local on-call procedures, including:
- Administration of urgent prophylaxis,
- Handover before and after on-call.

4 Experience of practicalities of working with others out of hours, particularly:
- Local and national health protection agency,
- Microbiology laboratory,
- Environmental Health department.

5 Up to date knowledge of relevant aspects of natural history, epidemiology, clinical presentation, laboratory diagnosis and methods of transmission and control of common hazards that may require public health intervention out of hours, including:
- Meningococcal disease and meningitis,
- Gastrointestinal infections, including STEC,
- Respiratory infection, including Legionella and TB,
- Blood-borne viruses (HBV, HCV, HIV),
- Infections requiring prophylaxis/advice, (e.g. pertussis, hepatitis A, measles),
- Most common chemical/environmental hazards (asbestos, CO, smoke, mercury, ammonia, chlorine),
- Other hazards with increased local/regional occurrence.

6 Ability to interpret national guidelines and local policies for the most common scenarios that present on-call and to effectively co-ordinate public health action. Includes single cases of infections listed in item 5.

7 Awareness of the basic principles of control and sources of advice and support (particularly out of hours) for serious, less common public health problems that may present out of hours, including:
- Imported infections (e.g. VHF, diphtheria, rabies exposure, possible MERS/avian flu),
- Exposure of particularly vulnerable groups (e.g. chickenpox in immunosuppressed/neonates; rubella in pregnancy),
- Exposure to blood-borne viruses or TB in community or health care settings (including needlestick injuries and potential lookback exercises),
- Potential public health emergencies (e.g. food-borne botulism),
- Potential deliberate release (e.g. 'White powder' exposures),
- Exposure to contaminated water,
- Acute exposure to chemical hazards,
- Urgent travel health enquiries,
- Major emergencies (e.g. floods, explosions),
- Recently emerged diseases/hazards.

8 Understanding of the principles and practice of outbreak and incident management.

Box 1.5.1 (*Continued*)

9 Ability to effectively co-ordinate the public health investigation and control of common local outbreaks and incidents out of hours, including:
- Potentially linked cases of meningococcal disease,
- Potential community outbreaks of gastrointestinal Illness,
- Chemical incidents.

10 Ability to contribute effectively to the control of:
- Hospital outbreaks/incidents,
- Radiological incidents,
- Major emergencies,
- Deliberate release incidents.

11 Ability to communicate effectively on public health issues, including:
- Preparing appropriate press releases out of hours,
- Giving effective media interviews,
- Communicating directly with public.

Source: UK Faculty of Public Health, 2006; accessed 2 April 2018 www.fph.org.uk/uploads/FPH%20on-call%20HP_training_generalist.pdf.

Public health response to a case of infection

The two key questions in dealing with a case of communicable disease are:
- *Where did the case get it from?* This is important because there may be a continuing source which needs to be controlled and because there may be others who have also been exposed and need advice and/or treatment. Others exposed may be known to the case (e.g. household or fellow tourists), but this is not always the case (e.g. a *Legionella* source in the environment).
- *Is the case likely to pass it on?* This may be to close contacts (e.g. household or sexual contacts) that need to be protected by advice to the case and perhaps prophylaxis for the contacts (some of whom may be particularly vulnerable), or it may be via the patient's occupation (e.g. a food handler who has a gastrointestinal infection).

Syndromes and diseases

At the time that health protection issues emerge, the causative agent may not yet be clear, for example an outbreak of diarrhoea and vomiting in a hospital, or an outbreak of respiratory disease at a nursing home. This may be especially true out-of-hours. Section 2 of this book looks at problems from this angle. The important issues to consider are:
- What investigations are needed to identify the agent (e.g. *Salmonella*), the cause of the incident (e.g. poor hygiene practices) and, if relevant, the vehicle of infection (e.g. a particular food served to guests)? Such investigations usually have microbiological, environmental and epidemiological components.
- What generic control measures can be applied to limit morbidity, whilst awaiting confirmation, for example enhanced handwashing, environmental cleaning and excluding ill food handlers in outbreaks of gastrointestinal illness?

Public health action on-call

There are two key questions that define what action is taken on-call:
- Is public health action necessary?
- Does it need to be done now?

The factors in deciding whether public health action is necessary are a combination of

- Is the index case at risk of a poor outcome? A death from meningitis or any case of a viral haemorrhagic fever are examples that lead to public anxiety and media interest.
- Is the index case likely to pass infection on to others? If so, action may be required to limit onward transmission from the index case and any infected contacts.
- Is there likely to be an ongoing source that needs controlling? Some stages in investigating possible sources take considerable time, so the earlier they are started, the sooner the result.
- Do contacts or others exposed to the same source need to be traced? This will be important if their outcome can be improved by an intervention or if it will help limit onward transmission.
- Does the public need information or reassurance? This is often affected by the 'scariness' of the disease, whether particularly vulnerable groups are exposed (e.g. children) and issues of 'blame'.

If public health action is necessary, it does not automatically follow that it should take place out-of-hours. Issues that affect timing include:

- The seriousness of the disease. Some infections such as viral haemorrhagic fevers, diphtheria or Shiga-toxin producing *Escherichia coli* (STEC) may require prompt action to prevent even one more additional case in vulnerable groups, whereas others such as norovirus or mumps are less of a threat to most individuals.
- How transmissible is the infection? Not only are some infections more transmissible than others, but some cases with the same infection can transmit more easily than others (e.g. e-antigen positive hepatitis B or smear positive TB).
- How long is the incubation period? Secondary (or co-primary) cases of meningococcal infection may present very quickly, but the incubation period for TB is weeks or months.
- How vulnerable are the people that may have been exposed? Some pathogens are particularly likely to lead to infection or a poor outcome in particular groups, for example STEC in young children and the frail elderly, or chicken pox in immunosuppressed patients. This will heavily influence speed of response.
- What is the public, media or political reaction? Even if not a health protection priority to react on-call (e.g. on HIV positive healthcare worker), action may be required if information becomes public.
- What is 'expected' or good practice?
- When will normal service be resumed? The risk of delaying until 'normal' office hours is obviously proportional to the length of time until a 'normal' response can be activated. Thus, action is more likely on a Saturday morning before a national holiday Monday than on a Sunday night before a normal working Monday.

Collection of baseline data

Collecting information and recording it in a systematic way is important in order to

- aid management of the incident: the information will be useful to you and to others who take over management later in the incident.
- be available for later scrutiny, either for professional purposes (audit, lessons learned) or legal purposes (Public Inquiries or civil actions).

A good basic minimum dataset is usually required, preferably by completion of a standard form/dataset, covering:

- Administrative details for those providing information (name, organisation/position, contact details) and cases and contacts (name, address, phone, GP, hospital).
- Epidemiological information on cases in relation to person (age, sex, occupation), place (residence, travel, institution) and time (onset and exposures).
- Diagnosis, consisting of clinical and laboratory information.
- Record of advice given.

Risk assessment

The next stage is usually to undertake a risk assessment, which includes the principles identified earlier (see 'public health on-call'), but may involve the use of a standard framework for assessing the need for action (ranging from gathering more information to implementing an immediate intervention), such as one using the following four criteria:

- *Uncertainty/Confidence* – how confident are you in the diagnosis of the suspected/confirmed illness or in the identification of the hazard? Are there other areas of uncertainty in assessing the situation?
- *Severity* – How severe is the illness in the individual(s) and/or how severe (and likely) is the potential range of illnesses caused by the suspected/confirmed pathogen?
- *Spread* – how likely are others to be exposed to the same source or to people/objects infected or contaminated by it?
- *Intervention* – what interventions are available, how effective are they, when do they need to be implemented for maximum effectiveness and how feasible is it to intervene?

It is often necessary to assess how likely contacts are to have been put at significant risk. The three general questions that are asked in assessing the likelihood of transmission are:

- How infectious is the source (or case)?
- How close is the contact?
- How susceptible are those exposed?

An example of how this is applied for a particular disease is given in Box 3.78.2.

Possible interventions

If it is decided that action is required, possible interventions include:

- Action to improve the outcome for cases by ensuring appropriate care is provided: this may include provision of immunoglobulins (rabies), antitoxins (diphtheria), antidotes (chemicals) or different antibiotics to usual (e.g. *Legionella*).
- Action to trace others exposed to source or cases in order to provide advice, antibiotics or vaccines (e.g. in contacts of meningococcal disease, all three may be provided).
- Action to prevent others being exposed to cases or contacts, for example by: rendering them non-infectious by use of antibiotics and/or isolation (e.g. diphtheria or TB); by provision of hygiene advice and/or exclusion from work or school (e.g. gastrointestinal illness); or by closure of premises associated with incident (e.g. cooling tower or food premises).
- Action to identify a possible source so that control measures can be implemented and monitored.

Communications

Communication is vital in public health incidents. Communication needs can be considered from a number of perspectives:

- Who needs to know for public health purposes? Some may need to be contacted on-call (may include the case [or parents], contacts or clinicians) and some can wait until the next working day (e.g. school).
- Who needs to know for information purposes (e.g. who needs to know before the press/public/politicians become aware)? This may include officers of local public health organisations (press officer, chief executive, Director of Public Health) and regional or national organisations (e.g. the national public health or health protection agency and the Department of Health may sometimes need to be told).
- Who can offer advice or help in management of the incident? Such individuals may be able to contribute from a microbiological, epidemiological or environmental health aspect. Occasionally an Incident Management Team meeting by teleconference may need to be set up out of hours.

Is there any advantage in wider dissemination of information or advice? This may be to primary or secondary health care services (e.g. identification and treatment of cases) or the public and press (e.g. to allay anxiety).

Governance issues

Ensuring an appropriate quality of response on-call can be considered as a mixture of preparation and follow up.

Preparation for on-call includes:

- access to an up-to-date on-call pack,
- access to up-to-date local policies and contingency plans,
- undertaking appropriate training and updating,
- exercising contingency plans and multi-agency response,
- ensuring effective authorisation for use of legal powers,
- ensuring access to required support, including surge capacity and access to additional resources (e.g. an Incident Room), if needed.

Follow-up issue include:

- debrief to review individual cases with local health protection team as learning exercise,
- systematic audit,
- adverse incident reporting,
- written reports, including any lessons learnt,
- review of policies and plans.

Section 2
Common topics

2.1 Meningitis and meningism

Meningitis is inflammation of the meninges. Meningism is the group of signs and symptoms that accompanies the inflammation. The symptoms of meningism are headache, neck stiffness, nausea or vomiting and photophobia. The classical physical sign of meningism is a positive Kernig's test; however this may be negative in mild cases. Typical features of meningism are uncommon in infants and young children, who are usually simply floppy and pale, with fever and vomiting. A bulging fontanelle may be present in a young infant.

Meningitis is a notifiable disease in most countries in Europe. This is however a rather unhelpful term for communicable disease control purposes, as bacterial meningitis (particularly due to *Neisseria meningitidis*), can present as septicaemia without any features of meningitis, and many types of meningitis require no public health action. Meningococcal septicaemia presents with a typical haemorrhagic rash, which may be accompanied by shock, circulatory collapse, and confusion or coma. Many patients with meningococcal disease will have features of both meningitis and septicaemia (see Chapter 3.47).

Infectious and other causes

Meningitis is the most common cause of meningism; however, meningism can occur in the absence of meningitis (Table 2.1.1). It may accompany upper lobe pneumonia, urinary tract infection and other febrile conditions. Cerebrospinal Fluid (CSF) examination is normal in these conditions. Meningism without fever can also occur in non-infectious conditions, the most important of which is subarachnoid haemorrhage; malignancy affecting the meninges can also present as meningism.

Clinical and epidemiological differences

Many infectious agents can cause meningitis. Acute meningitis is nearly always viral or bacterial; fungal and protozoal infections occasionally occur, mainly in the immunosuppressed patient.

The overall incidence is relatively stable across Europe, having declined since 2000 due to both the introduction of meningococcal group C vaccine and a general reduction in serogroup B infections. The recent introduction of serogroup B vaccine in the UK has further contributed to the decline. Hib meningitis is well controlled as all countries in Europe routinely vaccinate in infancy; vaccination with pneumococcal conjugate vaccination has also had an impact.

Viral meningitis

Viral meningitis (Table 2.1.2) is common. However, most cases are mild or inapparent. Notifications are an unreliable estimate of incidence as only the more severe cases are investigated.

The most common cause is an enterovirus infection (either an echovirus or coxsackie virus). In enterovirus meningitis there is sometimes a history of a sore throat or diarrhoea for a few days before the onset of headache, fever and nausea or vomiting. The headache is severe; however, there is no alteration of neurological function. Meningism is usually present to a greater or lesser degree. Recovery is usually complete and rapid (within a week). The CSF is clear, with 40–250 cells, all lymphocytes, elevated protein and normal glucose. An enterovirus infection can be confirmed

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

Table 2.1.1 Differential diagnosis of meningism

Cause	Distinguishing features
Viral meningitis	Fever. Clear CSF with a lymphocytosis and raised protein
Bacterial meningitis	Fever. Purulent CSF with a neutrophil pleiocytosis, raised protein and lowered glucose
Other febrile conditions	Fever; Normal CSF
Subarachnoid haemorrhage	No fever. Abrupt onset, rapid deterioration. Bloodstained CSF
Meningeal malignancies	No fever. Insidious onset. Variable CSF features

Table 2.1.2 Causes of viral meningitis

Common
Echovirus
Coxsackievirus
Rare
Poliovirus
Mumps virus
Herpes simplex type 2
Herpes zoster
Influenza types A or B
Arbovirus
Rubella
Epstein–Barr virus

by detection of virus in a faecal sample or by serology. Enterovirus meningitis occurs mainly in later summer. It affects all age groups, although it is commonest in preschool children.

Mumps can cause meningitis, although it is now rare due to widespread use of the MMR vaccine. It is easily recognised by the accompanying parotitis. The diagnosis can be confirmed by detection of specific IgM in blood or saliva, or by serology.

In herpes simplex meningitis the illness is more severe and may persist for weeks. It is usually associated with primary genital herpes.

Non-paralytic poliomyelitis can present as meningitis, indistinguishable clinically from other causes of enteroviral meningitis. Poliovirus is detectable in faeces or CSF.

Bacterial meningitis

Bacterial meningitis (Table 2.1.3) is a medical emergency. The clinical presentation depends on the age of the patient, and the infecting organism. In the neonate, the presentation is non-specific, with features of bacteraemia. The infant is febrile, listless, floppy and does not feed. There may also be vomiting, drowsiness, convulsions, or an abnormal high-pitched cry. In this age group, the commonest causes are *Escherichia coli* and group B streptococci.

Signs and symptoms in older infants and young children are also non-specific. Meningococcal infection is the commonest cause at this age and is often accompanied by a haemorrhagic rash (see Chapter 3.47).

Table 2.1.3 Causes of bacterial meningitis

Neonate	Infant/preschool child	Older child/adult
Common		
Escherichia coli	*Neisseria meningitidis*	*N. meningitidis*
Group B streptococci		*Streptococcus pneumoniae*
Uncommon		
Listeria monocytogenes	*Haemophilus influenzae*	*L. monocytogenes*
N. meningitidis	*S. pneumoniae*	Staphylococci
Staphylococci		*H. influenzae*
		Mycobacterium tuberculosis

In older children and adults, the symptoms are more specific. Fever, malaise and increasing headache are accompanied by nausea and often vomiting. Photophobia may be extreme. Meningism is usually present. Meningococcal infection is also the commonest cause in this group and the typical rash of meningococcal septicaemia may be present. Patients with rapidly advancing meningococcal disease may, over the course of a few hours, develop hypotension, circulatory collapse, pulmonary oedema, confusion and coma.

Other causes of acute bacterial meningitis in older children and adults are uncommon. *Haemophilus influenzae* meningitis occasionally occurs in unvaccinated children or adults; it has a slower onset than meningococcal meningitis and a rash is rare. Pneumococcal meningitis also has a more insidious onset and the symptoms are less specific than meningococcal meningitis. It usually occurs in adults with an underlying risk factor, such as dura mater defect due to trauma or surgery, chronic intracranial infection, asplenia, terminal complement deficiency or alcoholism.

Listeria meningitis presents either as a neonatal infection following intrapartum exposure or as a food-borne illness in older children and young adults, often in the immunosuppressed.

Tuberculous meningitis is a manifestation of primary tuberculosis, which occurs mainly in children and young adults. It has an insidious onset; meningism is usually mild and other features (except fever) are often absent.

Laboratory diagnosis

With the exception of tuberculosis, bacterial meningitis causes neutrophil pleiocytosis in the CSF, with raised protein and lowered glucose. A Gram stain will often demonstrate the typical appearance of the infecting organism, allowing a definitive diagnosis to be made.

Conventional culture of CSF and blood should always be carried out; however, these may be negative, particularly if the patient has been given antibiotics before hospital admission. In addition, a CSF specimen may not be available, as clinicians are often reluctant to undertake a lumbar puncture.

Polymerase Chain Reaction (PCR) diagnosis for meningococcal disease (see Box 3.47.1) for suggested investigations) and serology are available. Other useful investigations include throat swab and microscopic examination of a rash aspirate if present.

General prevention and control measures

Hygiene. Enteroviral meningitis usually spreads as result of environmental contamination, particularly under conditions of crowding and poor hygiene. General hygiene measures such as hand washing will help prevent spread. This is particularly important in hospitals.

Pregnancy. Group B streptococcal meningitis in neonates may be prevented by intrapartum antibiotic treatment of colonised women (see Chapter 3.76).

Immunisation. Childhood immunisation schedules in Europe ensure protection against meningitis caused by mumps, polio, and *H. influenzae* type b (Hib). In many countries, *N. meningitidis* group C and tuberculosis are also in the schedule. Quadrivalent vaccines *N. meningitidis* serogroups A, C, Y and W135 are increasingly replacing serogroup C vaccines, and a serogroup B vaccine is now available and has been introduced into the UK infant immunisation programme. 7, 10 and 13 valent conjugate pneumococcal vaccines are licensed in Europe and have been implemented in most countries (mainly 13 valent).

Chemoprophylaxis is indicated for close contacts of meningococcal and Hib disease (see Chapters 3.36 and 3.47) and investigation for close contacts of TB (Chapter 3.78). It is not necessary for contacts of pneumococcal or viral meningitis.

Food safety. *Listeria* meningitis is preventable by avoiding high-risk foods such as soft cheese, pate and cook-chill foods, particularly for the immunosuppressed and in pregnancy.

Optimising case management. In cases of suspected meningococcal disease, a parenteral antibiotic should be given urgently (see Chapter 3.47).

Response to a case or cluster

The first priority when a case is notified is to establish the diagnosis. This requires close liaison with clinicians and microbiologists to ensure that appropriate investigations are carried out. If the initial diagnosis is viral meningitis, then no further action is needed at this stage, although it may be necessary to provide information to GPs and parents if the case appears to be linked with others.

If bacterial meningitis is suspected, then further measures will depend on the cause. Again, optimum investigation is essential as the nature of the public health response differs for each organism. Typing of the organism is needed to determine whether cases are linked. Chemoprophylaxis, and sometimes also vaccination, is indicated for cases due to *N. meningitidis* or *H. influenzae* (see Chapters 3.36 and 3.47). With the widespread introduction of Hib and group C meningococcal vaccines, meningococcal group B infection is the most likely diagnosis in a patient with acute bacterial meningitis and it may sometimes be appropriate to initiate control measures before laboratory confirmation.

2.2 Gastrointestinal infection

Every year in the UK, approximately 1 in 30 people attend their general practitioner with an acute gastroenteritis (usually diarrhoea and/or vomiting) and many more suffer such an illness without contacting the health service. Although an infectious cause is not always demonstrated, there is strong epidemiological evidence to suggest that most of these illnesses are caused by infections. A wide variety of bacteria, viruses and parasites may cause gastrointestinal infection: commonly identified ones in the EU are listed in Table 2.2.1. Less common but highly pathogenic infections may be imported from abroad including amoebic dysentery, cholera, typhoid and paratyphoid fevers, as well as milder causes of travellers' diarrhoea, such as *Plesiomonas* and various *Escherichia coli*. Other infectious causes of gastroenteritis include other *E. coli*, *Bacillus subtilis*, *Clostridium difficile, Listeria monocytogenes*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica* and viruses, such as sapovirus, adenovirus, astrovirus, and coronavirus. Non-infectious causes of acute gastroenteritis include toxins from shellfish (see Chapter 3.89.8), vegetables (e.g. red kidney beans) and fungi (such as wild mushrooms), and chemical contamination of food and water.

Laboratory investigation

Identification of the causative organism is dependent upon laboratory investigation, usually of faecal samples. As well as microscopy and culture, testing may also be undertaken using a PCR panel, which tests for numerous pathogens: PCR can give rapid results, although follow up culture should also be undertaken It is important that such samples are taken as soon after the onset of illness as possible, as the likelihood of isolating some pathogens (e.g. viruses) decreases substantially within a few days of onset. Collecting at least 2 ml of faeces and including the liquid part of the stool will increase the chances of a positive result. Delay in transport to the laboratory, particularly in warm weather should be minimised: if delay is likely, samples should be refrigerated and/or stored in a suitable transport medium. A local policy on sampling and transport should be agreed with the local microbiology laboratory. Samples of vomit may sometimes be helpful. In both cases, the patient should receive instructions on the collection and storage or transport of the specimen. Serum samples may occasionally be helpful, particularly if some cases become jaundiced. It is often difficult to distinguish between bacterial and chemical food-borne gastroenteritis on clinical grounds, although some toxins cause an unpleasant taste and/or burning in the mouth or throat. If a chemical cause is

Table 2.2.1 Differential diagnosis of common gastrointestinal infection

	Laboratory Confirmed Cases from EU/EEA in 2014[a]		Incubation Period (Approx.)		Clinical clues in outbreaks		
Organism	**Cases (No.)**	**Notification rate per 100000 population**	**Usual**	**Range**	**Symptoms[b]**	**Severity**	**Other features**
Campylobacter	240379	59.8	1–7 days	1–10 days	D often with blood. Abdominal pain ± fever.	Usually lasts 2–7 days.	Peaks in early summer.
Salmonella	91408	25.4	12–48 hours	4 hours–10 days	D often with fever. May be myalgia, abdominal pain, headache.	Can be severe. Lasts several days to 3 weeks.	Peaks in late summer.
Norovirus	n/a	(10.0)	15–50 hours	6–72 hours	Nausea/vomiting, cramps, mild D common. Malaise, headache, fever may occur.	Usually mild lasts 1–2 days.	Secondary spread common. More common in winter.
Rotavirus	n/a	(7.5)	2–4 days	1–4 days	Watery D, fever, vomiting ± respiratory symptoms.	Usually lasts a few days, but occasionally severe.	Usually children, common in winter.
Giardia	17278	5.4	5–16 days	1–28 days	D, malaise, flatulence, smelly stools, cramps, bloating.	Often prolonged. May be malabsorption and weight loss.	Often travel associated. Possibility of water-borne outbreak.
Hepatitis A	13724	3.0	mean = 28 days	15–50 days	Fever, nausea, malaise, possibly diarrhoea in children. Jaundice fairly specific but not sensitive.	Worse in adults Lasts up to 4 weeks.	Children may be asymptomatic.
Cryptosporidium	7285	2.4	5–30 days	1–28 days	D, bloating and abdominal pain common.	Usually self-limiting in 5–14 days, but can lasts much longer.	Severe in immunocompromised. Increase in spring and autumn.

(*Continued*)

Table 2.2.1 (*Continued*)

Organism	Laboratory Confirmed Cases from EU/EEA in 2014[a]		Incubation Period (Approx.)		Clinical clues in outbreaks		
	Cases (No.)	Notification rate per 100 000 population	Usual	Range	Symptoms[b]	Severity	Other features
STEC	6167	1.4	2–4 days	6 hours – 10 days	D.[b] Often abdominal pain, fever and/or vomiting; blood not uncommon	Variable, may be very severe e.g. HUS, TTP.	Consider in all cases of bloody diarrhoea.
Shigella	6125	1.4	24–72 hours	12–96 hours	*S. sonnei*: Often watery D. May be mucus.	*S. sonnei*: Self-limiting in 3–5 days.	*S. sonnei:* Often children or institutions: secondary spread common
				possibly up to 1 week for *S. dysenteriae*	Other shigellae: D, mucus, blood, fever and colic common.	Other shigellae: Lasts average of 7 days, often severe.	Other shigellae: Often imported, secondary spread common.
Clostridium perfringens	n/a	n/a	8–18 hours	5–24 hours	D, abdominal pain common (vomiting and fever are rare).	Usually mild and short-lived lasts approx. 1 day.	Usually failure of temperature control post cooking.
Bacillus cereus	n/a	n/a	0.5–6 hours (Vomiting); 6–24 hours (diarrhoea)		Syndrome of nausea, vomiting + abdominal pain. *or* Syndrome of diarrhoea + abdominal pain.	Usually mild and short-lived lasts approx. 1 day.	Often from rice or pasta. High attack rate.
Staphylococcus aureus	n/a	n/a	2–4 hours	0.5–8 hours	Nausea, vomiting, abdominal pain and often diarrhoea. Often abrupt onset.	May be very acute.	Food handler may have skin infection.

[a] ECDC, Annual Epidemiological Report on communicable diseases in Europe; note number of reporting states may vary by organism, so rates more comparable than numbers. Case ascertainment also varies markedly by organism. Rates in (brackets) are for England and Wales only (source PHE).
[b] D = Diarrhoea, which can be defined as three or more loose stools in 24 hours.

suspected, advice on sampling should be obtained from a toxicologist (e.g. public analyst).

A suitable list of organisms to test for in all community outbreaks of gastroenteritis is:

- *Salmonella* species
- *Campylobacter* species
- *Shigella* species
- Shiga-toxin Producing *E. coli* (STEC)
- Norovirus
- Protozoa (*Cryptosporidium* and *Giardia*)

Plus, if food poisoning is suspected or if clinical features suggest (see Table 2.2.1):

- *Bacillus* species
- *Clostridium perfringens*
- *Staphylococcus aureus*

Also consider if clinical or epidemiological features suggest or if the first list above negative.

- Rotavirus
- *Vibrio* species
- *Yersinia* species
- *C. difficile*
- Other *E. coli* (see Chapter 3.69)
- Other viruses
- Toxins or poisons

In hospitals, the most common causes of outbreaks are:

- Norovirus
- *C. difficile*
- *Salmonella*
- Rotavirus

Prevention and control

Vaccines are not yet available against most of the major causes of gastrointestinal infection and so public health efforts concentrate on reducing exposure to the organisms responsible. Most gastrointestinal infections are either food-borne or spread person to person. The role of the consumer in demanding safe food via pressure on government and food retailers is under-developed in many countries:

At the local level, prevention of gastrointestinal or food-borne infection is achieved by:

- Working with food businesses and staff to reduce the likelihood of contamination of food (from the environment, food handlers or cross-contamination) and avoid inadequate cooking and storage at inadequate temperatures. The Hazard Analysis Critical Control Point (HACCP) system is used by the food industry in identifying and assessing hazards in food, and establishing the control measures needed to maintain a cost-effective food-safety programme. Important features are that HACCP is predictive, cheap, on-site and involves local staff in the control of risk. In the UK, this approach is reinforced by inspection of premises by the Environmental Health Department of the Local Authority and other enforcement agencies.
- Use of statutory powers: For example, UK Local Authorities can exclude cases or carriers of infection from work or school and compensate them for any loss of earnings. Other powers include seizure of food and closure of premises that present an 'imminent risk to Public Health'. Officers of the Environmental Health Department usually exercise these powers. The Food Standards Agency (FSA) is the enforcing authority for licensed fresh meat/poultry premises in Great Britain.
- Advising the public on safe food handling and the reduction of faeco-oral spread. This includes the importance of handwashing immediately after going to the toilet and before handling or eating food. This is of vital importance, as approximately 80% of people with gastrointestinal infection do not consult the health service when ill.
- Adequate infection control policies in all institutions, such as hospitals, nursing and residential homes, schools and nurseries, including use of enteric precautions (see Box 1.3.3) for cases of diarrhoea or vomiting.
- Regular surveillance to detect outbreaks and respond to individual cases. Food poisoning (proven or suspected and including water-borne infection), dysentery and viral hepatitis are all statutorily notifiable, as are cholera, paratyphoid and typhoid fever in almost all European countries. However, there may often be no laboratory confirmation

of the organism responsible and it is often necessary to initiate action before the causative organism is known. Arrangements should also be in place for reporting of isolates of gastrointestinal pathogens from local microbiology laboratories (see Table 4.1.2). However, around 90% of cases seen by general practitioners are not identified by either of these systems: obtaining surveillance data from computerised primary care providers may help address this.

Response to individual case

It is not usually possible to identify the organism causing gastroenteritis on clinical grounds in individual cases. The public health priorities in such cases are:

- To limit secondary spread from identified cases by provision of general hygiene advice to all and by specific exclusion from work/school/nursery of those at increased risk of transmitting the infection (see Box 2.2.1),
- To collect a minimum dataset to compare to other cases to detect common exposures or potential outbreaks. It is best to collect such data on standardised forms and a subset should be entered on a computerised database for both weekly and annual analysis. A possible dataset is given in Box 2.2.2,
- Ideally, a faecal sample would be collected from all clinical notifications of food poisoning or dysentery to detect clusters by organism/type, to detect potentially serious pathogens requiring increased intervention, and to monitor trends.

A local policy to address these priorities should be agreed with local Environmental Health Officers, microbiologists and clinicians. The role of the primary care practitioners in public health surveillance and in preventing secondary spread is of particular importance and needs to be emphasised regularly (e.g. via a GP newsletter).

Response to cluster

The most common setting for a cluster of clinical cases of gastroenteritis is in an already defined cohort, for example a nursing home or amongst attendees at a function. Such a situation is slightly different to investigating a laboratory identified cluster:

- It is important to discover the microbiological agent. Following discussion with the relevant microbiologist stool specimens should be obtained without delay from 6 to 10 of the patients with the most recent onset of illness and submitted to the laboratory for testing for all relevant organisms, (see list above: the laboratory may not test for all

Box 2.2.1 Groups that pose an increased risk of spreading gastrointestinal infection

(a) Any person who is unable to perform adequate personal hygiene due to lack of capacity or ability to comply OR has lack of access to hygiene facilities.

(b) All children aged five years old or under (up to the sixth birthday*) who attend school, pre-school, nursery or other similar child care or minding groups.

(c) People whose work involves preparing or serving unwrapped ready to eat food (including drink).

(d) Clinical, social care or nursery staff who work with young children, the elderly, or any other particularly vulnerable people, and whose activities increase the risk of transferring infection via the faecal-oral route.

* *Guidelines in some countries may specify 'under-5' only.*

Source: *Principles and Practice Recommendations for the Public Health Management of Gastrointestinal Infections. A joint guideline from Public Health England and the Chartered Institute of Environmental Health.*

Box 2.2.2 Possible local dataset for investigation of cases of gastrointestinal infection

Administrative details (Name, address, telephone, Date of birth, GP, unique number)
Formally notified? Yes/No
Descriptive variables (Age, sex, postcode)
Date and time of onset

Symptoms:	Diarrhoea	Yes/No
	Nausea	Yes/No
	Vomiting	Yes/No
	Fever	Yes/No
	Abdominal pain	Yes/No
	Blood in stool	Yes/No
	Malaise	Yes/No
	Headache	Yes/No
	Jaundice	Yes/No
	Others (specify):_____	

Duration of illness
Stool sample taken? (Source, date, laboratory)
Microbiological result (Organism details, laboratory, specimen date)

Food history: Functions, restaurants, takeaways;
Food consumed in five days before onset (if microbial cause known, use organism incubation period);
Raw water consumed outside the home in previous 14 days.

Travel abroad?
Animal contact?
Occupation, place of work/school/nursery
Advised not to work?
Formally excluded?
Part of outbreak?

Organism specific questions may be added if microbiological investigation reveals an organism of particular public health importance (e.g. STEC, *Cryptosporidium*, *Salmonella* Typhi, *Salmonella* Paratyphi).

these unless requested). The identity of the agent will dictate the urgency of the investigation (e.g. to prevent further exposure to a source of STEC), the control measures to be introduced (e.g. to limit person to person spread of norovirus in institutions) and provide valuable clues as to how the outbreak may have happened (e.g. inadequate temperature control in a *Bacillus cereus* outbreak).

- As microbiological results will not be available for a number of days, clinical details should be collected from all reported cases so that the incubation period, symptom profile, severity and duration of illness can be used to predict which organism(s) are most likely to be the cause (Table 2.2.1). The likelihood of different microbiological causes also varies by season (Figures 2.2.1 and 2.2.2). There may also be clues as to whether the illness is likely to be food-borne or spread person to person (Box 2.2.3). In many such outbreaks a formal hypothesis-generating study is not necessary, and it is often possible to progress to an analytical study to investigate possible food vehicles early in the investigation (see Chapter 4.2).

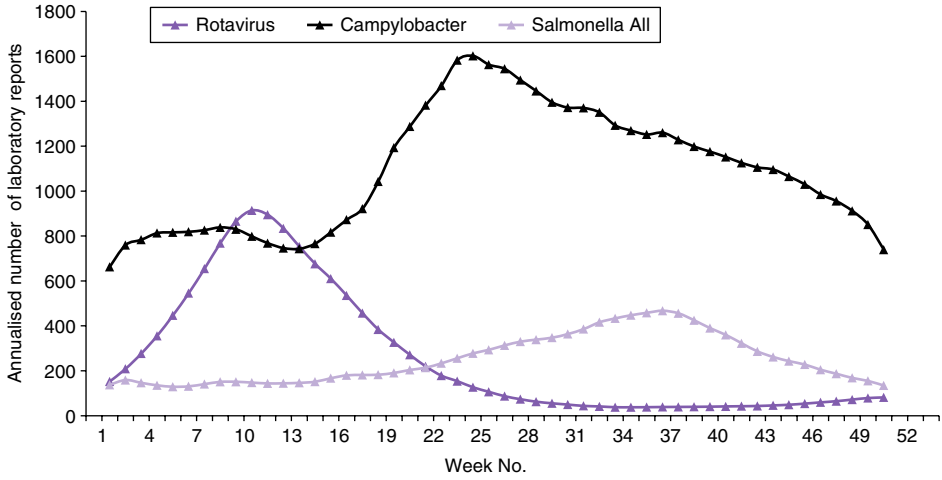

Fig 2.2.1 Seasonal distribution of gastrointestinal pathogens (Rotavirus, Campylobacter, Salmonella All) 1998–2017, England, Wales & Northern Ireland (3-week moving average).

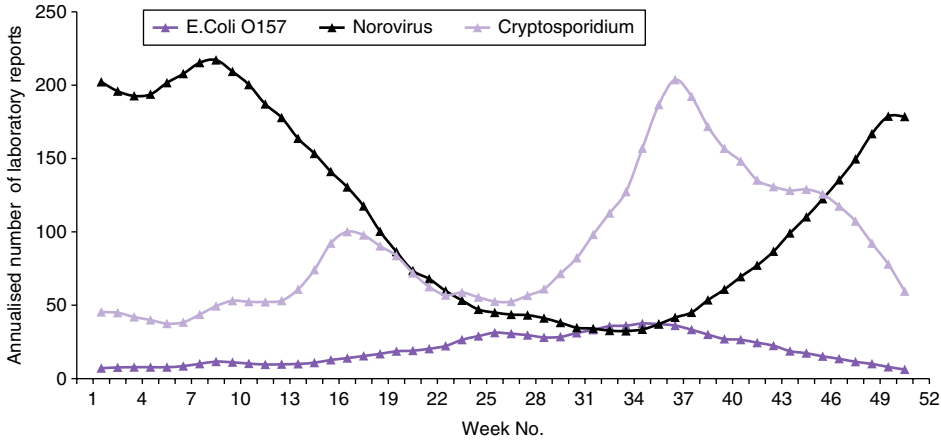

Fig 2.2.2 Seasonal distribution of gastrointestinal pathogens (*E. Coli* O157, Norovirus, Cryptosporidium) 1998–2017, England, Wales & Northern Ireland (3-week moving average).

- The environmental component of the investigation is often illuminating as to why the outbreak happened, in other words, how did an infectious dose of the organism occur in the identified food vehicle? This investigation will look at:
  - food sources, storage, food preparation, cooking procedures, temperature control after cooking and reheating,
  - symptoms of gastrointestinal or skin disease, or testing for faecal carriage in food handlers,
  - general state of knowledge of the staff and condition of the premises,
  - examination of records of key controls, such as temperatures and pest controls,
  - whether samples of food are available for examination/analysis and whether environmental swabbing or water sampling is appropriate.
- General control measures to prevent spread from those affected can be instituted early, as can addressing important problems identified in the environmental investigation.

Box 2.2.3 Clues as to whether an outbreak of gastroenteritis could be food-borne or spread person to person

May suggest food-borne	May suggest person to person
Dates of onset (epidemic curve) clustered indicating a point source outbreak.	Dates and times of onset do not cluster but occur in waves coinciding with the incubation period of the responsible pathogen.
All wards, classes, buildings or units supplied by the kitchens or food supplier are affected.	Patients and staff in a single ward, class, building, or unit are affected.
Food handlers and catering staff are affected.	People in the households of staff-members or pupils are also affected.
Clinical features and laboratory tests indicate an organism predominantly spread via food and water rather than person to person, e.g. *C. perfringens*, *B cereus*.	Clinical features and laboratory tests suggest organism predominantly spread person to person, e.g. rotavirus, *Shigella*.
Environmental investigation reveals poor food handling practices or premises.	Environmental investigation reveals poor infection control practice or hygiene facilities.

Warnings:

These are not invariable rules, assess each outbreak on its own merits, for example:

- Some food-borne outbreaks may be prolonged by person-to-person spread,
- Food-borne outbreaks may be due to a continuing source,
- Some outbreaks may be augmented by environmental contamination.

This includes the exclusion from work of infected foodhandlers and measures to avoid secondary spread from cases. More specific measures can be instituted when the organism and vehicle are identified (see disease-specific chapters in Section 3).

- In institutions, such as hospitals and nursing homes, institute measures to reduce risk of person-to-person spread (see Chapter 3.51, 'Control of an Outbreak' section for details).

2.3 Community acquired pneumonia

Respiratory tract infections are the most common infectious disease in developed countries and pneumonia remains one of the most common causes of death. Community (as opposed to hospital) Acquired Pneumonia (CAP) affects all ages, although its incidence increases dramatically beyond 50 years of age. Other risk factors include chronic respiratory disease, smoking, immunosuppression (including HIV/AIDS) and residence in an institution. Approximately 20% of cases require hospitalisation, of which 5–10% die.

In general, the symptoms of CAP are fever, cough, sputum production, chest pain and shortness of breath, with accompanying chest X-ray changes. The most common causes of CAP are listed in Table 2.3.1. Although the clinical picture cannot be used to diagnose individual cases, clues may be obtained to help identify the causes of outbreaks. Some organisms may be more likely to cause 'typical' pneumonia (e.g. pneumococcus, *Haemophilus*, *Moraxella*, *Klebsiella*) and others 'atypical' with significant non-pulmonary features (e.g. *Mycoplasma*, *Chlamydia*, *Legionella*, *Coxiella*).

Rare causes of pneumonia for which there may be an environmental cause (most likely abroad, but perhaps due to deliberate

Table 2.3.1 Differential diagnosis of community acquired pneumonia

Organism	Percentage of cases[a]	Incubation period	Clinical clues[b]	Epidemiological clues
Streptococcus pneumoniae	29	1–3 days (exogenous)	Acute. Mucopurulent or bloodstained sputum, fever, pleuritic chest pain. Prominent physical signs. Respiratory symptoms may be less prominent in elderly.	More common in infants, elderly, unvaccinated, in winter and during influenza A epidemics.
Mycoplasma pneumoniae	9	6–32 days (median 14)	Gradual onset, fever, malaise, and headache with coryza, sore throat or unproductive cough. 10% progress to LRTI[c] .	May be 4 yearly epidemics. More common in winter. Often affects younger patients or military.
Influenza A	8	0.3–3 days (median 1.4)	About half have classic flu: headache, myalgia, fever, malaise. May also be dry cough, sore throat, and coryza. 10% progress to pneumonia. About 20% are asymptomatic and 30% have URTI[d] only.	May be seasonal community epidemic. Particularly affects the unvaccinated (nb elderly may be vaccine failures).
Chlamydia pneumoniae	6	Unclear: 10–30 days?	Pharyngitis, sinusitis, either in isolation or together with chest infection with insidious onset and prolonged cough, with scanty sputum. High incidence of laryngitis.	Often affects young adults. No obvious seasonality. Outbreaks common in residential and educational institutions.
Gram negative bacteria	6	Variable	Severe. Acute onset. Bloody 'redcurrant jelly' sputum.	Particularly common in Nursing Homes. More likely if chronic respiratory disease, diabetes, alcohol.
Haemophilus influenzae	5	Unclear: 2–4 days?	Purulent sputum. Onset may be insidious.	Often associated with chronic lung disease and elderly.
Legionella pneumophila	4	2–10 days (median 6–7)	Anorexia, malaise, myalgia, headache, fever. Some with diarrhoea, confusion and high fever. Upper respiratory symptoms rare. Often severe.	May be associated with aerosol source. More common in summer and autumn. Mostly over 30; Male excess.
Staphylococcus aureus	4	1–4 days (exogenous)	Often serious. May be ring shadows on X-ray.	May complicate influenza infection. More common in nursing homes.
Parainfluenza	2	1–6 days (median 2.6)	Croup, wheezing, or hoarseness. Ear or upper respiratory infection.	Mostly affects children and immunocompromised. Paraflu 1 and 2 more common in autumn or early winter (but paraflu 3 endemic).

Chlamydia psittaci	2	4–28 days (median 10)	Fever, headache, unproductive cough, myalgia. May be rash. Often severe.	Possible link to birds. Mostly adults, more often male.
Influenza B	1	0–2 days (median 0.6)	Headache, myalgia, coryza, fever, sore throat. Children may have gastrointestinal symptoms.	May be seasonal community epidemic. Affects the unvaccinated.
Coxiella burnetii	1	7–32 days (median 18)	Fever, headache, myalgia, cough. May be fatigue, chills, anorexia, arthralgia, nausea. Possibly neurological symptoms or hepatitis. Asymptomatic infection common.	Possible link to sheep, other animals or animal products. May increase in April–June. Male excess, rare in children.
RSV	1	2–8 days (median 4.4)	Wheezing, rhinitis, fever, cough. Children may get otitis media and/or pharyngitis. Bronchiolitis, pneumonia, or croup may develop after a few days.	Peaks every November to January. Causes outbreaks in nursing homes and neonatal units.
Adenovirus	0.7	4–8 days (median 5.6)	Fever, sore throat, runny nose.	Usually children or young adults (e.g. military recruits). Highest in January–April.

[a] Average from a number of prospective studies of patients admitted to hospital (Farr, B. M., and Mandell, G. L.. (1988). Gram positive pneumonia. In: *Respiratory Infections: Diagnosis and Management*, 2e (ed. J. E. Pennington), 298–313. New York: Raven Press.). Will vary according to epidemic cycles.
[b] Clinical picture is not a reliable indicator of organism in individual cases.
[c] LRTI Lower respiratory tract infection
[d] URTI Upper respiratory tract infection

aerosol release) include anthrax, brucellosis, hantavirus, histoplasmosis, leptospirosis, tularaemia, Q fever and plague. Respiratory infection may also be caused by rare or emerging organisms such as MERS-CoV, SARS-CoV, avian influenza, metapneumovirus and *Moraxella catarrhalis* or, in immunosuppressed individuals, opportunistic pathogens such as *Pneumocystis carinii*. Similar symptoms may also be seen in exacerbations of chronic respiratory disease and non-infective respiratory conditions, for example pulmonary oedema, pulmonary infarction, alveolitis (may follow exposure to inorganic particles) and eosinophilic pneumonias (may be associated with drugs or parasites).

Laboratory investigation

Microscopy and culture of sputum was traditionally the mainstay of diagnosis for typical pneumonia. However, about a third of pneumonia cases do not produce sputum, culture is only moderately sensitive and contamination with oropharyngeal flora is not an uncommon event. Blood culture is highly specific but relatively insensitive.

Serology was the mainstay of diagnosis for viral and 'atypical' causes for many years, but has gradually been replaced by newer tests: serology is often not diagnostic until two to six weeks into the illness, although *Mycoplasma* specific IgM (Immunoglobulin class M) may be apparent earlier. PCR tests on respiratory samples can now be carried out for viruses, *Mycoplasma*, *Chlamydia* and *Legionella* (not just *L. pneumophila* serogroup 1): lower respiratory samples are preferred. Influenza and respiratory syncytial virus (RSV) may be cultured from nasopharyngeal swabs or aspirates, and viral antigen may also be detected from these specimens. Antigen tests are available for *L. pneumophila* (serogroup 1 only) in urine and pneumococcus in urine, sputum or serum, even if antibiotics have already been given.

A proportion of cases may be infected with more than one pathogen.

Prevention and control

- Immunisation of elderly and those with chronic disease and the immunocompromised with influenza and pneumococcal vaccines.
- Immunisation of children with influenza vaccine and conjugated vaccines against *Haemophilus influenzae* type b and pneumococcus.
- Use of specific prophylaxis (e.g. antivirals for influenza or palivizumab for RSV) for specific clinical risk groups when appropriate virus circulating.
- Reduction of smoking.
- Promotion of breastfeeding.
- Avoiding overcrowding, especially in institutions.
- Good infection control in institutions.
- Environmental measures to reduce *Legionella* exposure.
- Surveillance of community acquired pneumonia, especially for influenza, *Mycoplasma, Legionella, Coxiella* and *Chlamydia psittaci*. Surveillance of antibiotic-resistant pneumococci.
- Reporting of outbreaks in institutions to public health authorities.

Response to a case

- If resident or attender at institution, or if severely ill, investigate to obtain microbiological cause.
- Follow up individual cases of legionellosis, psittacosis and Q fever for source of organism.
- Advise personal hygiene, particularly handwashing, coughing, and disposal of secretions.
- Limit contact with infants, frail elderly and immunocompromised.
- Clinical assessment and treatment in line with national guidelines.

Response to a cluster

- Discuss investigation with microbiological colleagues. A suitable set of investigations could be:
  - Take nasopharyngeal aspirates or nose and throat swabs from the most recently infected cases for viral culture, PCR and antigen testing;
  - Send sputum samples for microbiological culture and possibly pneumococcal antigen;
  - Send blood cultures from febrile cases;
  - Send urine for *Legionella* and pneumococcal antigen;
  - If antibody testing is available, take serum samples from recovered cases or those with date of onset 10 days or more ago.
- If an institutional cluster, isolate or cohort cases until cause known. Stop new admissions. Avoid discharges to institutions containing elderly, frail, or immunocompromised individuals. Measures should aim to limit transmission by large droplets, droplet nuclei, respiratory secretions, and direct contact. In RSV season, also consider transmission via inanimate objects.
- Collect data on immunisation history (influenza, pneumococcus), travel, exposure to water and aerosols, animals, birds and other potential sources of *legionellosis, Q fever, psittacosis* and *brucellosis*.
- Advise community cases on hygiene measures (handwashing, coughing, discharges, etc.) and to avoid individuals susceptible to severe disease (e.g. elderly, chronically ill).
- Specific interventions as appropriate to identified organism (see organism-specific chapter).
- During influenza season, may wish to give anti-influenza prophylaxis to contacts in residential care institutions for elderly, whilst awaiting diagnosis (see chapter 3.38).
- A cluster of community acquired pneumonia could arise as a result of a deliberate release of an aerosol of a serious or rare infection such as anthrax or plague (see chapter 4.17).

2.4 Rash in pregnancy

Infectious and other causes

There are many possible causes of a rash in a pregnant woman. Most causes are non-infectious and include drug reactions and allergies. The important differentiating feature from an infectious cause is the absence of fever. Infectious causes are relatively uncommon, but important because of the potential harm to the developing foetus. Rubella, Parvovirus B19, Varicella, Cytomegalovirus (CMV) and Syphilis can all cause severe congenital disease or intrauterine death.

Clinical and epidemiological differences

Viral infections in pregnancy are often mild or inapparent with variable or absent fever. The exceptions are varicella, which presents with a characteristic rash, and measles. Bacterial infections are more severe and usually accompanied by a high fever (with the exception of syphilis). The clinical presentation of each of the infections in Table 2.4.1 is described in more detail in the relevant chapters.

The most common infections presenting with a rash in pregnancy are parvovirus B19

Table 2.4.1 Infections that may present with a rash in pregnancy

Viral
Rubella
Parvovirus B19
Varicella-zoster
Measles
Enterovirus
Infectious mononucleosis
Cytomegalovirus
Bacterial
Streptococcal
Meningococcal
Syphilis

(1 in 400 pregnancies), varicella (1 in 500 pregnancies) and the enteroviruses. CMV is common in pregnancy and is the most common cause of viral congenital infections (an estimated birth prevalence of 3 per 1000), but rarely presents with a rash. Rubella and measles are now both rare in pregnancy, due to successful immunisation programmes. Enterovirus infections and measles during pregnancy do not carry a specific risk for the foetus, although measles may result in intra-uterine death and preterm delivery.

Infectious mononucleosis sometimes presents with a rash but poses no risk to the foetus. Bacterial causes of rash in pregnancy are very uncommon.

Laboratory investigation

The laboratory investigation of suspected meningococcal and streptococcal disease and syphilis is described in Chapters 3.47, 3.72 and 3.26, respectively.

Where a viral infection is suspected, it is important to exclude varicella, parvovirus B19, rubella and CMV. Varicella can usually be diagnosed on the basis of the typical vesicular rash, but where there is doubt, laboratory confirmation should be sought. Rubella and parvovirus B19 can both be diagnosed by detection of IgM or rising IgG (Immunoglobulin class G) in saliva or serum. PCR testing is also available. Testing should be carried out irrespective of previous testing or vaccination.

The investigation of a pregnant woman who has been in contact with someone with a rash illness is more complex. The aim of investigation is to determine whether the contact case has varicella, rubella or parvovirus B19, and whether the pregnant patient is susceptible to these three infections. A significant contact is defined as being in the same room for over 15 minutes, or face-to-face contact. Testing algorithms have been published by Public Health England (http://www.gov.uk/government/publications/viral-rash-in-pregnancy)

Prevention and control

Rubella infection in pregnancy can be prevented both directly, by vaccination of susceptible women of childbearing age, and indirectly, by universal childhood immunisation (which reduces circulation of wild virus and thus prevents exposure). Rubella vaccine (usually given as MMR) is a live vaccine and should not be given during pregnancy, although the risk to the foetus is theoretical and immunisation in pregnancy is no longer an indication for termination of pregnancy.

Varicella vaccine is licensed in most countries in Europe and can be used for both direct prevention of varicella in pregnancy (by vaccination of susceptible women) and indirect prevention (universal childhood immunisation). A specific Varicella-Zoster Immunoglobulin (VZIG) is also available for postexposure prophylaxis of susceptible women exposed in pregnancy (see Chapter 3.7).

No specific measures are available for prevention of parvovirus B19 in pregnancy, although pregnant women may wish to avoid outbreak situations, and healthcare workers who have been in contact with B19 infection should avoid contact with pregnant women for 15 days from the last contact or until a rash appears (see Chapter 3.53).

Response to a case

Laboratory investigations should be undertaken, as described above. Pregnant women with varicella, rubella or parvovirus B19 should be counselled regarding the risks to the foetus and managed accordingly. Oral acyclovir should be considered for pregnant women after 20 weeks gestation who present within 24 hours of onset of varicella. The risk to the foetus of rubella in the first 16 weeks is substantial; rubella prior to the estimated date of conception or after 20 weeks carries no documented risk; and rubella between 16 and 20 weeks gestation carries a minimal risk of deafness only. Parvovirus B19 in the first

20 weeks of pregnancy can lead to intrauterine death and hydrops foetalis; so regular ultrasound screening/Doppler assessment is recommended for such cases. The public health management of the close contacts is the same as for non-pregnant cases (see Chapters 3.7, 3.53 and 3.64).

Response to a cluster

As for response to a case but consider community-wide vaccination programme for clusters of rubella or measles.

2.5 Rash and fever in children

Rashes in children are common. Where fever is present, this usually means the cause is infectious. Rashes with fever in children are most commonly caused by a virus. In the absence of fever, a non-infectious cause (e.g. allergy, drug reaction) is most likely, although in some infections, for example enterovirus infections, the fever may be mild or absent. A rare cause of febrile rash in children is Kawasaki disease, a vasculitic syndrome in children that is believed to be an abnormal immunological response to an infectious disease in genetically susceptible individuals.

Clinical and epidemiological differences

In addition to fever, other features that suggest an infectious cause are the presence of swollen lymph nodes, general malaise, and a history of recent contact with another infectious case. A full clinical history (including vaccination and travel history) and physical examination should always be obtained from a child with a rash. Consider the time of onset of the rash relative to the fever and the characteristics of the rash (morphology, location and distribution).

There are four main types of infectious rash in children: maculopapular/punctate, petechial/purpuric, vesicular/bullous and scaly. Maculopapular rashes are flat or slightly raised and there is sometimes joining together of areas of the rash. Punctate rashes have small, discrete pinpoint lesions. Petechial and purpuric rashes look like bruising or bleeding under the skin. Vesicular and bullous rashes have a blister-like appearance and sometimes contain fluid. Scaly rashes are flat, hard and may be shiny. The main causes of each type are shown in Table 2.5.1.

laboratory investigations

General investigations which are useful in differentiating infectious from non-infectious causes are a full blood count, erythrocyte sedimentation rate, blood culture, specimens for viral culture, serology and PCR. Most viral exanthems can now be diagnosed by PCR of blood. Other investigations will depend on the possible differential diagnoses. A saliva test should be obtained if measles or rubella is suspected.

Prevention and control

General hygiene measures such as handwashing may help limit the spread of some infectious causes of rashes. Transmission of measles, rubella, meningococcal and pneumococcal disease, and chickenpox are all preventable by vaccination (see Chapters 3.46, 3.64, 3.47, 3.55 and 3.7, respectively).

Response to a case

- Obtain clinical details, especially whether fever is present. The key to diagnosis is the nature of the rash (Table 2.5.1)
- Check vaccination status.
- Obtain history of contact with other case(s).
- Most childhood rashes are mild and do not warrant any specific public health action.

Table 2.5.1 Causes of different types of rash in children

Type of rash	Viral	Bacterial	Other infectious causes	Others
Maculopapular	Measles Rubella EBV[a] Parvovirus B19 Roseola infantum Enterovirus Adenovirus Gianotti-Crosti syndrome Unilateral laterothoracic syndrome Dengue fever Acute HIV West Nile virus	Staphylococcal and streptococcal toxic shock Scarlet fever Syphilis Leptospirosis *Borrelia* Typhoid Brucellosis *Arcanobacterium haemolyticum*	Toxoplasmosis *Rickettsia* Ehrlichosis *Mycoplasma* Psittacosis	Kawaskai disease Pityriasis rosea Juvenile chronic drug reaction Eczema SLE[b] Dermatitis
Petechial/ Purpuric	Enterovirus EBV Papular purpuric Gloves and Socks syndrome VHFs[d] Congenital CMV/rubella	Meningococcus Pneumococcus Leptospirosis Bacterial endocarditis	*Rickettsia* Malaria Leishmaniasis	Henoch-Schönlein purpura HUS[c] Idiopathic thrombocytopenic purpura Leukaemia
Vesicular/ bullous	Varicella Herpes simplex Smallpox Enterovirus esp. coxsackie	Staphylococcal scalded skin Staphylococcal and streptococcal impetigo	*Mycoplasma*	Stevens-Johnson syndrome
Scaly			Fungal e.g.tinea	Eczema Psoriasis Pityriasis rosea

Source: Adapted from Sharland, M. (ed.) (2016). *Manual of Childhood Infections. The Blue Book*. 4e. Oxford: Oxford University Press, Table 26.1. Reproduced by permission of Oxford University Press (global.oup.com).

[a] *Epstein-Barr virus*

[b] *Systemic lupus erythematosus*

[c] *Haemolytic uremic syndrome*

[d] *Viral haemorrhagic fevers*

- If rubella or chickenpox is suspected, a history of contact with pregnant women should be sought and further action may be warranted (see Chapters 3.64 and 3.7)
- Exclusion from school is indicated for the vaccine-preventable diseases (see earlier) and for scarlet fever (see Chapter 3.72).
- Exclusion of contacts of a case of Parvovirus B19 who are non-immune health care workers may be indicated (see Chapter 3.53).
- If meningococcal infection is suspected ensure rapid admission to hospital and administration of pre-admission antibiotics and chemoprophylaxis for close contacts (see chapter 3.47).

Response to a cluster

As per a case, although it may be important to give out information to parents and GPs to allay anxiety and to increase disease awareness.

2.6 Illness in returning travellers

In 2015, the World Tourism Organization recorded 1186 million international arrivals (half of which coming from Europe). Of these arrivals, 53% were for holiday, recreation and leisure, 14% for business and professional purposes and another 27% for other reasons such as visiting family and friends. International tourist arrivals are expected to increase by 3.3% a year between 2010 and 2030 to reach 1.8 billion. Of the arrivals, 608 million were to Europe, 279 million to Asia and the Pacific, 193 million to the Americas, 54 million to Africa and 53 million to the Middle East.

Data from the GeoSentinel network reveal that of travellers to the tropics, 20–60% self-report health problems. These are mainly mild and self-limited such as diarrhoea, respiratory infections and skin disorders, but around 8% are ill enough to seek health care.

Before departure to any destination with a higher risk of infection, the traveller should obtain health advice (including advice about immunisation) and if they are ill when they return they should seek appropriate medical attention. Their medical attendants should be aware of the infections that may affect the returning traveller (see also Chapter 4.11).

Travel-related infections

The likelihood of a travel-related infection will depend on the presence of risk factors and these should be assessed by a careful travel history including the following:

- Countries and areas that were visited (rural, urban),
- Duration of stay,
- Exact times and dates (in relation to incubation periods),
- Accommodation (luxury hotels, hostel, camping),
- Activities (hiking, walking, work, contact with local population, contact with animals, looking after ill persons or animals),
- Health status,
- Vaccinations,
- Protection against insect bites,
- Malaria prophylaxis,
- Incidents (animal bites, healthcare, sexual contact, injections, consumption of exotic foodstuffs),
- Exposure to healthcare activities/facilities.

A specific risk group is settled immigrant travellers returning to their country of origin to relatives and friends. This group is less inclined to seek pre-travel medical advice, more often visits developing countries, mixing with the local population and staying for a prolonged period. As a group they are more likely to be diagnosed with systemic febrile illnesses (including malaria), non-diarrhoeal intestinal parasitic infections, respiratory syndromes, tuberculosis, and sexually transmitted diseases.

It may be helpful to make enquiries about the local epidemiology of infections and any

unusual infections or outbreaks that have been reported in the area. There are several websites that may help with this (see websites listed inside back cover). The common presentations of travel-related infections are fever, diarrhoea and skin rash, and all of these may be due to conditions common in non-travellers such as pneumonia, urinary tract infection or neoplasia. The travel-related causes of these presentations are summarised in Table 2.6.1.

Response to a case

- From the detailed travel history, assess risk and determine possible exposures.
- Exclude malaria.
- Follow relevant algorithms (where available) to ensure that diagnostic tests and infection control measures are appropriate.
- Manage contacts, carers and health staff appropriately.
- In the case of suspected Viral Haemorrhagic Fever (VHF), Severe Acute Respiratory Syndrome (SARS) or MERS or other serious imported infections ensure that the relevant public health authorities and specialist secure infectious disease unit are alerted and follow their advice.
- Ensure timely reporting of notifiable diseases.

Investigation of a cluster

In Europe, due to good sanitary conditions and the rareness of appropriate biological vectors, onward transmission is unusual for most imported infections and secondary cases are therefore uncommon. If a cluster

Table 2.6.1 Presentations of travel-related infections

Fever	Malaria (see Chapter 3.45)
	Dengue (see Chapter 3.19)
	Enteric fever (see Chapters 3.52 and 3.80)
	Legionellosis (see Chapter 3.40)
	Rickettsial infections spotted fever (see Chapter 3.89.2)
	Epidemic typhus (see Chapter 3.89.3)
	Chikungunya (see Chapter 3.8)
	Viral haemorrhagic fever (see Chapter 3.82)
	Influenza (see Chapter 3.38)
	Coronavirus including MERS and SARS (see Chapter 3.15)
	Zikavirus (see Chapter 3.88)
Diarrhoea	STEC and other diarrhoeagenic *Escherichia. coli* (see Chapter 3.69)
	Salmonellosis (see Chapter 3.65)
	Campylobacteriosis (see Chapter 3.6)
	Shigellosis (see Chapter 3.68)
	Cryptosporidiosis (see Chapter 3.16)
	Giardiasis (see Chapter 3.24)
	Amoebic dysentery (see Chapter 3.1)
	Cyclosporiasis (see Chapter 3.17)
	Vibrios (see Chapters 3.11 and 3.81)
Jaundice	Hepatitis A, B, C and E (see Chapters 2.7, 3.30–3.34)
Rash	Rickettsial infections (see Chapter 3.89.2)
	Zikavirus (see Chapter 3.88)
	Chikungunya (see Chapter 3.8)
Pharyngitis	Diphtheria (see Chapter 3.20)
Skin lesions	Diphtheria (see Chapter 3.20)
	Leishmaniasis (see Chapter 3.89.4)
Other	Encephalitis (see Chapters 3.35, 3.75, 3.39, 3.84, 3.59)
	Intestinal helminths (see Chapter 3.89.5)
	Schistosomiasis (see Chapter 3.67)

does occur urgent investigation is required to determine whether it is the result of primary exposure abroad or secondary transmission in the home country. Clusters of vector-borne infections should be immediately reported to health authorities in regions with competent vectors.

Surveillance

Surveillance of travel-related infection is largely unsystematic, but networks of travel medicine clinics like the GeoSentinel network compile and publish data that can be useful when estimating the risks of acquiring an infection when visiting a particular location. Laboratory surveillance systems rarely capture accurate travel data and when these data are available they are subject to reporting bias. Single cases of notifiable infections and clusters of cases should be reported to the public health authorities and may be publicised on dedicated websites such as *ProMED-mail*. ECDC regularly publishes rapid risk assessments related to infections of concern to Europe.

2.7 Jaundice

Differential diagnosis

The differential diagnosis of jaundice includes many infectious and non-infectious causes (Boxes 2.7.1 and 2.7.2). Traditionally, for diagnostic reasoning based on clinical chemical laboratory tests, a division is made between pre-hepatic, hepatic, and post-hepatic (obstruction) causes. Here, we simply make a distinction between non-infectious and infectious causes. In a previously well patient with acute onset of jaundice, the most likely non-infectious cause is biliary obstruction, and the most likely infectious cause is viral hepatitis. Pseudo-jaundice due to high vegetable or fruit intake (e.g. papaya, carrots) should also be considered.

Box 2.7.1 Non-infectious causes of jaundice

- Drug reaction (paracetamol, phenothiazine, alcohol)
- Toxins (khat, herbs, mushrooms e.g. Amanita phalloides 'the death cap')
- Recent exposure to anaesthetic
- Haemolysis (e.g. due to G6PD deficiency, sickle cell disease)
- Physiological (in the neonate)
- Toxin causing liver damage (including chronic alcohol abuse)
- Primary biliary cirrhosis
- Autoimmune liver diseases (autoimmune hepatitis [AIH], primary biliary sclerosis [PBS], primary sclerosing cholangitis [PSC], sarcoidosis)
- Gallstones
- Biliary or pancreatic cancer
- Genetic disorders (e.g. Gilbert's disease. Mild forms may first become apparent due to the stress of an infection)

Box 2.7.2 Infectious causes of jaundice

Common
- Viral hepatitis A, B, C, E
- Malaria

Uncommon
- Acute infections of the biliary system (cholecystitis, cholangitis, pancreatitis)
- Leptospirosis
- Epstein–Barr virus infection (and other viruses causing mononucleosis)
- Cytomegalovirus
- Schistosomiasis
- Herpes hepatitis
- Yellow fever
- Rare viruses (e.g. Ebola, Marburg)
- Common viral infections can occasionally cause hepatitis
- Hepatitis D (delta), only as superinfection in chronically infected hepatitis B patients

The worsening of a pre-existing (hitherto unknown and undiagnosed) liver disease, for example chronic hepatitis B or C ('acute on chronic disease'), should also be included in the differential diagnosis of acute jaundice.

Viral hepatitis can be clinically distinguished from other causes of jaundice by the presence of a prodrome of fever, anorexia, nausea and abdominal discomfort. The liver is often enlarged and tender. There may be a history of travel to endemic areas, contact with a case, or high-risk behaviour. Bilirubin is present in the urine, and serum transaminase levels (ALT, AST) are markedly elevated.

In viral hepatitis, the fever usually subsides once jaundice has developed. If the fever persists, other liver infections should be considered, such as Epstein–Barr virus or leptospirosis.

Laboratory investigations to distinguish between the different types of viral hepatitis and other liver infections are covered in the relevant chapters.

Prevention and control

General measures for the prevention of gastrointestinal infection (see Chapter 2.2) and blood-borne virus infection (see Chapter 4.9) will help prevent jaundice due to viral hepatitis. Malaria prophylaxis is covered in Chapter 3.45. Vaccines are available for hepatitis A (see Chapter 3.30), hepatitis B (see Chapter 3.31) and yellow fever (see Chapter 3.86).

Response to a case

Determine whether an infectious or non-infectious cause is suspected. If toxins might be involved, it is wise to check if others may have also been exposed. Contact the occupational health department if exposure in the work place is suspected. No specific public health measures are needed for other non-infectious causes. For infectious causes, specific measures will usually be indicated, depending upon the causal agent. Assume blood, body fluids and (until one week after start of jaundice) stools are infectious until the cause is known.

Investigation of a cluster and response to an outbreak

Investigate to determine whether infectious or non-infectious cases. For non-infectious cases, consider a common toxic exposure. For infectious cases, the response will depend upon the causal agent. As there is massive underdiagnosis, and that mild and asymptomatic infections occur, look for other possible undiagnosed cases. Asymptomatic cases can contribute to finding the common source.

2.8 Infection in the immunocompromised

Immunocompromise is a deficiency in a person's immune response that results in an ineffective response to infections. This includes persons with chronic multi-system disorders such as diabetes, haematological malignancies, those receiving therapeutic immunosuppression, and patients with HIV infection, patients with the rarer primary immunodeficiency disorders, as well as solid organ and haemopoietic stem cell transplant recipients.

Immunocompromise is common and has increased over the past decades partly due to improvements in transplantation science and the development of novel immunosuppressive and biological therapies. It may be congenital or acquired (ageing, treatments, and underlying disease), or physiological (during pregnancy). Pregnancy can be characterised by cellular immune dysfunction and there are a number of infections that are more common and/or very severe during pregnancy.

Infection should always be considered in an unwell immunocompromised person (and immunocompromise in unusual or

recurrent infection). Infection can be caused by both common and unusual pathogens and may present in unusual ways and in unusual sites. Particular infections may be associated with specific immune defects (e.g. invasive aspergillosis with neutropenia and intracellular organisms with T-cell defects); knowledge of the immune defect may guide preventative measures, investigation and therapy.

Infections with common organisms usually respond to routine treatment. Immunocompromised patients are often exposed to healthcare facilities, and to courses of antimicrobials, and are at increased risk of infection with antimicrobial resistant organisms.

Treating infection in the immunocompromised is highly specialised and expert advice should be sought. This chapter concentrates upon issues of concern to a health protection specialist whose major role is ensuring systems are in place to minimise the risk of infection in the immunocompromised.

Specific causes of immunocompromise

Groups at increased risk of immunocompromise include:

- Extremes of age,
- Impaired anatomical barriers: burns, catheters, intubation,
- Impaired host defence: genetic or acquired, underlying malignancy, solid organ transplantation, Haemopoietic Stem Cell Transplantation (HSCT), chronic infection, immunosuppressive drugs, and HIV.

Human immunodeficiency syndrome

HIV-positive persons are particularly at risk when they come into contact with other immunocompromised patients in healthcare surroundings. Services should be organised to minimise transmission of likely pathogens, in particular TB, *Pneumocystis*, *Cryptosporidium*, Cytomegalovirus (CMV). Outbreaks of drug-resistant TB associated with healthcare have occurred.

Splenectomy or hyposplenism

Patients are at risk of infection from encapsulated bacteria, particularly *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae*. Asplenic children under 5, especially those with sickle cell anaemia or splenectomised from trauma, have an infection rate of over 10%. Most infections occur within two years following splenectomy; however, the increased risk of dying of serious infection is probably lifelong.

Hyposplenic patients should receive:

- Pneumococcal immunisation (conjugate vaccines) every five years,
- *H. influenzae* type b vaccine (if not already immune),
- Vaccines against invasive meningococcal disease (meningococcal Group B vaccine, meningococcal conjugate ACWY vaccine and meningitis C conjugate vaccine if not previously received as part of childhood immunisation),
- seasonal influenza immunisation,
- prophylactic antibiotics, probably life-long (oral phenoxy-methyl penicillin or an alternative),
- advice on prevention of malaria,
- A Medic Alert bracelet or a splenectomy-warning card to carry.

Cause of infections

A search for infection, including blood and urine cultures and a chest X-ray, will be necessary as soon as an immunocompromised patient develops a fever. Opportunistic organisms that do not cause disease in the immunocompetent must be sought but it should be remembered that immunocompromised patients are most often infected by common pathogens.

Acute febrile illness

In a febrile immunocompromised patient, an infectious cause for the fever is only confirmed microbiologically and clinically in around a third to one-half of patients.

Invasive mycoses

There are several opportunistic fungi capable of causing serious, potentially fatal infection. These organisms include *Candida*, *Aspergillus*, and *Cryptococcus* species, and non-*Candida* yeast species such as *Pneumocystis jirovecii* (formerly known as *Pneumocystis carinii*).

The most important fungal pathogens identified among patients in Europe are *Candida* spp. (60%) and *Aspergillus* spp. They can cause a spectrum of disease including skin infections, respiratory disease, and bloodstream infections such as candidemia which is considered the fourth most common healthcare associated infection. *Candida auris* is a recently identified *Candida* spp. that has been associated with infection and outbreaks in healthcare settings on five continents and is a growing problem particularly in critically unwell patients in high dependency settings.

Most fungal infections arise from the endogenous flora of patients with risk factors following disruption of skin and mucosal barriers. Less commonly, these organisms can be transmitted via healthcare workers' hands or contaminated medical devices.

Outbreaks of fungal infection have been associated with contaminated ventilation systems and building work occurring close to healthcare areas that immunocompromised patients have frequented.

Prevention and control

Immunisation

The following infections can be prevented through immunisation of the immunocompromised patient:

- Pneumococcus
- *H. influenzae* (Hib)
- Seasonal influenza
- Meningococcus (Group A, B, C, W and Y)
- Varicella risk can be reduced by offering vaccination to close non-immune contacts of immunocompromised persons where continuing contact is unavoidable (e.g. sibling of a child with leukaemia).

Live vaccines are contraindicated in many immunocompromised patients. Avoid giving live vaccines (except MMR and BCG) to siblings of immunocompromised patients.

The Oral Polio Vaccine (OPV) is no longer routinely used in the UK. In countries where it is still used for primary and booster immunisation, immunocompromised children should avoid close physical contact with children vaccinated with OPV for four to six weeks following administration (this does not require school withdrawal).

Prophylaxis

The following chemoprophylaxis is available to reduce risk of infection in appropriate cases:

- Pneumocystis (oral trimethoprim/sulphamethoxazole) in HIV/AIDS
- Malaria chemoprophylaxis
- Penicillin in hyposplenism
- Antifungal prophylaxis can be used in high-risk patients (e.g. HSCT).

Managing the environment

- Patients with T-cell deficiency are advised to boil their drinking water. This group includes:
  - HIV-positive patients with a low T-cell count,
  - Children with Severe Combined Immunodeficiency (SCID),
  - Others with specific T-cell deficiencies.
- In healthcare settings, staff should follow standard infection control practices to minimise transmission risk from one patient to the other.
- Avoid healthcare staff who are varicella zoster susceptible working with immunocompromised individuals, or vaccinate non-immune health-care workers.
- Consider using High-Efficiency Particulate Air (HEPA) filters in isolation rooms to protect immunocompromised patients.
- Consider relocating services for high-risk patients away from major building works.

Travel advice

Immunocompromised patients are at increased risk of travel-related infection. Asplenic/hyposplenic patients are at risk of severe malaria and patients with AIDS are at risk from gastrointestinal (GI) parasites. The advice given will be dependent upon the epidemiology of disease in the area to be visited and the cause and severity of immunosuppression.

Surveillance

All units treating significant numbers of immunocompromised patients should have ongoing surveillance of infection and be aware of the risk of outbreaks in the patient population.

Investigation of a cluster

Clusters of infection in the immunocompromised should be investigated with urgency. A cluster suggests a group of vulnerable people exposed to a common source.

Control of an outbreak

Rapid identification and control of any source. If necessary close the ward if environmental contamination is suspected.

Section 3
Diseases

3.1 Amoebic dysentery

Entamoeba histolytica is a cause of intestinal infection, which may include dysentery.

Suggested on-call action

- Exclude cases in high-risk groups for transmission of gastrointestinal infections (Box 2.2.1).
- If other non-travel related cases known to you or the reporting laboratory/clinician, consult the local outbreak plan or Standard Operating Procedure (SOP).

Epidemiology

Although much more common in tropical countries, amoebiasis does occur in Europe. Approximately 50–100 cases a year are reported in the UK, where infection is most common in young adults and unusual in preschool children. Most cases occur in travellers to developing countries, where amoebiasis is endemic in areas with poor sanitation.

Clinical features

Intestinal infection may be asymptomatic (90% of infections); an intermittent diarrhoea with abdominal pain; amoebic colitis presenting as bloody diarrhoea; or a fulminant colitis with significant mortality in the malnourished, pregnant, immunosuppressed or very young. Extra-intestinal disease includes liver, lung, and brain abscesses. About 4–10% of asymptomatic cases later develop invasive disease.

Laboratory confirmation

PCR is the method of choice because of high sensitivity and specificity. *E. histolytica* is morphologically indistinguishable on microscopy from *Entamoeba dispar* (which is the more common in developed countries, but is non-pathogenic) and *Entamoeba moshkovskii* (which may cause diarrhoea, but is non-invasive), and so a positive PCR or antigen test or demonstration of trophozoites containing red blood cells is required for confirmation. Stool microscopy requires three samples on separate days to achieve similar sensitivity to stool PCR. Invasive disease may be diagnosed by serology.

Transmission

E. histolytica is predominantly spread by environmentally resistant cysts excreted in human faeces. Transmission may occur via contaminated water or food or direct faeco-oral contact. Cysts resist standard water chlorination.

Acquisition

The incubation period is usually two to four weeks, but a range of a few days to years has been reported. The infectious period depends upon the excretion of cysts in the stool and may last several years. In acute dysentery, only trophozoites are passed in the stool: these die within minutes in the environment and do not survive gastric acid exposure. Almost all recovered patients appear to be immune to reinfection.

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

Prevention

- Avoidance of faecal contamination of water supplies, combined with adequate water treatment (e.g. filtration).
- Good personal, toilet and food hygiene.
- Care with food and water for travellers in developing countries.
- Sterilisation of reusable colonic or rectal equipment (e.g. colonic irrigation or medical investigation).

Surveillance

- Cases of dysentery should be reported to the local public health department and confirmed *E. histolytica* to local and national surveillance systems.

Response to a case

- Liaise with laboratory to confirm case is *E. histolytica*, rather than *E. dispar*.
- Exclude cases in groups at increased risk of spreading infection (Box 2.2.1) until 48 hours after first normal stool.
- If no history of travel abroad (this may be some months before) or link to known case, then obtain detailed food history for the period two to four weeks before onset, including drinking water.
- Enteric precautions. Hygiene advice to case and household.
- Identify household, co-traveller and sexual contacts of confirmed cases for screening. Consider treatment for those with prolonged excretion of pathogenic cysts, especially if in risk group for spreading infection.

Investigation of a cluster

- Ensure not due to travel abroad: inform relevant national centre if associated with particular country.
- Organise further testing to ensure that reported cases have infection with pathogenic *E. histolytica*.
- For symptomatic cases, obtain detailed food and water consumption history for period two to four weeks before onset of symptoms. Check home/work/travel against water supply areas (water-borne outbreaks have occurred rarely in Europe).
- Look for links with institutions with potential for faeco-oral spread, for example young adults with learning difficulties or camps with poor hygiene facilities.
- Consider sexual transmission.

Control of an outbreak

- Rarely a problem in developed countries. Response will depend upon source identified.
- Enteric precautions for cases and carriers. Exclusion of those in risk groups (Box 2.2.1). Consider treatment if confirmed as *E histolytica*. Ensure that treatment includes an agent that eliminates cysts (e.g. diloxanide).
- Sanitary disposal of faeces, handwashing, food hygiene and regular cleaning of toilet and kitchen areas.

Suggested case-definition for an outbreak
Diarrhoea with demonstration of trophozoites or cysts (speciation preferable) or PCR positive.

3.2 Anthrax

Anthrax is a potentially serious infection caused by *Bacillus anthracis*, an organism that forms spores that may survive for many years. It is a potential agent of bioterrorism.

Suggested on-call action
Ensure case admitted and treated. Identify likely source of exposure and other individuals who may have been exposed. Ensure exposed individuals are clinically assessed.

Epidemiology

Anthrax is a zoonosis, acquired from contact with infected herbivores or their products. It is endemic in the Middle East, Africa and in countries of the former Soviet Union, where it is usually a disease of rural herdsmen. In most of Europe it has been eliminated from livestock and is therefore rare as are imported infections. Between 2011 and 2015 30 cases were reported in Europe (United Kingdom [8], Bulgaria [5], Romania [5], Germany [4], Denmark [2], Greece [2], France [1], Croatia [1], Portugal [1] and Spain [1]). The sporadic cases reported in Europe, usually result from occupational exposure to animal products, carcasses, hides, hair and wool. Fatal cases in 2009/2010 were associated with the injection of contaminated heroin. Other than those drug-related cases, concern is occasionally raised about renovating old buildings where animal hair was used in the construction: these have not been associated with cases.

Clinical features

The clinical features depend upon the route of infection:

Cutaneous anthrax (over 90% of cases): Infection is through the skin. Over a few days a sore which begins as a pimple grows, ulcerates and forms a black scab, around which are purplish vesicles. There may be associated oedema. Systemic symptoms include rigours, headache and vomiting. The sore is usually diagnostic.

Inhalation/Pulmonary Anthrax: spores are inhaled, with subsequent invasion of mediastinal lymph nodes. An abrupt onset of flu-like illness, rigours, dyspnoea and cyanosis, is followed by shock and usually death over the next two to six days.

Intestinal Anthrax: occurs following ingestion of spores, with severe gut disease, nausea, vomiting, anorexia, fever and then septicaemia.

Pulmonary and intestinal diseases are usually recognised late and have poor outcomes.

Laboratory confirmation

Swabs from cutaneous lesions, nasal swabs (if inhalational anthrax suspected), blood cultures, lymph node or spleen aspirates, or cerebrospinal fluid (if meningitic) show characteristic bacilli on staining with polychrome methylene blue. Colonies may be grown overnight. The definitive test for *B. anthracis* is PCR.

Transmission

Transmission is usually from contact with contaminated animal products. Spores can remain viable in the soil for many years. Transmission may be by direct contact, inhalation or ingestion (e.g. of spores in meat). Person to person spread via the inhalational route has not been reported.

Acquisition

The incubation period varies between one and seven days, inhalation anthrax usually occurs within 48 hours, but cutaneous anthrax may rarely take up to seven weeks. Secretions from cutaneous lesions may be infectious. Environmental spores may be infectious for decades.

Prevention

- Pre-treatment of animal products and good occupational health cover are the mainstays of control.
- Animals believed to have died of anthrax should be disposed of under supervision. Mass vaccination of animals may reduce disease spread.
- Non-cellular vaccines for human use are available for individuals at risk from occupational exposure, such as veterinarians working in endemic areas, zoos and so on. Workers handling potentially infectious raw material should be aware of the risks. In the event of a deliberate release, individual risk would be assessed on a case-by-case

basis. Post exposure prophylaxis with antibiotics can be very effective in preventing disease if given early enough.

Surveillance

- Anthrax is a compulsory notifiable disease in all EU countries. Cases should be reported on clinical suspicion as a matter of urgency to the local Public Health authorities and to national authorities.
- A suspected case includes any previously healthy person with:
  - Rapid onset of severe, unexplained febrile illness or febrile death.
  - Rapid onset of severe sepsis not due to a predisposing illness, or respiratory failure with a widened mediastinum.
  - Severe sepsis with Gram-positive rods or *Bacillus* species identified in the blood or cerebrospinal fluid and assessed not to be a contaminant.

Response to a case

- Set up incident team.
- Remove potentially contaminated clothes to reduce possibility of secondary cutaneous cases. Instruct exposed persons to shower thoroughly. Use standard universal precautions for care.
- Investigate source: search for history of potentially infected animals or animal products and trace to place of origin. Liaise with veterinary officers. Particularly enquire as to travel and occupational exposure – include exposure to mail.
- Consider bioterrorism if:
  - single confirmed case of inhalational anthrax;
  - single confirmed case of cutaneous anthrax in individual with no contact with animals or animal hides;
  - two or more suspected cases linked in time and place.
- Initial therapy of inhalational anthrax should be with Ciprofloxacin 400 mg iv every 12 hours or Doxycycline 100 mg every 12 hours plus additional antibiotics (rifampicin, vancomycin, chloramphenicol, penicillin, amoxicillin, imipenem, clindamycin, clarithromycin). Benzylpenicillin or amoxicillin should not be used alone.
- Other possible contacts of the source should be identified and placed under clinical surveillance for seven days since last exposure.
- Contacts of cases are not at risk.

Investigation of a cluster

Check for history of exposure in endemic countries. If none:

- undertake full hypothesis-generating study, using semi-structured interviews of all cases and re-interviewing as potential sources identified by other cases. Include full occupational history;
- institute case-finding, both locally and nationally;
- consider bioterrorism.

Control of an outbreak

- Trace exposure as a matter of urgency.
- Remove source.

Response to a deliberate release

- Report to local and national public health authorities.
- Define exposed zone and identify individuals exposed within it (some may have left scene).
- Cordon off exposed zone.
- Decontaminate those exposed: remove clothing and possessions, and then shower with soap and water.
- Chemoprophylaxis (currently ciprofloxacin) as soon as possible for those exposed.
- Record contact details for all those exposed.
- Some health and emergency workers may also need prophylaxis.
- Police may take environmental samples.

More general information in Chapter 4.17.

Suggested case-definition for an outbreak of inhalational anthrax

Suspected

- Rapid onset of severe, unexplained febrile illness or febrile death.
- Rapid onset of severe sepsis not due to a predisposing illness, or respiratory failure with a widened mediastinum.
- Severe sepsis with Gram-positive rods or *Bacillus* species identified in the blood or cerebrospinal fluid and assessed not to be a contaminant.

Confirmed case

A case that clinically fits the criteria for suspected anthrax, and in addition, definitive positive results are obtained on one or more pathological specimens by the reference laboratory.

3.3 Bacillus cereus

Bacillus cereus is a rare cause of food poisoning that manifests as one of two mild gastrointestinal syndromes. It is not spread from person to person.

Suggested on-call action

- If you or the reporting clinician/microbiologist knows of associated cases, consult the local outbreak control plan or SOP.

Epidemiology

Bacillus cereus food poisoning occurs worldwide, accounting for around 0.2% of sporadic gastroenteritis cases presenting to general practitioners in the UK. A much higher incidence has been reported from Finland, Hungary, Netherlands, France and Norway. Reported outbreaks are usually linked to institutions, including restaurants, schools and hospitals.

Clinical features

Two clinical syndromes may occur, caused by different toxins:

i A short incubation illness consisting of vomiting accompanied by nausea, abdominal pain and, occasionally, diarrhoea later. This is usually a mild illness, which lasts less than 24 hours and is difficult to distinguish clinically from staphylococcal food poisoning.

ii A short-medium incubation illness consisting of diarrhoea usually accompanied by abdominal pain and perhaps tenesmus, nausea or vomiting. Diarrhoea may be profuse and watery and lasts around 24 hours. It is difficult to distinguish clinically from *Clostridium perfringens* food poisoning.

Bacillus cereus may also cause serious local and systemic infections – bacteraemia is often associated with intravascular catheters.

Laboratory confirmation

Bacillus cereus may be cultured from stool or vomit samples (may need to be specifically requested), but is also found in a small number of healthy controls. It may be cultured from suspect foods: however large numbers (e.g. $>10^4$/g) are necessary to prove that food was the source of infection. Serotyping is available to compare strains from different cases or with food isolates: however, more than one strain can be associated with an individual outbreak. Phage-typing may also be available. Reference laboratories can test the potential of the isolate for toxin production.

Bacillus subtilis, *Bacillus licheniformis* and *Bacillus thuringiensis* may also occasionally be identified as causes of gastrointestinal infection associated with poor temperature control.

Transmission

Bacillus cereus is widespread in the environment and is found at low levels in many

foodstuffs. Contamination of food may easily occur prior to cooking and spores can survive normal cooking (optimum temperature for spore activation is 65–75 °C) and they are resistant to drying. Cell growth usually occurs between 7 and 50 °C (optimum 28–35 °C) and so storage of food at ambient temperature after cooking allows multiplication of the organism. *B cereus* can produce two types of toxin, a heat stable emetic toxin associated with the short incubation vomiting illness, and a heat labile enterotoxin associated with the longer incubation diarrhoeal illness. Both toxins occur preformed in food, but the latter may also be produced in the gut after digestion.

Emetic outbreaks are often associated with starchy foods, such as rice and pasta, including fried rice dishes, where boiled rice is stored at room temperature and later flash fried which fails to destroy preformed heat-stable emetic toxin. Attack rates of near 100% have been reported from such outbreaks.

The diarrhoeal syndrome is often associated with proteinaceous foods, such as meat, milk or vegetable dishes. Attack rates of 50–75% are reported for these outbreaks.

Bacteraemia and local infections can be contracted though inadequately sterilised medical or injecting equipment.

Acquisition

The incubation period is 0.5–6 hours for the vomiting illness and 6–24 hours for the diarrhoeal syndrome. *B. cereus* is not considered communicable from person to person. People at increased risk of severe infection include those with sickle-cell disease, patients with intravascular catheters, intravenous drug users and those with immunosuppressive or debilitating medical conditions.

Prevention

- Store cooked foods at above 60 °C or below 7 °C before re-heating or consumption.
- Limit storage time and reheat thoroughly.

Surveillance

- Infection by *B. cereus* should be reported to local public health departments and to national surveillance systems.
- Ensure laboratories test for *B. cereus* when an increase in cases of vomiting or diarrhoea with abdominal pain is noted.

Response to a case

- Collect data on food consumption in 24 hours before onset of symptoms. Ask particularly about meals out of the house.
- Although secondary spread of *B. cereus* does not occur, it is prudent to exclude risk groups with diarrhoea or vomiting. Microbiological clearance is not necessary before return.
- No need to screen contacts.

Response to a cluster

- Discuss further investigation, for example serotyping and toxin production, with microbiologist.
- Undertake hypothesis generating study covering food histories particularly restaurants, social functions and other mass-catering arrangements.

Control of an outbreak

- Identify and rectify faults with temperature control in food preparation processes.

Suggested case definition for an outbreak

Clinical: Either:
1 Vomiting occurring 1–6 hours, *Or*
2 Diarrhoea occurring 6–24 hours
after exposure to potential source
Confirmed: As above plus *B. cereus* of correct serotype cultured from stool or vomit.

3.4 Botulism

Botulism is caused by a neurotoxin produced by *Clostridium botulinum*. In Europe it is a rare cause of food-borne infection with a potentially high mortality. One suspected case warrants immediate investigation. It is also a potential bioterrorism agent and a cause of severe illness in intravenous drug users.

Suggested on call action

A suspected case of botulism should be viewed as an emergency for investigation:

- Ensure case admitted to hospital.
- Obtain food history as a matter of urgency.
- Obtain suspect foods.
- Identify others at risk.
- Inform appropriate local and national authorities.

More details in 'Response to a Case' section.

If deliberate release suspected:

- See 'Response to Deliberate Release' section at the end of this chapter.

Epidemiology

Between 85 and 137 cases of botulism were reported in the EU each year from 2010 to 2015, giving a reported incidence of 0.02 cases per 100 000 population, with the highest number of cases reported in Italy and Romania, The age-sex and ethnic distribution of cases will usually reflect the consumption patterns of the implicated foods (or drugs). There is no obvious seasonality.

In recent years, cases of wound botulism have been reported in intravenous drug users in Europe: this is now the most common type of botulism in some European countries, such as the UK and Ireland.

Infant botulism is very rare in Europe. It affects children under two years of age, with most being under six months old.

Clinical features

Botulism is characterised by symmetrical, descending flaccid paralysis of motor and autonomic nerves. This initially affects cranial nerves and may present with a dry mouth, difficulty in swallowing, double vision, slurred speech and blurred vision. Weakness in the neck and arms follows, after which the respiratory muscles and muscles of the lower body are affected. Respiratory dysfunction may be severe enough to require ventilation. Autonomic symptoms may include dry mouth and gastrointestinal, cardiovascular and urinary dysfunction. There is usually no fever or sensory loss. Mortality of up to 10% is reported. Other syndromes have been confused with botulism (Table 3.4.1): deep tendon reflexes (may be present initially but diminish or disappear in ensuing days in botulism), brain scan, CSF examination, nerve conduction tests and tensilon test for myasthenia gravis may help eliminate these other diseases.

Food-borne botulism may present with gastrointestinal symptoms, such as nausea, vomiting, constipation, diarrhoea and abdominal cramps, or neurological symptoms.

Wound botulism cases may present with local inflammation at an injection site, followed by hypotension and circulatory collapse, as seen during the outbreak in the UK and Ireland in 2000. There was usually a very high white blood cell count, cases usually had a temperature of less than 40 °C (there may be a local wound co-infection) and they often looked and felt quite well before deteriorating dramatically over a period of a few hours.

Infant botulism may present as constipation, lethargy, feeding difficulties, hypotonia, increased drooling and a weak cry.

Laboratory confirmation

Urgent confirmation of the diagnosis is important. Laboratory confirmation is usually by detection of toxin in faeces, serum, stomach contents or wound swab, or by

Table 3.4.1 Differential diagnosis of botulism

Disease	Distinguishing features
Guillain–Barré and Miller–Fisher syndromes	Anteceding febrile illness, parasthesia, paralysis may be ascending, early loss of reflexes, increased CSF protein, EMG findings.
Myasthenia gravis	Recurrent paralysis, sustained response to anticholinesterases, EMG findings.
Stroke	Usually asymmetric paralysis, abnormal brain scan.
Intoxication (carbon monoxide, organophosphates, mushrooms)	Drug detected in body fluid.
Tick paralysis	Parathesias, ascending paralysis, tick bite (or tick in-situ).
Poliomyelitis	Anteceding febrile illness, asymmetric paralysis, CSF changes.
Viral syndrome	No bulbar palsies or flaccid paralysis.
Psychiatric illness	EMG findings.
Paralytic shellfish poisoning	Food history (onset <1 h), paresthesia.

detection of the organism in faeces, stomach contents or wound swab (rapid PCR testing is available). Sensitivity of tests decreases with time since onset (particularly for toxin). Suspect food samples may also be tested (10 g usually required). The aid of the reference laboratory should be enlisted and suspect foods (or drugs) and clinical specimens sent immediately by courier. As *C. botulinum* is present in the environment, any isolate in food should be shown to be of the same 'cultural group' or produce the same toxin type as the cases (there are eight toxin types, designated by letters A–H). Toxin types A, B, E, F and H are associated with human disease, with type B being the most common in Europe. Rarely other *Clostridium* species (e.g. *C. butyricum*, *C. noyvi* or *C. baratii*) may also cause botulism. It may take up to five days for negative results to be available, although this does not exclude the diagnosis.

For wound botulism, pus (or wound swab) and tissue biopsy (from surgical debridement) should also be sent for anaerobic culture.

Transmission

Clostridium botulinum spores are ubiquitous in the environment and can be found in dust, soil, untreated water and the digestive tracts of animals and fish. Toxin type E is particularly associated with fish products. There are three naturally occurring forms of botulism: food-borne botulism, wound botulism and infant botulism.

Food-borne illness results from the ingestion of preformed toxin. Although boiling inactivates the toxin, spores may resist 100 °C for many hours. These may multiply (producing toxin) when conditions are favourable, that is anaerobic, above pH 4.6 and at room temperature (usually 10–50 °C, but in some cases as low as 3 °C). Underprocessed foods or foods contaminated after processing that are then held at room temperature in anaerobic, non-acidic conditions are at particular risk. The contaminated food may be consumed directly or used as an ingredient for another product.

Food vehicles reported in outbreaks include meat products such as sausage and cured ham; canned, vacuum-packed, smoked or fermented fish products; vegetable products preserved by canning or storing in oil; and baked potatoes, honey and cheese. Many outbreaks are associated with home preserved foods.

Intestinal or infant botulism usually results from the ingestion of *C. botulinum* spores, which then germinate in the gut, producing toxin. The source of the organism may be food-borne, for example from contaminated honey or herbal infusions; soil and pets have been reported as rare causes.

Wound botulism usually results from the inoculation of *C. botulinum* spores (most

commonly from injecting drug misuse), which then germinate in the anaerobic conditions of the wound, producing toxin that can cause systemic symptoms. Inhalation of toxin may also cause disease, but this is extremely rare under natural conditions. Iatrogenic botulism from therapeutic or cosmetic overdose can also occur.

Acquisition

The incubation period ranges from a few hours to at least eight days and there are reports of potentially longer incubations. Most cases occur between 12 hours and three days after exposure. Gastrointestinal symptoms may precede neurological signs by a few hours and shorter incubations may be associated with higher doses and more severe disease. The incubation for wound botulism may be longer (4–21 days following trauma) and for inhalational botulism may be shorter (a few hours up to four days).

Although demonstrable in the faeces of cases, botulism is not communicable from person to person. The dose of toxin needed to cause symptoms is very low, with illness resulting from nanogram quantities of ingested toxin. Type F toxin is about 60 times more toxic than type B (order: F > C > A > D > B). Estimated lethal doses of type A toxin are 0.1 µg given intravenously or intramuscularly, 0.8 µg inhaled and 70 µg ingested. Therapeutic botulinum toxin preparations contain only about 2% of the lethal intravenous dose. There appears to be no acquisition of immunity to botulinum toxin, even after severe disease. Repeated illness is well recognised.

Prevention

- Care with commercial or home canning processes and with home preservation of fish, to ensure spores destroyed before storage.
- Avoid consumption from food containers that appear to bulge (possible gas from anaerobic organisms) or containers that are damaged. Avoid tasting potentially spoilt food.
- Refrigeration of incompletely processed foods. Boiling for 10 minutes before consumption would inactivate toxin in home-canned foods.
- High index of clinical suspicion and urgent investigation and response to cases.
- Prevention work with intravenous drug users.

Surveillance

- Botulism is statutorily notifiable in almost all EU countries.
- Clinicians should report suspect cases to local public health authorities for urgent investigation.
- Laboratories should report positive toxin or culture results from patients to the relevant local and national centres as a matter of urgency.

Response to a case

- Clinicians or laboratories should report suspected cases immediately to the relevant public health officer for urgent investigation.
- Take urgent food history from case or, if not possible, from another reliable informant (e.g. spouse). Take details of all foods consumed in the week before illness. Ask specifically about any canned foods or preserved foods. A standard questionnaire may be available from national centres.
- Inform others who ate the suspect foods with the case to seek medical help if symptoms develop.
- Obtain any leftovers of any foods eaten in the last week, including remains from uncollected domestic waste and unopened containers from the same batch. This prevents further consumption and allows storage under refrigeration by the laboratory in case later testing appropriate.
- Organise testing of foods at highest suspicion (e.g. canned food eaten 12–72 hours before onset) with reference laboratory.

- Inform appropriate national public health authority and, if commercial food product suspected, the national food safety agency.
- Case-finding: any other suspected cases in local hospitals or laboratories or known to national centre? If so, compare food histories.
- Ensure case admitted to hospital for investigation and treatment.
- Antibiotics are not effective against preformed toxin, such as occurs in food-borne disease. Botulinum antitoxin is available and reduces duration of illness and fatality rate. Antitoxin can have serious side-effects, although these may be lower with modern preparations and doses. It can be given without waiting for microbiological confirmation if a strong clinical diagnosis has been made. Appropriate antibiotics (e.g. penicillin and metronidazole) and surgical debridement are also indicated for wound botulism.
- Person-to-person spread unlikely, but universal precautions sensible for carers, laboratory staff and post-mortems.
- No exclusions required for cases or contacts if well enough to work.
- If no obvious food source, consider intravenous drug use via contaminated illegal drugs; intestinal botulism, especially if child under two years of age; mis-injection of pharmaceutical preparation or a deliberate bioterrorism incident.

Investigation of a cluster

- Treat individual cases as indicative of a significant public health risk and investigate as above.
- Instigate case-finding with local clinicians and laboratories, and national centre.
- Compare food histories: specifically ask *each* case about *each* food reported by any of the other cases.
- Organise laboratory testing of *any* food reported by more than one case.
- Check preparation details of any food reported by more than one case to see if anaerobic conditions could have been created for any component and/or it was stored at room temperature after cooking.
- Remember, as well as canned, bottled or preserved produce, unexpected food vehicles have been reported from recent incidents, including sautéed onions (kept under butter), hazelnut yogurt (canned puree used in preparation), baked potatoes (kept in foil) and honey.
- Consider possibility that cases may be intravenous drug users exposed to contaminated illegal drugs (cases may not just be young males or homeless people).
- Consider possibility of bioterrorism: this could be via air-borne release or contamination of foodstuffs. Consider if cases have similar geographic exposure but no common food exposure; multiple simultaneous outbreaks with no obvious common source; unusual toxin type (C, D, F or G, or E without exposure to aquatic food); or similar cases in animals (liaise with veterinary agencies).

Control of outbreak

- Identify and remove any implicated food.
- If commercially produced food, organise recall of product.
- If food vehicle identified, organise medical assessment of others who have consumed it.
- If linked to intravenous drug use, liaise with local community drug workers to get public health messages on safer drug use out to users and to promote early diagnosis and treatment of cases.

Response to deliberate release

- Activate local and national plans and procedures.
- Decontaminate exposed people, clothing and fomites if air-borne release.
- Identify and monitor exposed individuals, including those who may have left the scene.
- No prophylaxis indicated for those exposed if remain asymptomatic.

- Ensure access to antitoxin and supportive therapy for those who develop symptoms.
- Full biological protective equipment for those entering 'exposed zone'.
- Contaminated area to be made out-of-bounds for few days after release (toxin loses activity during this period).
- Household bleach solution or 0.5% solution of hypochlorite (5000 ppm) are adequate decontamination.
- More general information given in Chapter 4.17 and more specific information available on PHE website

Suggested case definition for an outbreak

Confirmed: Clinically compatible case with demonstration of botulinum toxin in blood, faeces, vomit or gastric aspirate.

Clinical: Acute bilateral cranial neuropathy with symmetrical descending weakness, but no sensory loss in a responsive and afebrile patient. *(nb – drop afebrile from case definition if wound infection).*

Provisional: Any three from dysphagia, dry mouth, diplopia, dysarthria, limb weakness, blurred vision or dyspnoea, in an alert, non-febrile patient with no sensory deficit. Review when clinical investigations complete.

3.5 Brucellosis

Brucellosis is a zoonosis caused by a Gram-negative coccobacillus of the genus *Brucella*. A wide variety of mammals are susceptible to *Brucella* species. *Brucella abortus* (cattle, camels), *Brucella melitensis* (goats, sheep, camels) and *Brucella suis* (pigs) are the usual causes of brucellosis (undulant fever, Malta fever, Mediterranean fever) in humans. Other *Brucella* species such as *Brucella canis* (dogs) and those associated with marine mammals are rare causes of human disease.

Suggested on-call action

Not usually required, but if you or the reporting clinician/microbiologist knows of associated cases, consult the local outbreak control plan or SOP.

Epidemiology

Human brucellosis has a worldwide distribution, with the highest reported incidence in the Middle East and Central Asia. In 2015, 439 cases were reported in Europe; the highest rates were reported from Greece (1 per 100 000 population), Bulgaria, and Portugal. Males aged 25–64 years have the highest rates suggesting an occupational risk factor. In much of northern Europe, brucellosis in domestic animals has been eradicated and most cases are now acquired abroad or via products from abroad (e.g. dairy products). In countries where *Brucella* is still endemic, farmers, veterinarians, abattoir workers and consumers of unpasteurised milk products are at risk. Outbreaks of human infection were reported from Mexico (unpasteurised cheese), Russia, and Kyrgyzstan (infected livestock).

Clinical features

Symptoms are generally non-specific. In acute brucellosis there is a systemic febrile illness with hepatosplenomegaly which may be complicated by bone and joint manifestations (in all joints but mostly sacroiliitis and spondylitis), orchitis, epididymitis, neurological involvement and endocarditis. Also 'acute' infections tend to develop slowly, with moderate temperature increase. Most cases will recover but some develop chronic or relapsing disease (also after adequate antibiotic treatment) characterised by malaise, depression, and localised infection. In non-endemic countries, diagnostic delay may be prolonged and can lead to more serious symptoms and chronicity.

Laboratory confirmation

Serological methods are used, including specific IgG/IgM enzyme immunoassays. Interpretation of results is often difficult and should be informed by clinical and local prevalence data. Definitive diagnosis is by culture of *Brucella* from blood, bone marrow or pus but yield is often poor. Extended culture may be necessary although rapid culture technologies may be helpful. In some countries laboratories have developed a PCR to identify and classify strains that are difficult to type. PCR can also be used directly on clinical material (blood, bone marrow).

Transmission

Transmission is by contact with infected animals or tissues (blood, urine, aborted foetus, placenta) as a result of inoculation, mucous membrane exposure, aerosol inhalation or consumption of unpasteurised dairy products. Infection can follow accidental self-inoculation by veterinarians with animal vaccine strains. Laboratory-acquired infections causing outbreaks in (mostly clinical diagnostic) laboratories have been described.

Brucella is a potential bioterrorism agent because it survives well in the environment and is highly infectious in aerosol form or as a contaminant of food, milk and water or by direct inoculation.

Acquisition

The incubation period is 5–60 days and depends on the species, route of transmission and infective dose which may be as low 10–100 organisms. Person-to-person transmission is rare. The duration of acquired immunity is uncertain.

Prevention

- The prevention of human disease depends on the control of brucellosis in food animals by vaccination, testing and slaughter of infected animals and pasteurisation of dairy products. Pastures and animal accommodation on farms may remain contaminated for prolonged periods.
- *Brucella* infection is a significant biohazard for laboratory workers and guidelines should be followed.
- Others at occupational risk (veterinarians, abattoir workers and farmers) should take suitable precautions. This includes people who handle marine mammals.
- Visitors to endemic countries should avoid unpasteurised dairy products.

Surveillance

- Brucellosis is a notifiable disease in many countries. In the UK, it is statutorily notifiable if occupationally acquired.
- Cases should be reported to public health authorities.
- Due to its non-specific symptoms, cases are often underdiagnosed and thus underreported.

Response to a case

- Cases should be investigated to determine the source of infection, including travel and food history.
- If the case has not been abroad, possible animal exposure should be sought in collaboration with veterinary authorities. Suspect animals may be tested.
- Contacts who may have been exposed to the source of infection should be offered investigation.
- Following laboratory exposure, all workers at risk should be monitored for symptoms and offered repeated serological testing over a six-month period. Post-exposure prophylaxis may be offered with an appropriate antibiotic.
- Following the accidental inoculation of an animal vaccine to a human, antibiotic chemoprophylaxis is recommended.

Investigation of a cluster

- As most cases in northern Europe are imported, a cluster usually results from a common exposure at a single point source.
- An investigation to identify the source of infection, usually milk or cheese from an infected herd, should be initiated.
- Implicated products should be recalled, production should cease and pasteurisation should be enforced.

Control of an outbreak

Control requires the identification and eradication of infected livestock, pasteurisation of dairy products, and control of domestic animals and animal products moving between countries.

Suggested case-definition for an outbreak

Clinical: an acute illness characterised by fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia.

Confirmed: clinical case with isolation of *Brucella* spp. from a clinical specimen, or demonstration by immunofluorescence of *Brucella* spp. in a clinical specimen, or fourfold or greater rise in *Brucella* agglutination titre between acute and convalescent serum specimens obtained at least two weeks apart.

3.6 Campylobacter

Campylobacter species cause diarrhoeal and systemic illnesses in humans and animals, and are the most common bacterial cause of infectious intestinal disease in developed countries. Although food-borne outbreaks are rarely identified, occasional outbreaks due to contaminated food or water may occur.

Suggested on-call action

- If you or the reporting clinician/microbiologist are aware of potentially linked cases, consult your local outbreak control plan or SOP.

Epidemiology

About 230 000 cases of *Campylobacter* infection are reported annually in EU/EEA countries, with half of those occurring in Germany and the UK, and the highest rate in the Czech Republic. True community incidence is much higher at an estimated 870 per 100 000 population in the UK. Deaths are rare. Infections occur at all ages, but are highest in children under five. Reported cases are higher in men and in some ethnic groups (e.g. south Asians in the UK).

Campylobacter infections occur all year round, but with the highest incidence of domestic cases from June to September; this peak is slightly earlier than that seen for *Salmonella* (Figure 2.2.1). Outbreaks occur, but are rarely identified.

Certain groups are at increased risk of *Campylobacter* infection due to increased exposure, including those with occupational contact with farm animals or meat, travellers abroad, gay men (including infection with other *Campylobacter* species) and family contacts of cases. *Campylobacter* infection is the most commonly identified cause of travellers' diarrhoea in Scandinavia and the second most common (after Enteropathogenic *Escherichia coli*) in the UK. *Campylobacter* infection is hyper-endemic in developing countries.

Clinical features

Campylobacter infection may vary from asymptomatic (estimated 25–50% of cases) to a severe disease mimicking ulcerative colitis or acute appendicitis. Most diagnosed cases present as acute enteritis, with symptoms of diarrhoea, abdominal pain and fever. There

may be a prodromal period of fever, headache, myalgia and malaise for approximately 12–24 hours before the onset of intestinal symptoms. Diarrhoea varies from loose stools to massive watery stools. About a quarter of cases have blood in the stool (usually appearing on the second or third day) and a similar number have vomiting. Abdominal pain may be prominent, is often described as constant or cramping rather than colicky, and may be relieved by defaecation.

Most cases settle after two to three days of diarrhoea and 80–90% within one week. However, some cases may be prolonged or severe. Complications include reactive arthritis (1–5% of cases), Guillain–Barré syndrome (0.1% of cases) and haemolytic uraemic syndrome.

Although difficult to distinguish from other causes of intestinal infection in individual cases, *Campylobacter* might be suspected as the cause of an outbreak due to the combination of abdominal pain and fever, and/or the presence of bloody diarrhoea or faecal leukocytes. However, Shiga-toxin producing *E. coli* may cause a similar picture.

Campylobacter jejuni is responsible for most campylobacteriosis and *Campylobacter coli*, which may be less severe, for most of the rest. Other species such as *Campylobacter fetus* and *Campylobacter lari* are uncommon causes of diarrhoea in immunocompetent individuals, but can cause severe systemic illness in debilitated or immunosuppressed patients.

Laboratory confirmation

The mainstay of diagnosis is culture of the organism from faecal samples. Sensitivity is increased if samples are delivered to the laboratory on the day of collection: if this is not possible, samples should be either refrigerated or stored in a suitable transport medium. Culture of *Campylobacter* requires different conditions than for other enteric pathogens. Provisional results may be available after overnight incubation. PCR or mass spectrometry ('MALDI-TOF') can be used to identify the species. Genotyping (by whole genome sequencing [WGS], pulsed-field gel electrophoresis [PFGE] or multilocus sequence typing [MLST]) may be available from reference laboratories if required for epidemiological purposes, however, more than one subtype can occur in outbreaks. Serological tests are in development.

Microscopic examination of fresh diarrhoeal stool specimens may permit a rapid presumptive diagnosis, although sensitivity is only 60% compared to culture. *Campylobacter* is sometimes isolated from blood cultures in acute illness. Resistance to antibiotics, especially fluoroquinolones, is high in southern Europe as well as from many holiday destinations outside Europe. *Campylobacter* may be isolated from food or environmental specimens after enrichment culture.

Transmission

Campylobacteriosis is a zoonosis. It is found worldwide in the gastrointestinal tract of many animals, including poultry, cattle, pigs, birds, wild mammals and domestic pets. Humans are not an important reservoir. Transmission from animals to man occurs predominantly via ingestion of faecally contaminated food or water. Campylobacters are sensitive to drying, acid, high salt concentrations, chlorine and temperatures over 48 °C.

The main routes of infection are as follows.

Poultry and other foods

In the majority of sporadic cases in developed countries, *Campylobacter* probably entered the kitchen on contaminated meat. Chicken carcasses are the most commonly contaminated, but pork, lamb and beef (including meat products such as sausages) may also be affected. Contamination of these meats is usually with *C. jejuni*, with the exception of pork for which almost all are *C. coli*. The contamination can lead to illness in one of three ways: contamination of hands leading to accidental ingestion; inadequate cooking, especially of chicken and a particular risk for

barbecues (numerous outbreaks in the UK have been linked to chicken liver pate); and cross-contamination of foods that will not be cooked, either via hands or via utensils such as knives and chopping boards. Fortunately *Campylobacter* does not multiply on food, which reduces the risk of large food-borne outbreaks. Normal cooking kills *Campylobacter*, and viable organisms are reduced 10-fold by freezing, although freezing cannot be assumed to have made contaminated poultry safe. Other food vehicles that have been reported include shellfish contaminated by sewage and mushrooms contaminated by soil. Consumption of contaminated food and water is the likely cause of most cases of travel associated campylobacteriosis.

Water-borne

Campylobacter excretion by wild birds causes contamination of open waters, and the organisms can survive for several months in water below 15 °C. Large outbreaks have occurred from the use of untreated surface water in community water supplies. There may also be failures in 'treated' water supplies. Smaller outbreaks have occurred from the storage of water in open-topped tanks. Deliberate or accidental ingestion of raw water can cause infection in those undertaking outdoor activities, for xample trekkers and canoeists.

Milk-borne

Campylobacters are commonly found in bulked raw milk samples. Infected animals may contaminate milk with faeces or excrete the organism via infected udders. *Campylobacter* can survive in refrigerated milk for three weeks and, when ingested, milk protects the organisms from the effect of gastric acid. Properly conducted pasteurisation destroys the organism. Consumption of raw or inadequately pasteurised milk has caused large outbreaks of campylobacteriosis, and contributes to endemic infection. Contamination of milk after pasteurisation may also occur: in the UK, home delivery of milk in foil-topped bottles left on the doorstep may be contaminated by pecking by wild birds.

Direct transmission from animals

Approximately 5% of cases in the UK and the USA are thought to occur through contact with infected pets. The most likely source is a puppy with diarrhoea or, less often, a sick kitten and the most likely victim a young child. Transmission from asymptomatic pets has also been reported. Children may also be exposed to excreting animals on farm visits. Occupational exposure to excreting animals or contaminated carcasses is also well recognised.

Person-to-person spread

Although the transmissibility of *Campylobacter* is low, person-to-person spread does occur. The index case is usually a small child who is not toilet trained. The victim may be the person responsible for dealing with soiled nappies. Vertical transmission has also been documented as has spread by blood transfusion. Secondary spread has not been documented from asymptomatic food handlers or hospital staff.

Acquisition

The incubation period is usually between one and seven days (median three) and inversely related to the dose ingested. Incubation periods up to 10 days are reported. The infectious period lasts throughout the period of infection, although once the acute symptoms have passed, the risk of transmission is very low if adequate hygiene is practised. The average duration of excretion is two to three weeks, with some cases excreting for two months and occasional cases for three months. Antibiotic treatment (e.g. with erythromycin) usually terminates excretion but it is rarely necessary to attempt to do this. The infective dose is usually 10^4 organisms or above, but food vehicles

which protect the organism against gastric acid (e.g. fatty foods, milk, water) can result in an infectious dose of as little as 500 organisms. Immunity develops in response to infection, with antibodies that protect against symptomatic infection against similar strains. Patients with immune deficiencies or chronic illnesses may develop severe disease and those with HIV infection may suffer repeated illness with the same strain

Prevention

- Chlorination of drinking water supplies and prevention of contamination.
- Pasteurisation of milk for retail sale.
- Reducing infection in poultry and animal farms.
- If unable to prevent contaminated meat leaving the slaughterhouse, gamma-irradiation of carcasses is effective, although not popular with the public.
- Adequate hygiene in commercial and domestic kitchens, particularly the avoidance of cross-contamination.
- Adequate cooking of meat, especially poultry.
- Protecting doorstep milk against birds.
- Handwashing after contact with faeces, nappies, meat or animals, including on farm visits.
- Conventional disinfectants are active against *Campylobacter*.
- Advice to travellers abroad and to immunocompromised patients to reduce exposure.

Surveillance

- Campylobacter infection is statutorily notifiable in almost all EU countries.
- Laboratory isolates of Campylobacter species should be reported to local public health departments and the national surveillance system.

Response to a case

- Enteric precautions for case (see Chapter 1.3).
- Report to public health authorities (by clinician and laboratory).
- Exclude from work/nursery if in risk group (see Box 2.2.1) until 48 hours after first normal stool. No microbiological clearance necessary.
- Antibiotic treatment unnecessary unless severe or prolonged illness.
- Obtain history of food consumption (particularly chicken, unpasteurised milk or untreated water), travel and contact with animals.
- Investigate illness in family or other contacts.

Investigation of a cluster

- Discuss further microbiological investigations of epidemiological relevance with reference laboratory, for example typing of isolates to see if similar. Ensure that local laboratories retain isolates for further investigation.
- Obtain details from cases on:
  - Source of water supply (failure of treatment?);
  - Source of milk supply (failure of pasteurisation?);
  - Functions attended (food-borne outbreak?);
  - Foods consumed, particularly consumption of undercooked chicken or, if *C. coli*, pork;
  - Bird pecked milk;
  - Farm visits (age-distribution of cases may support this);
  - Occupation/school/nursery;
  - Travel.

Control of an outbreak

- Exclude symptomatic cases if in risk groups and ensure enteric precautions followed.
- Re-enforce food hygiene and handwashing.
- Check for ways in which food or water could have become contaminated. Also check for animal contact.
- Prevent use of unpasteurised milk, untreated water or undercooked poultry.

Suggested case definition for outbreak

Clinical: Diarrhoea or any two symptoms from abdominal pain, fever, nausea/vomiting, with onset one to seven days after exposure in person with link to confirmed case.

Microbiological: Isolate of outbreak strain from faeces or blood. As carriage of any type of *C. jejuni* in asymptomatic controls in the UK is only about 1%, but 25–50% of cases of *Campylobacter* infection are asymptomatic, clinical component of case-definition could be waived if appropriate typing results are available.

3.7 Chickenpox and shingles (varicella–zoster infections)

Chickenpox is a member of the group of common childhood exanthems that include measles and rubella. It is a systemic viral infection with a characteristic rash caused by varicella–zoster virus (VZV), a herpes virus. Its public health importance lies in the risk of complications in immunosuppressed and pregnant patients, and the potential for prevention by vaccination. Herpes zoster (shingles) is caused by reactivation of latent VZV whose genomes persist in sensory root ganglia of the brain stem and spinal cord.

Suggested on-call action

Assess clinical status of close contacts and arrange for exclusion/Varicella-zoster immunoglobulin (VZIG) if appropriate

Epidemiology

Chickenpox occurs mainly in children. There are epidemics every one to two years, usually in winter and early spring. More than 90% of adults in the industrialised Western world have natural immunity. In the (sub)tropics seroprevalence at age 12 years is 50%. Herpes zoster occurs mainly in middle or older age. Mortality is low (in Europe around 0.1 per million), although it increases with age.

Clinical features

There is sometimes a prodromal illness of fever headache and myalgia. The diagnostic feature is the vesicular rash, which usually appears first on the trunk. They start as small papules, develop into clear vesicles which become pustules and then dry to crusts. There are successive crops of vesicles over several days. The hands and feet are relatively spared

A more fulminant illness including pneumonia, hepatitis or disseminated intravascular coagulation may affect the immunocompromised, neonates and occasionally healthy adults, particularly smokers. Congenital varicella syndrome, with skin and eye defects, hypoplastic limbs and central nervous system (CNS) defects in the neonate, occurs following infections in the first five months of pregnancy, although most risk (2%) appears to be in weeks 13–20 and is zero after 24 weeks. Of VZV infections in pregnancy, 5% end in premature delivery. Herpes zoster begins with pain in the dermatome supplied by the affected sensory root ganglion. The trunk is a common site. The rash appears in the affected area and is vesicular and rapidly coalesces. It is very painful and persists for several days and even weeks in elderly people.

Laboratory confirmation

This is rarely required as the clinical features are so specific. If necessary, VZV is readily demonstrable by PCR or culture from vesicular fluid in both chickenpox and shingles; serology (VZV-IgG) is also available and can be used to demonstrate immunity.

Transmission

Man is the only reservoir. Carriage does not occur. Chickenpox is highly infectious; up to 96% of susceptible people exposed develop the disease. Herpes zoster is much less infectious. Transmission is by direct person-to-person contact, by air-borne spread of vesicular fluid or respiratory secretions, and by contact with articles recently contaminated by discharges from vesicles and mucous membranes. Infections also occur in neonates whose mothers develop varicella around the time of birth (five days prior to two days after delivery).

Acquisition

The usual incubation period for chickenpox is 14–16 days (range 7–24 days). Cases are infectious for up to five days before the onset of the rash (usually one to two days) until five days after the first crop of vesicles. Infectivity may be longer in immunosuppressed patients. Most transmission occurs early in the disease.

Patients with herpes zoster are usually only infectious if the lesions are exposed or disseminated. Infectivity is increased in immunosuppressed patients.

Prevention

- Live attenuated vaccines are available, either as monovalent vaccines or in combination with measles/mumps/rubella.
- The recommended schedule is two doses. In some countries of Europe, mass vaccination has been introduced, but in the majority of European countries a selective vaccination policy has been adopted. The aim of selective vaccination is to prevent varicella among those in close contact with individuals who are most at risk from complications of the disease, for example non-immune health care workers and household contacts of the immunosuppressed, seronegative women going for infertility treatment, children before starting immunosuppressive therapy.
- A live attenuated vaccine is available for the prevention of shingles and postherpertic neuralgia in adults over 50 years; a killed vaccine has recently been granted approval for use in Europe.

Surveillance

- Chickenpox is notifiable in many EU countries. (In the UK, only notifiable in Scotland and Northern Ireland).
- Laboratory diagnosis is rare, so local surveillance depends on informal sources such as schools. The public health practitioner may also be contacted with a request for specific immunoglobulin in an immunosuppressed or pregnant contact. Trend data can be obtained from sentinel general practices.

Response to a case

- Consider exclusion of children with chickenpox from school/nursery until five days from the onset of rash, particularly if there are immunocompromised children in the group Healthcare workers with chickenpox should stay off work for the same period.
- Non-immune health care workers with significant exposure to VZV should be excluded from contact with high-risk patients from 8 to 21 days after exposure, or report to the occupational health department if they feel unwell or develop a fever or rash.
- No exclusion criteria need to be applied to individuals with herpes zoster in the community. Healthcare workers with shingles should inform their Infection Control Team; they may continue working if the lesions are localised and be covered with a bandage or clothing. If they are in contact with high risk patients an individual risk assessment should be carried out.
- In most circumstances, no further action is required. There are, however, some situations

in which post exposure prophylaxis with (VZIG) is indicated. VZIG is indicated for non-immune individuals with a clinical condition that increases the risk of severe varicella (e.g. immunocompromised, neonates, very premature or low birth weight infants, pregnant women without history of chickenpox [more common in those who have lived in the (sub) tropics in childhood] especially before 20 weeks and in the three weeks before delivery) and who have significant exposure to chickenpox or herpes zoster (at least 15 minutes in same room, face to face or on the same ward). A positive history of varicella is usually reliable; a negative history requires confirmation by serology. Detailed advice on the use of VZIG is available in a number of European countries; supplies are often limited.

Investigation of a cluster

- Look for links to institutions with high levels of susceptible individuals.

Response to an outbreak

- In most outbreaks there will be no specific action in addition to the exclusion criteria and issue of VZIG described earlier.
- Hospital outbreaks pose special problems because of the risk of transmission to immunosuppressed and pregnant patients. All staff in contact with these high-risk groups should be screened for VZ antibody. Non-immune staff could then either be vaccinated or, excluded from contact with high-risk patients for 8–21 days after exposure (see earlier).

Suggested case definition for an outbreak
Physician diagnosis of chickenpox or herpes zoster.

3.8 Chikungunya

Chikungunya is a mosquito-borne viral disease caused by an alphavirus from the *Togaviridae* family and first described during an outbreak in southern Tanzania in 1952.

Suggested on-call action
Autochthonous cases should immediately be reported to the health authorities.

Epidemiology

Chikungunya is endemic in sub-Saharan Africa, the Indian Ocean, South-East Asia and the Pacific Region, sometimes causing very large outbreaks of disease. In late 2013, the disease was identified for the first time in the Caribbean, and by May 2016 local transmission had been identified in 45 countries and territories throughout the Americas, with more than 1.7 million reported cases. In Europe, local transmission was reported for the first time in 2007 during an outbreak in northern Italy with 217 cases. Since then smaller numbers of autochthonous cases have been reported from France (in 2010 and 2014) and Spain (2015). The number of reported Chikungunya cases in travellers returning to Europe (1450 cases in 2014) is likely to be a significantly under-ascertainment.

Clinical features

A variety of clinical manifestations may occur. Symptoms are often mild; the infection may go unrecognised, or be misdiagnosed in areas where dengue fever is endemic. Classically, there is abrupt onset of fever with joint pain, which can be very debilitating; often combined with muscle pain, headache, nausea, fatigue and rash. It usually lasts for days or weeks. Most patients recover fully. In some cases joint pain

may persist for months or years. Cases of eye, neurological, heart complications and gastrointestinal complaints have been reported. Serious complications are uncommon. Nevertheless, it has been described as contributing to the cause of death in elderly patients.

Laboratory confirmation

Chikungunya virus can be identified using reverse transcription polymerase chain reaction (RT-PCR) or viral isolation during the first week of illness. Serological tests, such as enzyme-linked immunosorbent assay (ELISA) can detect specific IgM antibodies in serum specimen from day four to five after the onset of symptoms, preferably confirmed by neutralisation. IgM antibody levels are highest three to five weeks after the onset of illness and persist for approximately two months. Confirmatory diagnosis can also be done by detection of a fourfold rise of specific chikungunya antibodies titre in paired (acute and convalescent) serum samples.

Transmission

The virus is transmitted by the bite of female mosquitoes, most commonly *Aedes aegypti* (present also in Madeira and the Black Sea Region) and *Aedes albopictus* (present also along the Mediterranean coast of Europe) which bite throughout daylight hours, with peaks of activity in the early morning and late afternoon. Transmission of chikungunya virus infection through transfusion and transplantation has not been reported in humans. However, this mode of transmission is described for Ross River disease, caused by an infection with a similar alphavirus, and has been shown for chikungunya in animal models.

Acquisition

The incubation period varies between 2 and 12 days. Person-to-person transmission is unlikely.

Preparedness

Chikungunya preparedness in the EU builds on the capacity to detect possible cases in areas with presence of the competent vectors and rapid notification of such cases. Other preparedness elements include review of contingency plans for mosquito-borne outbreaks and education of the general public on how to control mosquito breeding sites.

Prevention

- Reduce the proximity of mosquito vector breeding sites to human habitation. For mosquito protection see Chapter 1.3.
- The possibility of chikungunya transmission via blood donations calls for preventive safety measures to be applied to donors returning from affected areas. Blood safety authorities need to be vigilant regarding the epidemiological situation in outbreak areas.
- No vaccine is available.

Surveillance

- Chikungunya is mandatory notifiable in most countries in Europe, not including the UK.
- ECDC undertakes surveillance of the competent vector in Europe.

Response to a case

- Treatment is directed primarily at relieving the symptoms, including joint pain.
- Rapid implementation of vector control measures around each case identified in areas with presence of the competent vector (see Chapter 1.3).

Case-definition
Confirmed: a patient meeting the laboratory criteria, irrespective of the clinical presentation.

Probable: patient meeting both the clinical and epidemiological criteria.
Possible: a patient meeting clinical criteria.

Clinical criteria – acute onset of fever >38.5 °C and severe/incapacitating arthralgia not explained by other medical conditions.

Epidemiological criteria – residing or having visited epidemic areas, having reported transmission within 15 days prior to the onset of symptoms.

Laboratory criteria – at least one of the following tests in the acute phase: virus isolation; presence of viral ribonucleic acid (RNA) by RT-PCR; presence of virus specific IgM/IgG antibodies in single serum sample; seroconversion to virus-specific antibodies in samples collected at least one to three weeks apart.

3.9 Chlamydia pneumoniae

Chlamydia pneumoniae, also known as *Chlamydophila pneumoniae or* TWAR (Taiwan Acute Respiratory Agent), is a relatively common cause of atypical pneumonia and other respiratory infections.

Suggested on-call action
None required unless outbreak suspected.

Epidemiology

Infection probably occurs worldwide and has been demonstrated in many European countries. Data from the USA suggests annual incidence rates of 6–9% in 5–14 year olds, falling to 1.5% for adults, leading to an overall seroprevalence of 50% by about age 30. Incidence is low in the under-fives but infection/re-infection may occur at any age. No seasonal pattern has been demonstrated but there is evidence of two- to four-year cycles of high and low endemicity. Outbreaks commonly occur in residential or educational institutions.

Clinical features

Chlamydia pneumoniae can cause atypical pneumonia or bronchitis, which is usually mild but often slow to resolve. Approximately 10% of community acquired pneumonia (CAP) is caused by this organism. Upper respiratory symptoms, such as pharyngitis and sinusitis, may occur in isolation or together with chest infection and these together with a usually insidious onset, prolonged cough and a high incidence of laryngitis may help to distinguish an outbreak from other causes of atypical pneumonia. Asymptomatic infection is common. Prolonged infection has also been demonstrated. Illness may be severe in elderly or debilitated patients. Various non-infectious chronic diseases have been linked to *C. pneumoniae*, although definitive proof of causation is lacking.

Laboratory confirmation

Diagnosis can be confirmed by PCR, serology, culture or direct antigen detection. PCR has the best sensitivity and specificity and is the preferred method if a validated test is available: PCR testing may be available as part of a multiplex PCR respiratory panel. Serology using genus-specific IgG is unreliable, as these cross-react with *Chlamydia psittaci* and *Chlamydia trachomatis*: micro-immunofluorescence detection of *C. pneumoniae* specific antibody, including an IgM test for diagnosis of acute infection is required for confirmation. IgM rises can be detected after about three weeks. *C. pneumoniae* is difficult to culture, but respiratory samples may be positive on special cultures. Genotypic or phenotypic typing is not currently available. Co-infection with other respiratory pathogens is relatively common.

Transmission

No zoonotic or environmental reservoir for human infection has been discovered. Spread is likely to be person to person, mainly via respiratory tract secretions, although hand or environmental contamination may also occur.

Acquisition

The incubation period is unclear: estimates range from 10 to 30 days. The infectious period is also unclear but appears to be prolonged. Asymptomatic cases may also play a part in transmission. Although strong antibody responses occur, re-infection is common (sometimes even within the same outbreak). Most severe cases or deaths occur in those with underlying disease.

Prevention

General measures for respiratory infection including:

- Stay away from work or school when ill.
- Cover mouth when coughing or sneezing.
- Sanitary disposal of respiratory secretions and tissues.
- Handwashing.
- Avoid overcrowding.

Surveillance

- Sporadic infection with *C. pneumoniae* is not statutorily notifiable in most countries.
- Possible outbreaks or clusters should be reported to local public health departments.
- Laboratories should report all clinically significant infections to national surveillance systems.

Response to a case

- Hygiene advice to cases and advice to stay at home whilst coughing/sneezing.
- Check for links to other cases.

Investigation of a cluster

- Seek microbiological advice to confirm as *C. pneumoniae* infection.
- Look for direct contact between cases or attendance at same functions or institutions.

Control of an outbreak

Likely to be difficult due to asymptomatic infectious cases, re-infection, prolonged infectivity and long incubation period. Could include hygiene measures, case-finding and treatment (with macrolides, quinolones or tetracyclines), but effectiveness not known.

Suggested case-definition for outbreak
Compatible illness with demonstration of *C. pneumoniae* specific IgM or fourfold rise in specific IgG or PCR positive.

3.10 Chlamydia trachomatis

Bacteria in the family *Chlamydiaceae* are obligate intracellular organisms that can infect mammals and birds. *Chlamydia trachomatis* (CT) serovars A–C mainly cause ocular infections; D–K mainly cause anogenital infections; and serovars L1–L3 cause lymphogranuloma venereum.

Suggested on-call action
Not usually applicable.

Epidemiology

In Europe genital chlamydial infection ('chamydia') is the most frequently diagnosed bacterial STI (see Table 3.10.1). The

Table 3.10.1 Epidemiology of acute Chlamydia and LGV in Europe and the UK

Chlamydia Infection	WHO estimates 146 million new infections each year. Chlamydia is the most frequently notified STI in Europe. The overall rate in 2013 of 182 (per 100 000 population) conceals wide variations. For example, the UK contributes 61% of all reported EU cases. Variations in surveillance systems prevent meaningful comparisons. The overall reporting rate is still increasing, due to increased case detection, improved diagnostic tools, improved surveillance systems, and the introduction of chlamydia screening programmes. More than two-thirds (67%) of all cases were reported in young people between 15 and 24 years of age, and 88% of cases were reportedly due to heterosexual transmission. In the UK, genital chlamydial infection is the most frequently diagnosed STI. In 2015, there were 200 288 reports from genitourinary medicine (GUM) clinics and other community-based settings that screen for chlamydia, a stable number for the last five years since the introduction of more sensitive tests and full scale implementation in 2008 of screening in the National Chlamydia Screening Programme (NCSP). In the UK, in 2015, over 1.5 million chlamydia tests were carried out and over 129 000 chlamydia diagnoses were made amongst young people aged 15–24 years, the target population for the NCSP.
Lymphogranuloma venereum	Anogenital CT infections are caused by CT-serotypes D–K, but serotypes L1, L2/L2a, L2b, L2c and L3 cause lymphogranuloma venereum (LGV). LGV is endemic in Western and Sub-Sahara Africa, India, South-East Asia, South America and the Caribbean America, and was introduced in Europe in the MSM community in 2004. Since introduction in the MSM community in 2004 the infection has spread all over Europe and the USA. In Europe, 1043 cases were reported in 10 countries in 2013. Compared with 2012, this is an increase of 22%. Not all European countries report LGV as the diagnosis requires specific microbiological testing that is not available everywhere. In the UK the LGV prevalence amongst CT-infected MSM was 9% (of which 27% had no symptoms). The majority of LGV infected MSM are HIV-positive.

highest rates of infection are in males aged 20–24 and females aged 16–24 years old. In European studies of the general population (i.e. without restrictions on age or sexual experience), the estimated prevalence of chlamydia in women ranged from 1.1 to 6.9% and in men, it ranged from 0.4 to 6.2%. Similar results have been reported in North American and Australian studies. Risk factors for infection include age 25 or less, multiple sexual partners, recent change of sexual partner, use of oral contraceptives, low socio-economic status and having had a previous infection.

Lymphogranuloma venereum (LGV) is endemic in Africa, Asia, South America and the Caribbean America, but was rare in twentieth-century Western Europe. Since 2004, outbreaks have occurred amongst men who have sex with men (MSM) in major cities in Europe, rapidly increasing with steepest rise during 2013–2015 (see Table 3.10.1). Most cases present as proctitis in HIV-positive white MSM, often with multiple sexual partners.

Clinical features

Many cases of infection in men and women are asymptomatic. In women, there may be a cervicitis and urethritis which may be complicated by pelvic inflammatory disease, tubal damage, infertility and ectopic pregnancy. In men, there is urethritis which may be complicated by epididymitis.

LGV infections can be asymptomatic (in 27% of diagnosed infections), but cause more invasive disease compared to CT D-K. In early infection severe mucosal inflammation and lymphadenopathy can occur, sometimes

leading to rupturing with fistulae as result. In later stages scar tissue may lead to irreversible complications (strictures, lymphedema). *Anorectal LGV* can cause pain, cramps, rectal blood loss and obstipation, proctocolitis, diarrhoea and systemic complaints (fever, weight loss). In *inguinal LGV* the external genitals and inguinal lymph glands are infected, with abscesses (buboes) with or without infection of the urethra or anus. *Pharyngeal LGV* (mucosal infection with cervical lymphadenopathy) is rare.

Laboratory confirmation

Nucleic acid amplification tests (NAATs) are available for the non-invasive laboratory diagnosis of *C. trachomatis* for urine or swab samples. Clinician-taken or self-taken samples can be used for testing. Less sensitive enzyme immunoassay tests should no longer be used.

A new variant of *C. trachomatis* (nvCT) was reported from Sweden in 2006. It is of public health importance because it is not detected by some NAATs and therefore gives false negative results. With better detection using multi-target NAATs, nvCT was reported incidentally in other Northern European countries but remains rare outside Sweden. Laboratories should ensure they are using an NAAT capable of detecting nvCT.

Transmission

Transmission is usually by direct sexual contact. However, adult eye infection can occur through *indirect* transmission (by fingers contaminated with infected genital discharges) and also anal infections can occur through *indirect* transmission (i.e. without anal sex through cervical fluid).

The majority of LGV cases in Europe occur in MSM having unprotected receptive anal sex with multiple partners, of which the majority are also HIV-positive. There is one report showing an association with the regular use of anal enemas. Also use of sex toys and attendance at sex parties are associated with LGV.

Acquisition

The incubation period is 7–14 days and the cases remain infectious until treated. Only limited short term immunity occurs and re-infection rates are high.

Prevention

- Programmes of opportunistic selective screening, case finding and partner notification are cost effective. Universal population screening is not recommended.
- Annual *C. trachomatis* testing in STI or sexual health clinics is recommended for all sexually active young women and men (<25 years of age), and should be considered for MSM.
- Repeated testing in three to six month intervals should be offered to young women and men (<25 years of age) who test positive for *C. trachomatis* to exclude re-infection.
- Anorectal testing should be routinely offered to MSM and selectively offered to women who report to have had anal sex in the past six months.
- Urine and self-taken vaginal swabs are tested with NAATs. The service is available in a variety of community settings. Use of condoms during sexual intercourse and avoiding shared use of sex toys will reduce individual risk.
- *C. trachomatis* positive rectal specimens from MSM are recommended to be genotyped for LGV, irrespective of the presence of anorectal symptoms.

Surveillance

- *C. trachomatis* infections should be notified to local, regional and national authorities as mandated by statute.
- ECDC is responsible for the EU/EEA-wide surveillance of communicable diseases including *C. trachomatis* infections.
- Laboratories should report positive results through laboratory reporting systems.

Response to a case

- Treatment to remove infectivity and reduce complications: check national guidelines for recommended antibiotic courses.
- Cases should avoid sexual intercourse for seven days after the completion of treatment.
- Patients identified with *C. trachomatis* should have partner notification discussed at time of treatment by a trained health care professional.

Investigation of a cluster and control of outbreaks

- This is not generally applicable but contact tracing, mapping sexual networks, treatment and education may be appropriate, especially in cases of LGV.

Suggested case definition

Cases are defined by the results of appropriate laboratory tests.

3.11 Cholera

Cholera is a life-threatening secretory diarrhoea resulting from infection with toxin-producing *Vibrio cholerae* O1 or O139.

Suggested on-call action

Cases should normally be admitted to an infectious diseases unit and enteric precautions instituted.

Confirm diagnosis and the toxin production status of the isolate.

Exclude cases in risk groups 1–4 (Box 2.2.1) for 48 hours after the first normal stool.

Identify household contacts and those with common exposure, place under surveillance for five days from last contact and exclude from food handling.

Epidemiology

Cholera is rare in Europe. In 2016, 23 confirmed imported cases were reported by the UK (16), Spain (3), and Belgium, Denmark, Germany and Norway (1 each). World-wide, cholera has become more widespread as the virulent El Tor biotype has spread, encouraged by international migration and the breakdown of public health measures especially associated with war, famine and other disasters. European visitors are unlikely to visit areas where cholera is common. *V. cholerae* O139 has been identified as causing epidemic cholera.

Clinical Features

Cholera is characterised by a sudden onset of copious, watery diarrhoea, and sometimes vomiting. Stool volumes of up to 30 l a day lead to rapid dehydration. There may be severe muscle pain as a result of hypokalaemia. This dramatic presentation is distinctive, but mild or subclinical infections are more common. The outcome depends on the amount of fluid and electrolyte loss and replacement; severe untreated cases have a case-fatality of 50%. With correct treatment less than 1% die.

Laboratory Confirmation

Vibrios are small, comma-shaped, motile, Gram-negative bacilli, which may be seen on direct microscopy of stools or cultured from stool or a rectal swab (still the gold standard). Various media have been described for culture; colonies can be recognised by fermentation reactions or by using antisera or fluorescent antibody tests. *V. cholerae* O1 is

divided into two biotypes – classical (Inaba and Ogawa) and El Tor. Determination of toxin production is important, non-toxin producing organisms are not of public health significance (most *V. cholerae* isolated in the UK are not toxin producers). PCR and other nucleic acid-based rapid techniques have been developed; as have rapid antigen tests with limited sensitivity and specificity.

Transmission

Infection is faeco–oral, commonly through contaminated water. Undercooked seafood can also act as a vehicle. Cholera vibrios are sensitive to acid: most die in the stomach, but achlorhydria increases susceptibility to infection. Following colonisation of the small bowel, an enterotoxin that interferes with intestinal epithelial cell metabolism is produced, causing secretion of electrolytes and water into the intestinal lumen. Person to person spread should not occur where sanitary conditions are acceptable.

Acquisition

The incubation period is 6–48 hours. Cases are infectious during the period of diarrhoea and up to seven days after.

Prevention

Control by sanitation is effective but may not be feasible in endemic areas.

- A parenteral vaccine of whole killed bacteria has been used widely, but is relatively ineffective and is not generally recommended.
- An inactivated oral vaccine (Dukoral) against Vibrio cholera O1 (classical and El Tor) is available in some European countries.
- Antibiotic prophylaxis is feasible for small groups over short periods in high-risk situations.
- Breastfeeding in endemic areas protects infants from disease.

Surveillance

- Cholera is a notifiable disease, and the public health authorities should be informed of any case.
- WHO should be informed by the national authority.
- Illnesses caused by strains of *V. cholerae* other than toxigenic *V. cholerae* O1 or O139 should not be reported as cases of cholera.

Response to a case

- See on-call box above.
- Individual cases should be investigated to determine the source.
- Microbiological clearance: when indicated, two consecutive negative stools taken at intervals of at least 24 hours are required.
- Hygiene advice to the case and contacts.

Investigation of a cluster

- Clusters should be investigated in case there is secondary transmission within the household or community. This is rare in Europe.
- Obtain history of foreign travel.

Control of an outbreak

Outbreaks are rare in developed countries and are controlled through the provision of safe drinking water supplies.

Suggested case-definition for an outbreak

Clinical: an illness characterised by diarrhoea and/or vomiting in a contact of a case.

Confirmed: clinical case with isolation of toxigenic *V. cholerae* O1 or O139 from stool or vomitus.

3.12 CJD and other human transmissible spongiform encephalopathies

Human Transmissible Spongiform Encephalopathies (TSEs) are a group of conditions characterised by progressive fatal encephalopathy, with typical spongiform pathological appearances in the brain. They include idiopathic diseases (classical Creutzfeldt–Jakob Disease [CJD] and sporadic fatal insomnia); familial diseases (fatal familial insomnia and Gerstman–Straussler–Scheinker disease); and acquired diseases: (variant Creutzfeldt–Jakob Disease [vCJD] and kuru). These conditions are believed to be caused by prion proteins, known as PrP in the case of vCJD.

Suggested on-call action
Undertake risk assessment May need to prepare for media interest

Epidemiology

CJD in its classical form is the commonest of the human TSEs, but is still rare, with an annual incidence worldwide of one per million population.

The first case of vCJD was first identified in 1996. Cases have occurred in a number of European countries, but particularly in the UK where 177 cases had been reported by May 2015. France has reported 27 cases; Ireland, Italy, the Netherlands, Portugal and Spain have each reported five or fewer cases. The number of cases peaked in 2000, and has been declining since then; in 2016 only two vCJD cases were reported in the EU (one in Italy and one in the UK). The age distribution of vCJD is younger than in classical CJD and cases have a different symptom profile and a different appearance of brain tissue on post-mortem. There are genetic differences in susceptibility: all cases of vCJD (except one) tested to date are homologous for methionine at codon 129 of the prion protein gene – about 38% of the UK population are of this genotype. No relationship with occupation is apparent.

Kuru is a disease that occurs exclusively in Papua New Guinea; it has now almost disappeared.

Clinical features

The onset of vCJD is with variable psychiatric symptoms. This is typically followed by abnormal sensation at two months, ataxia at five months, myoclonus at eight months, and akinetic mutism at eleven months, with death at fourteen months average.

Laboratory confirmation

The diagnosis of vCJD is made on the basis of typical clinical features (see http://www.cjd.ed.ac.uk/sites/default/files/criteria.pdf) and post-mortem findings of spongiform change and extensive PrP deposition with florid plaques throughout the cerebrum and cerebellum.

Transmission

Most cases of classical CJD are sporadic, about 15% are inherited and around 1% are iatrogenic, transmitted from human pituitary derived growth hormone injections, corneal transplants and brain surgery involving contaminated instruments. Classical CJD is not thought to be transmissible via blood transfusion.

The most likely source of vCJD in humans is cattle infected with Bovine Spongiform Encephalopathy (BSE). The PrP causing vCJD and BSE are indistinguishable from each other, but are different to those causing classical CJD or scrapie. The route of spread is unknown although consumption of infected bovine neural tissue is thought to be the

most likely. Such exposure is likely to have been at its greatest before the introduction of effective control measures in 1990. In addition to the CNS tissues (including eye and pituitary) that are infectious in all types of TSE, vCJD also involves the lymphoreticular system and so tissues such as tonsils, appendix, thymus, lymph nodes, spleen, Peyer's patches and possibly bone marrow could all be infectious. Cases possibly associated with blood transfusion have been reported; iatrogenic transmission from contaminated surgical instruments is also theoretically possible, with CNS and back of eye operations likely to pose the highest risk. Scrapie, the main TSE of sheep, is not thought to be transmissible to man.

Kuru is transmitted by cannibalistic consumption of infected human brain tissue; there is some suggestion that transmission may have occurred by spreading infected brain material over superficial cuts.

Acquisition

The incubation period for vCJD is unknown, but is probably several years; for iatrogenic CJD and kuru the mean incubation is 12 years. The infective dose is unknown, but is likely to be affected by route of exposure. Cattle under 30 months of age are thought to be significantly less likely to be infectious.

Prevention

- Prevent BSE in cattle and transmission of infected tissues to man. This includes banning consumption of potentially infected feed to cattle, avoiding human consumption of nervous and lymphoreticular tissues, safe preparation of carcasses and slaughter of affected herds.
- Standard infection control measures for decontamination of surgical instruments; use disposable instruments where possible.
- Incinerate surgical instruments used on definite or probable CJD cases and high-risk groups.
- Quarantine of surgical instruments used on possible cases.
- Effective tracking system for surgical instruments.
- Use of leucodepleted blood for transfusions.
- Use of synthetic clotting factor to treat patients with haemophilia.
- Avoid transplant and tissue donations and blood transfusions from certain high-risk groups.
- Infection control guidance for CJD patients undergoing surgery have been drawn up by the UK Advisory Committee on Dangerous Pathogens TSE subgroup (available via Public Health England web site).

Surveillance

European surveillance of vCJD is done by the ECDC funded network EuroCJD. The network undertakes surveillance that includes identification of risk factors, routes of transmission, and identification of novel forms of human prion disease. It also provides advice on diagnosis, including review of clinical data and examination of tissue samples.

Response to a case

- Neurologists should report to their local public health department who will report to ECDC via the national competent authorities.
- Investigate patient's medical history, especially recent surgery or organ or tissue donation and blood donations. Advise on infection control measures.
- A look-back exercise should be considered in any case of vCJD who has undergone an invasive procedure, particularly if involving nervous or lymphoid tissue. This should be based upon a risk assessment considering the type of exposure and how long previously the exposure occurred. Those at highest risk are probably those exposed to instruments on the first few occasions of use after the potential contamination.

Investigation of a cluster

- Seek advice from national public health institute and EuroCJD.
- The uncertain and prolonged incubation period make the identification and investigation of clusters difficult. For vCJD, look for common exposures over a wide period of time, particularly common sources of beef and bovine products since 1980, and consider the possibility of iatrogenic transmission.

Comprehensive guidance on the public health management of cases and clusters of CJD and vCJD was published on the PHE website in June 2014.

3.13 Clostridium difficile

Clostridium difficile is an anaerobic spore-forming, gram-positive, toxin producing bacterium widely distributed in soil and the intestinal tracts of humans and animals. The majority of *C. difficile* strains produce the virulence factors toxin A (TcdA) and toxin B (TcdB) whilst some are non-toxigenic. Strains like ribotype 027 produce a binary toxin that has been associated with severe illness and poorer outcomes. *C. difficile* Infection (CDI) is an important Healthcare Associated Infection (HCAI) which in 2008 was estimated to incur additional healthcare cost of £4000 per case in the UK, and between €4067 and €9276 per case in Europe, which equates to around €3000 million per year in Europe.

Suggested on-call action

Hospital outbreaks will be managed by the hospital Infection Control Team. The local health protection team should be prepared to participate in meetings of the outbreak control group.

The local health protection team may be called upon to investigate and manage incidents involving CDI in community-based healthcare settings like nursing homes.

Epidemiology

Elderly, hospitalised patients, especially those on broad spectrum antibiotics are at greatest risk. There is a background rate of CDI in most hospitals and outbreaks may occur. CDI incidence has increased over time in North America and Europe; rising from 2.45 per 10 000 patient days per hospital in 2005 to 4.1 in 2008 in Europe.

Across the EU/EEA, there is considerable variation in CDI incidence but they still remain at historically high levels. CDI was responsible for 48% of healthcare-associated gastrointestinal infections in acute care hospitals in the EU/EEA during 2011–2012. The burden of healthcare-associated CDIs was estimated at 123 997 cases annually with a 3% attributable mortality that equates to around 3700 deaths per year.

A number of reasons were adduced for this increase including greater awareness on the part of health professionals leading to increased testing and reporting, an older population, an increase in community-acquired CDI and the emergence of hypervirulent strains such as PCR ribotype 027 and to a lesser extent ribotype 078. In England, the ribotype 027 strain that emerged in the early 2000s and was associated with increased severity of CDI is no longer as prevalent and this may have resulted in a reduction in case fatality from CDI.

In the UK, there has been a considerable reduction in CDI incidence with 12 840 cases in patients aged two years and over reported in 2016/2017, a reduction of 76.9% compared with the 55 498 cases in 2007/2008.

Clinical features

CDI is a spectrum of disease comprising colonisation, toxin-production, watery diarrhoea and severe colitis. *C. difficile* accounts for up to 25% of cases of antibiotic-associated diarrhoea and a greater proportion of more severe disease. In a typical case of CDI, watery diarrhoea starts within a few days of commencing antibiotics, although antibiotics taken one to two

months previously may still predispose to infection. There may be abdominal pain (occasionally without diarrhoea), nausea and fever. Complications include dehydration, Pseudomembranous Colitis (PMC), toxic megacolon, and colon perforation. Around 15–25% (range: 5–45%) of patients with primary *C. difficile* infection may experience a re-occurrence (either re-infection or relapse) and in a small proportion of these patients, CDI may reoccur several times. Older persons, immunocompromise, use of multiple antibiotics and prolonged hospital stay are among risk factors of CDI re-occurrence.

Laboratory confirmation

Laboratory tests used to test stool specimens for *C. difficile* infection include Enzyme Immunoassay (EIA) to detect both toxin A and toxin B, cell culture cytotoxicity assay (toxin B only), or EIA for Glutamate Dehydrogenase (GDH) antigen detection.

Culture is labour intensive with a slow turnaround and cannot distinguish toxigenic from non-toxigenic strains.

Toxigenic culture (gold standard) can be considered, but it takes longer. Culturing the organism can provide isolates if typing is to be performed and for antibiotic sensitivity testing.

Molecular tests such as NAAT are rapid and can sensitively detect the presence of the organism. Due to the varying sensitivity and specificity of these tests across Europe, the use of two- or three-step testing algorithms have gained popularity in order to minimise under-diagnosis. In the UK, the two-step algorithm uses a highly sensitive test (GDH EIA [or NAAT]) as the first screening step and a highly specific test (EIA to detect toxins) as the second confirmatory test.

Transmission

Clostridium difficile is present in the faeces of 3% of healthy adults, 7% of asymptomatic care-home residents, 20% of elderly patients on long-stay wards and 66% of babies.

Clostridium difficile is transmitted from patients with symptomatic CDI either directly, via the hands of health care workers, through the accumulation of spores in the environment or on contaminated fomites such as commodes. *C. difficile* can live for long periods on surfaces. Spread does not occur from an asymptomatic carrier (colonisation) in the absence of diarrhoea. Transmission to medical and nursing staff has been reported, although this is unusual and the disease is usually mild and short-lived. There has been an increase in reports of community-associated CDI in individuals without a history of prior healthcare exposure or other key risk factors.

Acquisition

CDI occurs when a toxigenic strain of *C. difficile* colonises the gastro-intestinal tract of a susceptible patient. Predisposing risk factors are advanced age, antibiotic treatment, proton pump inhibitors, immunocompromise, prolonged stay in a healthcare setting, serious underlying illness and alteration in gut motility.

Prevention

- Antimicrobial stewardship: in hospitals there should be an antimicrobial stewardship programme that includes the use of restrictive antibiotic guidelines that promote the use of narrow-spectrum agents.
- Standard infection control procedures, including staff training and a high level of environmental cleanliness.

Surveillance

- Clinicians and other healthcare practitioners should have a high index of suspicion and should submit faecal specimens for laboratory testing when diarrhoea may be due to CDI.
- Laboratories should test diarrhoeal specimens for toxin A and B from patients aged two years and over.

- Include CDI in the mandatory surveillance of health-care-associated infection using the standardised European protocol.

Response to a case

- Treatment of primary infection is with an antibiotic such as metronidazole, vancomycin, or fidaxomicin.
- Test of cure is not advisable as most cases may continue to shed *C. difficile* in the stool for up to six weeks after treatment and this is not an indication of treatment failure.
- Recurrent infections may be managed with oral vancomycin or fidaxomicin, intravenous immunoglobulin, or bio-therapeutical interventions such as faecal microbiota transplant where available.
- Involve the hospital infection control and antimicrobial stewardship teams.
- Side room isolation with enteric and contact precautions, including the use of gloves and aprons and attention to hand washing by all staff. If side rooms are unavailable, cohort nurse with other CDI cases.
- Bowel function should be monitored daily for frequency and severity using the Bristol Stool Chart.
- Thorough environmental cleaning in line with extant hospital guidance for CDI control.

Investigation of a cluster

- All patients with diarrhoea should be identified, risk factors should be documented and faecal samples submitted for toxin tests, culture and ribotyping. In a hospital outbreak, typing may help to determine whether all patients are infected with the same strain, whether re-occurrences are due to the original outbreak strain (relapses) and whether patients are infected with more than one strain at a time.
- Routine environmental sampling is not recommended but may form part of an investigation, especially if isolates can be typed.

Control of an outbreak

- Antibiotic stewardship arrangements to support the appropriate use of antibiotics. Consider reviewing the local antibiotic formulary/policy if appropriate.
- Case finding through enhanced surveillance.
- Enteric and contact precautions including side room isolation and hand washing. If side rooms are unavailable, cases can be cohort nursed with other patients with CDI.
- Restrict movements and transfers of patients.
- Environmental cleaning and disinfection strategy that includes disinfection and sterilisation of shared (reusable) equipment using recommended sporicidal cleaning agent (example: hypochlorite-based disinfectant). Consider single use equipment.
- Screening for and treatment of asymptomatic patients who are CD carriers is unnecessary and not effective for decolonisation.
- There is no need to screen asymptomatic staff for carriage of CD: staff who are asymptomatic carriers do not present a risk to patients and they can continue in their normal duties.

Suggested case-definitions

Clostridium difficile infection must meet at least one or more of the following criteria: diarrhoeal stools (stool loose enough to assume shape of sample container or Bristol Stool Chart types 5–7) or toxic megacolon without other known aetiology AND a positive laboratory assay for *C. difficile* toxin A and/or B in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means, for example a positive PCR result;

OR

pseudomembranous colitis revealed by lower gastro-intestinal endoscopy;

OR

colonic histopathology characteristic of *C. difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy

Outbreak of *C. difficile* infection: two or more cases caused by the same strain related in time and place over a defined period that is based on the date of onset of the first case.

3.14 Clostridium perfringens

Clostridium perfringens (formerly *Clostridium welchii*) is primarily a food-borne pathogen, which causes a mild gastrointestinal illness due to an enterotoxin. It is a cause of outbreaks, usually associated with mass catering.

Suggested on-call action

If you, or the reporting laboratory/clinician, are aware of other potentially linked cases, consult the local outbreak plan or SOP.

Epidemiology

The incidence of *C. perfringens* food poisoning presenting to general practice in England is about 1.3 per 1000 person years. *C. perfringens* is identified as the cause of 1.4% of all gastroenteritis outbreaks reported in the UK, but this rises to 8% of those thought to be food-borne. There is little known variation by age, sex, ethnicity, occupation and geography. Reported cases are higher in autumn and winter months (especially December) than in summer, perhaps because of seasonal consumption of the types of foods often associated with infection. The association of infection with institutions or large gatherings likewise probably reflects patterns of food preparation. Outbreaks often have a high attack rate.

Clinical features

Almost all cases of *C. perfringens* food poisoning have diarrhoea (watery, often violent), usually with colicky, often severe, abdominal pain. Nausea may occur and a small proportion may have fever or vomiting. Blood in the stool is rare. Most cases recover within 24 hours, although elderly or debilitated patients may be more severely affected and occasional deaths are reported.

A much more serious disease (enteritis necrotans) is caused by different strains and is rare in Europe. *C. perfringens* is also the major cause of gas gangrene.

Laboratory confirmation

Clostridium perfringens can be isolated from anaerobic culture of stool samples. They are divided into five types (A–E) on the basis of toxin production. Type A causes almost all cases, with A2 strains, which form markedly heat resistant spores, the most common. A1 strains, whose spores are relatively heat sensitive, may also cause illness.

As asymptomatic carriage of *C. perfringens* is extremely common in healthy humans and carriage of heat resistant organisms not uncommon, isolation of the organism from sporadic cases is of little value. However, serotyping, which allows cases to be linked to each other and to strains from potential food vehicles, is useful in outbreak investigation. Other factors which may help separate cases from carriers are a quantitative culture of organisms (over 10^6 cfu g^{-1} faeces is usually significant) or the demonstration of enterotoxin in faeces. More than one serotype can be present in the same specimen.

Transmission

Clostridium perfringens is ubiquitous in soil and in the gastrointestinal tracts of mammals and birds. Many opportunities exist for spores to contaminate food, particularly meat and meat products, but provided contamination remains low, illness does not result. *C. perfringens* can grow at temperatures between 12 and 50 °C with optimal growth at about 45 °C, when a generation time of 10 minutes

can be achieved. Spores, particularly those of the A2 strains, can survive normal cooking, including boiling for longer than one hour. These 'heat activated' spores will then germinate in the protein rich environment as the food cools: the longer the food remains at the organism's preferred temperature, the larger the number of resulting organisms. If the food is not then reheated to at least 70 °C for two minutes throughout its bulk to kill the vegetative cells before eating, then a potentially infectious dose is ingested. The ingested organisms sporulate in the gut and (probably as a result of the initial heat shock) produce the enterotoxin, which causes disease. Bulk cooking of meat/poultry stews, roasts, pies and gravies appear to be particularly vulnerable to this chain of events.

Acquisition

The incubation period is usually 8–18 hours, although a range of 5–24 hours has been reported (possibly occasionally shorter). *C. perfringens* gastroenteritis is not spread from person to person, and asymptomatic food handlers are not thought to be infectious to others. The infectious dose in food is usually greater than 10^5 organisms. There is no evidence of effective immunity post infection.

Prevention

- Prevention is dependent upon adequate temperature control of food after (initial) cooking. Meat dishes should be served whilst still hot from initial cooking *or*, if not served immediately or kept above 63 °C until serving, they should be:
  - refrigerated to below 8 °C within two hours of end of cooking, then
  - reheated to achieve 70 °C for at least two minutes throughout the bulk of the food.
- Take particular care in large functions, or if consumers are likely to include elderly or debilitated people.

Surveillance

- Report cases of food poisoning to local public health authorities and positive samples from cases to national surveillance systems.

Response to a case

- As with all cases of diarrhoea, hygiene advice should be given and it is best if the case does not attend work or school until he/she has normal stools.
- Occupational details should be sought: cases in higher risk groups (Box 2.2.1) should be excluded until 48 hours after the first normal stool. No microbiological clearance is necessary.
- No action is necessary with asymptomatic contacts of cases.

Investigation of a cluster

A laboratory identified cluster is currently a rare event. Should one occur in a group of individuals with a compatible clinical illness, then analysis of person/place/time variables should be followed by a semi-structured questionnaire aimed at identifying common foods, especially cooked meat/poultry products and meals eaten outside the home, and functions.

Control of an outbreak

- As secondary spread from cases is unlikely, the aim of the outbreak investigation is to discover how it happened so that further outbreaks can be prevented. In practice this means trying to identify how an infectious dose resulted in a food presented for consumption.
- The vehicle of infection is identified by microbiological analysis of remaining food to find the same serotype as the cases (make sure you know how the food was stored after serving but before sampling) and/or

by an analytical epidemiological study to show that cases were statistically significantly more likely to have eaten the food than controls (and that the consumption of that food explains the bulk of the cases).
- The environmental investigation will concentrate on how the food was cooked, stored and reheated. It is worth remembering that type A1 spores should not survive adequate initial cooking.

Suggested case-definition for analytical study of *C. perfringens* outbreak

Clinical: Diarrhoea or abdominal pain with onset between 8 and 18 hours of exposure.
Confirmed: Clinical case with one of: isolate of outbreak serotype, demonstration of enterotoxin in faeces or spore count $>10^6 g^{-1}$.

3.15 Coronavirus (including MERS and SARS)

Coronaviruses form a large family of viruses that cause a number of diseases in animals and humans. In humans coronaviruses can cause diseases like the common cold, as well as Severe Acute Respiratory Syndrome (SARS) or Middle East Respiratory Syndrome (MERS).

Suggested on-call action

- Consult current national guidelines.
- Assess whether case fits current case-definition. If so, inform National Surveillance Centre.
- Samples should be taken urgently for laboratory diagnosis.
- Patient(s) should be immediately isolated and respiratory transmission-based precautions instituted.
- The response to the following groups should be considered: cases, potential cases, contacts of cases, the worried well.
- Contacts of persons under investigation for SARS or MERS should be traced and placed under observation for 10 days or until SARS has been ruled out, or 14 days or until MERS has been ruled out, respectively. A close contact for MERS is any person who had prolonged face-to-face contact (>15 minutes) with a symptomatic confirmed case of MERS-CoV in a household or other closed setting, health or social care worker who provided direct clinical or personal care or examination of a symptomatic confirmed case of MERS-CoV, or was within close vicinity of an aerosol generating procedure AND who was not wearing full Personal Protective Equipment (PPE) at the time.
- Individuals at high risk of exposure to a person or persons in a SARS or MERS cluster (e.g. healthcare workers) should be managed as contacts until the disease has been ruled out.
- Contacts within the healthcare setting should be managed as follows:
  (a) Inpatients should be isolated or cohorted and transmission-based precautions instituted (respiratory, body fluids and faecal). They should be placed on fever surveillance.
  (b) Exposed staff should be placed on active fever surveillance, and either cohorted to care for exposed patients (as above) or should self-isolate.
- Community contacts should be:
  (a) given information on the clinical picture, transmission, and so on, of SARS or MERS respectively;
  (b) placed under active surveillance for 10/14 days and voluntary self-isolation is recommended;

(c) visited or telephoned daily by a member of the public healthcare team;
(d) temperature recorded daily.

- If the contact develops disease symptoms, they should be investigated locally at an appropriate healthcare facility prepared for triage.

Epidemiology

SARS

An unusual respiratory illness that emerged in southern China in November 2002; the outbreak spread outside China in February 2003 and ended in July 2003. According to the World Health Organization (WHO), a total of 8098 people (21% of which were healthcare workers) worldwide were notified as having had SARS during the 2003 outbreak. Of these, 774 died. Healthcare workers and close (e.g. household or face-to-face) contacts of cases are at particular risk. The case fatality rate is about 10% and increases with age. For cases of SARS to reappear, the virus has to re-emerge (from a possible animal source, a laboratory accident or undetected transmission in humans). Since 5 July 2003 the only confirmed SARS-CoV infections resulted from laboratory accidents (Singapore and Taiwan), from exposure to animal sources or environmental contamination (China); none of these cases has been fatal nor resulted in secondary transmission.

MERS

The first cases were identified in 2012 in Saudi Arabia, from where a large proportion of cases have been reported. Other cases have been reported from other parts of the Arabian peninsula and many of the cases reported from outside the Middle East had links to this region. In 2015, the Republic of Korea experienced a large outbreak of MERS related to local transmission in health care settings. However, other countries outside the Middle East that have reported imported cases have reported no or limited secondary transmission. Approximately 35% of the reported cases of MERS have died.

Clinical features

In general, SARS begins with high-grade fever (temperature greater than 38.0°C [100.4°F]). Other symptoms may include headache, chills, rigour, dry cough, malaise and body aches. The symptoms are non-specific. Pulmonary symptoms, including dry cough and later breathlessness, are the most common primary manifestation during the early phase. Some 20–25% of cases develop severe respiratory failure requiring intensive care treatment. About 10–20% of patients have diarrhoea, which is the second most common manifestation. Most patients develop pneumonia and the majority of cases have an abnormal chest radiograph at some stage.

MERS-CoV infections can be asymptomatic or may cause only mild, severe or fatal respiratory disease. Typical symptoms are fever, cough and shortness of breath. Pneumonia is common. Gastrointestinal symptoms are also common. Severe illness can cause respiratory failure that requires mechanical ventilation and support in an intensive care unit. The clinical symptoms are more severe in older people and patients with pre-existing illnesses.

Laboratory confirmation

The most accurate diagnostic tests for SARS are RT-PCR or real-time PCR of genomic fragments or cultured virus. RT-PCR can be used to make a relatively early diagnosis. A positive RT-PCR test should be repeated by the national reference laboratory using a second, unopened aliquot. Respiratory, serum, stool and urine specimens should be taken for virus isolation and for acute phase serology. Sensitivity can be increased if multiple specimens/multiple body sites are tested. Respiratory samples should include

nasopharyngeal aspirates, provided full infection control procedures are in place to protect staff and other patients. Respiratory and stool specimens should be routinely collected for virus isolation or detection of viral genome utilising RT-PCR during the first and second weeks. Serum specimens should also be collected for serology in the second and third weeks to detect a rising titre by testing acute and convalescent sera in parallel. Clinical samples should be separated into three aliquots at the time of collection. One should be used by the local diagnostic laboratory; the second aliquot, received unopened, should only be used by the national reference laboratory; and the third should be retained for use by the WHO SARS Reference and Verification Laboratory, should verification be necessary.

For MERS, molecular tests (for active infections) and serological tests (for antibodies indicating previous infections) are available. The molecular test real-Time Reverse-Transcription Polymerase Chain Reaction (rRT-PCR) assays is used to detect viral RNA in clinical samples. Multiple specimens, including upper (e.g. nasopharyngeal and oropharyngeal swabs) and lower (bronchoalveolar lavage, sputum and tracheal aspirates) respiratory samples, serum, and stool specimens should be collected. Serology is used to detect antibodies to MERS-CoV in people who may have been exposed to the virus. The presence of these antibodies indicates that a person has been infected with the virus and developed an immune response. Often a two-phase approach for serology testing, using a screening test (ELISA) and two confirmatory tests (immunofluorescence assay and microneutralisation assay) is used. MERS-CoV serology tests are generally used for surveillance or investigational purposes, not for diagnostic purposes.

Transmission

SARS is mainly spread by respiratory droplets, SARS-CoV is also shed in faeces; faecal shedding is more prolonged than respiratory. The number of new cases (R_0) arising from each case of SARS in the absence of interventions is about three; public health interventions can reduce R_0 to below 1 and control the disease. Risk of transmission is greatest during the second week of illness. Transmission is greatly reduced if the case is isolated within three days of onset. Mild cases are less infectious than more severely ill patients. Super spreading events occur, but are not well understood or predictable. Hospitals act as amplification sites for SARS. Asymptomatic patients are not infectious and cases are no longer infectious 10 days after fever resolution. Children are rarely affected.

For MERS the route of transmission from animals to humans is not fully understood, but camels are likely to be a host for MERS-CoV and an animal source of infection in humans. In several countries MERS-CoV strains that are identical to human strains have been isolated from camels. The virus does not appear to pass easily from person to person unless there is close contact (e.g. unprotected care to an infected patient). There have been clusters of cases in healthcare facilities, where human-to-human transmission appears to be more probable, especially when infection prevention and control practices are inadequate. Thus far, no sustained community transmission has been documented.

Acquisition

The mean incubation period for SARS is five days (range 2–10 days), although incubation periods of up to 14 days have been reported. Serial interval is 8.4 days. Available information suggests that persons with SARS are likely to be infectious only when symptomatic.

Available information indicates that the mean incubation period for MERS is five to six days (range 2–14 days).

Prevention

Detailed infection control guidelines for MERS are available on the PHE website. Effective infection prevention and control

measures, including transmission-based precautions (air-borne, droplet and contact precautions), use of recommended PPE and appropriate cleaning and decontamination of the environment are essential.

SARS can be controlled by identifying and isolating all cases as early in the illness as possible, rigorous infection control at all stages and monitoring the health of close contacts, so that any infected cases are identified and isolated before they become infectious. This includes the following:

- Isolation and contact tracing to break chains of transmission.
- Care in laboratory handling of specimens (biosafety containment level 3).
- Good hospital infection control.
- WHO recommendations are that patients with probable SARS should be isolated and accommodated as follows in descending order of preference:
  - **(a)** negative pressure rooms with the door closed;
  - **(b)** single rooms with their own bathroom facilities; and
  - **(c)** cohort placement in an area with an independent air supply and exhaust system. Turning off air conditioning and opening windows for good ventilation is recommended if an independent air supply is unfeasible. Wherever possible, patients under investigation for SARS should be separated from those diagnosed with the syndrome.

Surveillance

- Report urgently to local and national public health authorities.
- National public health authorities should report every laboratory-confirmed case of SARS or MERS to the WHO.

Response to a case

See Suggested on-call action box.

No vaccine or specific treatment is available for MERS or SARS; treatment is supportive and based on the patient's clinical condition.

Investigation of a cluster

- Look for a history of travel abroad, contact with a case or recent exposure to a healthcare setting.
- If none of the above explains cases, undertake full hypothesis-generating study.

Control of an outbreak

- Deal with individual case as above.
- Set up dedicated triage area with adequate infection control arrangements. Patients under investigation for SARS or MERS should be separated from the probable cases.
- Provide suspected patients with a face mask to wear, preferably one that provides filtration of their expired air.
- Provide triage staff with a face mask, and eye protection.
- Ensure good infection control/handwashing procedures in place.
- Disinfectants, such as fresh bleach solutions, should be widely available in appropriate concentrations.
- Guidance for clinical and laboratory management, and case-definitions available on the WHO, ECDC, PHE and CDC websites.

3.16 Cryptosporidiosis

Cryptosporidia are protozoan host-adapted parasites, which usually cause an acute self-limiting diarrhoeal illness in man and/or animals. Their main public health importance lies in the severe illness caused in

immunocompromised individuals, the lack of specific treatment, and the potential to cause outbreaks, including large water-borne outbreaks.

Suggested on-call action

- If case in risk group for onward transmission (Box 2.2.1), exclude from work or nursery.
- If you, or the reporting laboratory/clinician, are aware of other potentially linked cases, consult the local outbreak plan or SOP.

Epidemiology

The annual notification rate for cryptosporidiosis in Europe is 2.5 cases per 100 000 population (2010–2014), but under-reporting is significant in many countries; much higher rates are reported from Ireland, the UK and Sweden. Seroprevalence rates of 20–35% are reported suggesting that exposure is widespread. Diagnosed infection rates are highest in children aged under 5 years and low in adults over 45: although different patterns may occur in some risk groups, for example travellers abroad and the immunosuppressed. Males and females are affected equally. The most common sources for outbreaks are drinking water and swimming pools, with subsequent human-to-human transmission.

Cryptosporidiosis has a marked seasonal pattern in Europe with a peak in late summer or autumn (mainly due to *Cryptosporidium hominis* infection) and, in some countries (e.g. Ireland and UK), an earlier peak in spring (mainly *Cryptosporidium parvum*) (Figure 2.2.2). Groups at particular risk of infection include animal handlers (*C. parvum*), travellers abroad, contacts of cases, homosexual men and the immunosuppressed. Rates may also be higher in rural areas.

Clinical features

The main presenting symptom is diarrhoea, which in immunocompetent individuals may last from 1 to 100 days, with reported medians of 5–14 days. Almost all presenting cases have abdominal cramps and many have vomiting, mild fever and loss of appetite. The diarrhoea is usually watery, may be mucoid and may wax and wane. The illness is usually self-limiting with low mortality. Mild or asymptomatic infection may also occur.

Immunosuppressed patients have difficulty in clearing the infection, particularly HIV infected individuals with CD4 cell counts below 150 cells μl^{-1}. Many such individuals have a prolonged and fulminant illness, which may be life threatening.

Laboratory confirmation

Testing for cryptosporidia may not be routine for all samples at all laboratories and should be specifically requested if suspected. The mainstay of diagnosis is microscopy of stool samples to detect cryptosporidia oocysts. It is important that such microscopy be undertaken by experienced personnel, both to maximise ascertainment and because a wide variety of microscopic structures can be confused with *Cryptosporidium* oocysts. Repeat sampling may improve ascertainment. Antigen detection assays may be available and have increased sensitivity, although some may have lower specificity.

Molecular testing (e.g. PCR) is now able to split human infections into *Cryptosporidium hominis* ('genotype 1'), which is found only in humans and *C. parvum* ('genotype 2'), found in animals, particularly cattle, and humans Rarely other cryptosporidia, such as *Cryptosporidium cuniculus* and *Cryptosporidium meleagridis* may be identified. Further genotyping may be available to provide detailed strain discrimination from some reference laboratories.

Transmission

Cryptosporidium parvum has been demonstrated in a wide variety of animals including cattle, sheep, goats, horses, pigs, cats, dogs, rodents and humans. Clinical disease and most oocyst excretion are thought to occur mainly in young animals. Transmission to humans is by faeco-oral spread from animals or other humans. The main routes of spread are:

Person to person

Cryptosporidiosis can be transmitted by cases to family members, nursery contacts, carers and sexual partners. Spread can be direct faeco-oral or via contaminated items such as nappies. *C. hominis* cases have higher excretion levels than *C. parvum*, although both are transmissible. Aerosol or droplet spread from liquid faeces may also occur. Secondary spread in households is common and may occur after resolution of clinical symptoms in the index case. Many outbreaks have been reported in nurseries.

Animal to person

Human infection with *C. parvum* may occur from contact with farm or laboratory animals and, occasionally, household pets. In addition to agricultural and veterinary workers, those at risk include children visiting farms on educational or recreational visits where they may handle lambs or calves. A number of outbreaks associated with such visits have been reported.

Drinking water

Contamination of drinking water may occur from agricultural sources or human sewage contamination. Oocysts passed in faeces can survive in the environment for months. They are resistant to chlorination and their removal relies on physical methods of water treatment such as filtration, coagulation and sedimentation. Over 50 drinking water related outbreaks have been reported in the UK and large water-borne outbreaks have been reported in other EU countries, but the largest such outbreak occurred in Milwaukee, USA in 1993 when an estimated 400 000 people became ill. A review of the UK outbreaks found a common thread of an inadequacy in the treatment provided or of the operation of the treatment process.

Other

Infection has been reported via food, such as salad, raw vegetables and milk. Many swimming pool outbreaks have been reported, usually as a result of faecal contamination of water and inadequate pool maintenance. Transmission has been reported from health care workers to patients (both immunosuppressed and immunocompetent) and between patients. About 13% of UK cases are associated with foreign travel, most commonly to holiday destinations in the Mediterranean or visits to the Indian subcontinent.

Acquisition

The incubation period is unclear: five to seven days would seem to be average, but a range spanning 1–30 days has been reported. The infectious period commences at onset of symptoms and may continue for several weeks after resolution. The infective dose can be as low as 10 oocysts in some cases (thus enabling autoinfection) with an ID_{50} of around 100 oocysts. The UK Expert Group found it was not possible to recommend a health-related standard for *Cryptosporidium* in drinking water. In immunocompetent individuals the immune response successfully limits the infection. AIDS patients are at increased risk of acquisition and increased severity. Relative immunosuppression due to chickenpox and malnutrition has also been associated with infection, but renal patients

do not appear to be at increased risk. Oocyst excretion may be very high in the immunosuppressed.

Prevention

- Handwashing after contact with faeces, nappies and animals (take particular care in contact with these if immunosuppressed).
- Safe disposal of sewage, taking particular care to avoid water sources.
- Risk assessment for water supplies, protection against agricultural contamination, adequate water treatment (e.g. coagulation aided filtration) and monitoring of water quality, particularly turbidity.
- Enteric precautions for cases (Chapter 1.3) and exclusion of those in at-risk groups (Box 2.2.1).
- Immunosuppressed patients to boil water (both tap and bottle) before consumption and avoid contact with farm animals and infected humans.
- Guidelines for farm visits by children have been developed and can be adapted for local use (e.g. Health and Safety Executive, UK). Guidelines have also been developed for swimming pools (e.g. Pool Water Advisory Group, UK).
- Cryptosporidium is resistant to many common disinfectants. Ammonia, sodium hypochlorite, formalin, glutaraldehyde and hydrogen peroxide may be effective. Heating to 72 °C for one minute inactivates the parasite.

Surveillance

- All gastrointestinal infections thought to have been acquired from food, water or public areas should be reported to local public health authorities and confirmed *Cryptosporidium* cases reported to national surveillance systems: reporting is mandatory in many EU countries, including the UK.
- The most important function of surveillance of cryptosporidiosis is the detection of outbreaks, particularly water-borne outbreaks. All diarrhoeal samples should be examined for oocysts (unless a bacterial or viral cause has already been identified) and all positives reported. Home postcode should be collected on all cases to be plotted on water supply zone maps, which can provided by water providers and need regular updating. Trigger levels can be calculated for districts and regions: a seasonal baseline can be set, based on historical data with confidence intervals. High figures for one week only may be the result of reporting delay (look at dates of onset). The age-distribution of cases should also be monitored.
- Water providers should also undertake appropriate monitoring of water quality and inform the local public health authorities of potentially significant failures, for example levels of one oocyst per 10 l of water (see Box 3.16.1).

Response to case

- Enteric precautions for case (see Boxes 1.3.1 and 1.3.3).
- Exclude from work/school if in risk group (Box 2.2.1) until 48 hours after first normal stool. No microbiological clearance necessary.
- Cases should not use swimming pools until two weeks after first normal stool.
- Investigate illness in family or other contacts.
- Obtain history of raw water consumption (including postcodes of premises on which consumed and any consumption from private water supplies), contact with other cases, contact with animals, nurseries, swimming pools, travel and food consumption in previous 14 days.

Investigation of cluster

- Check to see if neighbouring areas, particularly those sharing a water supply, have an increase.

Box 3.16.1 Response to detection of oocysts in water supply

The relationship between oocyst counts and the health risk to those who drink the water is unclear. However the water companies in the UK will inform public health authorities of breaches in water quality standards. An appropriate response would be (based on Hunter, 2000):

Collect information for risk assessment:

- When and where sample taken.
- Number of oocysts detected and results of any viability testing.
- Results of repeat testing (should be done urgently).
- Source and treatment of affected water supply.
- Any recent changes in source or treatment.
- Distribution of water supply.
- Any treatment failure or high turbidity identified?
- How long water takes to go through distribution system.
- History of *Cryptosporidium* sampling and results for this supply.
- Any previous outbreaks associated with this supply.

For a low oocyst count in a supply in which oocysts frequently detected and not associated with previous outbreaks, further action may not be necessary.

Call Incident Management Team if significant exposure is likely, for example:

- Unusually high oocyst count or demonstration of viability.
- Evidence of treatment failure or increased turbidity.
- Groundwater source.
- Association with previous outbreaks.

Possible actions:

- None.
- Advice to particular groups.
- Enhanced surveillance for human cases.
- Provision of alternative water supply.
- 'Boil water' notice to affected area.

'Boil water' notices are issued if risk is thought to be ongoing, for example:

- Repeat samples positive.
- Treatment or turbidity problems continue.
- Contaminated water not yet cleared from distribution system.

- Check age-range of affected cases: an increase in cases in adults could suggest water-borne infection, link with immunosuppressed patients or travel abroad. If most cases are in children, consider visits to farms or swimming pools and, if increase in under-fives, links to nurseries.
- Epidemic curve may suggest point source, continuing source or person-to-person spread.
- Check with water provider whether any recent evidence of increased contamination or failure of treatment.
- Plot cases by water supply zones. Check with water provider how cases relate to water sources (e.g. reservoirs, treatment centres) during relevant period: supply zones are not fixed and some areas may also receive water from mixed sources.
- Collect and review risk factor details from individual cases for hypothesis generation and further investigation as appropriate (see Chapter 4.2). Case finding may also be necessary.
- Organise confirmatory testing and genotyping by reference laboratory. If *C. hominis*,

look for potential human sources; if *C. parvum*, consider animal and human sources. Discuss whether more detailed genotyping is available.

Control of an outbreak

- If a water-borne outbreak likely then:
  - **(a)** Issue 'boil water' notice if contamination likely to be ongoing. A communications plan should already exist for public information. Water needs only to be brought to the boil: prolonged boiling is not necessary.
  - **(b)** Organise Outbreak Control Team to include relevant water company specialists/managers and Local Authority. If potentially serious, add appropriate experts. The addition to the team of an individual who has dealt with such an outbreak before should be considered.
  - **(c)** Consult Bouchier report in UK (see Appendix) for more detailed advice.
- Exclude symptomatic cases in risk groups (Box 2.2.1).
- Advise public on how to prevent secondary spread.
- Institute good practice guidelines at any implicated nursery, farm, swimming pool or hospital.

Suggested case-definition for analytical study of an outbreak

(a) *Cohort study* (e.g. nursery, school class):
Clinical: Diarrhoea within 1–14 days of exposure.
Confirmed: Diarrhoea and oocysts seen in faecal specimen or PCR/antigen positive.

(b) *Case–control study* (e.g. general population):
Diarrhoea plus oocysts (of correct genotype, if known) in faeces, with no other pathogen isolated, no previous cases of diarrhoea in family in last 14 days and date of onset since commencement of increase in cases.

3.17 Cyclosporiasis

Cyclospora cayetanensis is a protozoan parasite that causes human gastroenteritis.

Epidemiology

Infection is uncommon in Europe, with most cases related to travel to tropical or subtropical areas, such as Central America, South America, the Indian subcontinent and south-east Asia. Outbreaks may also occur from contaminated imported food.

Clinical features and diagnosis

Almost all cases have diarrhoea (usually watery) and most report anorexia, weight loss, fatigue, flatulence, nausea and abdominal pain. Headache, vomiting, fever, myalgia and constipation may also occur. Bloody diarrhoea is rare. Symptoms may be prolonged and relapses may occur. Illness may be more severe or prolonged in the immunosuppressed. Asymptomatic infection is possible, particularly after repeated exposures, for example in endemic areas.

Diagnosis is confirmed by detection of spherical oocysts of 8–10 μm diameter in faeces or by PCR. If *Cyclospora* is suspected, inform the laboratory, so that stool concentration can be carried out and the use of UV light or modified ZN stain considered. Repeat sampling may be required.

Transmission and acquisition

Humans are, so far, the only host species identified for *C. cayetanensis*. Oocysts are excreted in a non-infective unsporulated form; sporulation takes about 7–15 days in the environment (preferably at 22–32 °C) and infection results from ingestion of mature sporulated oocysts. Spread is therefore indirect via vehicles such as food, water and soil; person-to-person spread is unlikely. Oocysts are resistant to chlorination

and freezing, but are removed by water filtration and killed by adequate cooking. The infectious dose is unclear, but probably low. Outbreaks in developed countries have been associated with berries, salad vegetables and herbs, usually imported from endemic countries, with attack rates of about 90% for those consuming the implicated food. The incubation period is usually 5–9 days (median 7), with extremes of 1–19 days reported.

Prevention and response

Prevention and control in developed countries relies on sanitary disposal of faeces and advice to travellers. Should a cluster of cases occur within Europe, ask each case about travel abroad: if no history of travel, then take a food history asking specifically about raw fruit, salad, vegetables, herbs and imported food.

3.18 Cytomegalovirus

Infection with Human Cytomegalovirus (HCMV, Human Herpesvirus 5 [HHV-5]), a herpes virus, is frequently silent, but can also cause a variety of symptoms. Its major impact is in the newborn and the immunocompromised.

Suggested on-call action
No need for urgent action, but check for possible iatrogenic transmission (blood transfusion, transplantation).

Epidemiology

The prevalence of CMV rises with age: in Europe 60–90% of adults have antibodies. Prevalence is highest in lower socio-economic groups and in immigrants from areas of high endemicity. In Europe prevalence is highest around the Mediterranean basin. Congenital infections occur in 0.5–2% of all births.

Clinical features

In immunocompetent individuals most infection is asymptomatic. Occasionally a glandular fever like illness occurs. Rare complications include hepatitis and the Guillain–Barré syndrome. In the (cellular) immunocompromised, infection or reactivation of latent infection can disseminate, leading to interstitial pneumonia and hepatitis, and in HIV-infected individuals with low CD4, to colitis, retinitis and encephalitis.

Congenital infection may cause a variety of adverse pregnancy outcomes ranging from low birthweight, to severe brain damage, stillbirth, and perinatal death. Infection early in pregnancy has the highest risk. Infection in the third trimester rarely causes symptoms in the child. In some, the first symptoms show in the post-neonatal period: hearing loss, deafness, chorioretinitis, psychomotor retardation, convulsions. Later signs can include language and learning difficulties.

Most postnatal infections are asymptomatic, but in premature neonates, it can lead to pneumonia, hepatitis and thrombocytopenia; although CNS complications do not occur in this group.

A post-transfusion syndrome, resembling infectious mononucleosis, can develop following transfusion with infected blood.

Laboratory confirmation

In immunocompetent individuals, serology (IgM and fourfold rise in IgG) is sensitive. Specificity differs per test. CMV-IgG avidity testing can assist in defining the infection phase. CMV may be isolated from urine and other body fluids and tissues. CMV is excreted periodically by individuals without active disease. The demonstration of active disease may require biopsy. CMV-PCR is used to monitor infection in immunocompromised individuals. To diagnose fetal infection, amniotic fluid is tested with CMV PCR.

Transmission

Once infected, people excrete CMV periodically and transmit the virus through body fluids, blood, or transplanted organs. In the newborn, infection may have been acquired transplacentally or during birth. Most transmission takes place in early life through close contact. High-risk professions are those working with children.

Pathogenesis

The incubation period for transfusion or transplantation of CMV mononucleosis is 2–4 weeks; for other transmission routes 4–12 weeks. After infection CMV can be found in leucocytes, salivary glands and kidneys; in symptomatic patients, the liver, lungs and CNS may also be infective. After primary infection CMV will be excreted periodically for a few days by the majority of cases, but infectivity of body fluids may persist for many months.

Prevention

- Screening of transplant donors for active disease.
- Thrombocyte and erythrocytes concentrates should be reduced in leucocytes, minimising transmission risk. To prevent transmission by intrauterine transfusions, specific blood donors should be anti-CMV negative, and not incubating disease.
- Risk assessment for those receiving transplantation and consideration of antiviral prophylaxis.
- In healthcare and childcare institutions, standard hygiene precautions are essential, especially after contact with urine or saliva of children.
- Promising results of vaccine studies in guinea pigs have not yet resulted in vaccines close to licensure.

Surveillance

No need to report individual cases, other than through routine laboratory surveillance.

Response to a case

- Exclude iatrogenic transmission following transplantation or administration of blood products. Otherwise, no public health response is usually necessary.
- Standard hygiene precautions suffice for high-risk professions and for pregnant employees. However, in certain situations temporarily change of working environment for seronegative pregnant women should be considered.
- Treatment options include antivirals (ganciclovir), foscarnet and immune globulins.

Investigation of a cluster and control of an outbreak

Investigate to ensure that it is not caused by exposure to contaminated blood or blood products.

Suggested case definition for an outbreak

Pregnancy: laboratory confirmation following symptomatic disease or exposure to case.
Fetal: CMV PCR on amniotic fluid six weeks after maternal infection.
Neonatal: clinically compatible disease with laboratory confirmation.
Adult: clinically compatible disease with laboratory confirmation.
Laboratory confirmation may be by serology (IgM or fourfold rise in IgG), PCR, isolate or antigen detection.

3.19 Dengue fever

Dengue fever is a febrile disease caused by a flavivirus with four distinct serogroups and transmitted by the bite of *Aedes* mosquitoes.

Suggested on-call action
None usually necessary

Epidemiology

Dengue fever is endemic throughout the tropics and subtropics. A dramatic increase in the incidence has been seen worldwide. The WHO estimates that currently every year around 390 million people get infected of which around 96 million develop dengue fever. An estimated 500 000 people with severe dengue need hospitalisation each year, most of which are children. Dengue haemorrhagic fever is most common in children less than 10 years old from endemic areas. In 2012–2013, there was a large dengue outbreak in the autonomous province of Madeira, Portugal, with more than 2000 probable cases. In 2014, around 1800 cases were reported in Europe. Most cases were reported in Germany (626), the UK (376), France (212) and Belgium (110). Almost half the dengue fever cases imported into Europe come from Asia. Some recent studies suggest that some illnesses labelled as dengue may have been caused by flaviviruses such as Zika virus or alphaviruses.

Clinical diagnosis

Dengue presents with an abrupt onset of fever, chills, headache, backache and severe prostration, but up to 40–80% of cases may be asymptomatic. Aching in the legs and joints occurs during the first hours of illness. Fever and symptoms persist for 48–96 hours, followed by rapid defervescence, after about a further 24 hours, a second rapid temperature rise follows (saddleback temperature). Typical dengue fever is not fatal.

In Dengue Haemorrhage Fever (DHF), bleeding tendencies occur with shock two to six days after onset. Mortality for DHF ranges from 6 to 30%; most deaths occur in infants less than one-year-old.

Laboratory confirmation

Serologic diagnosis may be made by haemagglutination inhibiting and complement fixation tests, using paired sera.

Transmission

Spread by mosquito bites (e.g. *Aedes aegypti*).

Acquisition

The incubation period is 3–15 days. Human-to-human spread of dengue has not been recorded, but people are infectious to mosquitoes during the febrile period.

Prevention

- Avoidance of mosquito bites, for example with bed nets and insect repellent.
- Control or eradication of the mosquito vector.
- To prevent transmission to mosquitoes, patients in endemic areas should be kept under mosquito netting until the second bout of fever has abated.
- In December 2015 a first Dengue vaccine was registered in Mexico.

Surveillance

- Public health officials should be informed of individual cases. Dengue haemorrhagic fever is a reportable disease under EU legislation.

Response to a case

- Isolation not required.
- Specimens should be taken using universal precautions and the laboratory informed.

Investigation of a cluster and control of an outbreak

- Not relevant to European countries.

Suggested case-definition

A clinically compatible case confirmed by
- growth from or demonstration of virus in serum and/or tissue samples by immunohistochemistry or by viral nucleic acid detection; *or*
- demonstration of a fourfold or greater rise in IgG in paired samples or IgM antibody titres to one or more dengue virus antigens in a single serum sample.

3.20 Diphtheria

Diphtheria is an infection of the upper respiratory tract, and sometimes the skin. In Europe it is caused by toxin-producing (toxigenic) strains of *Corynebacterium diphtheriae* and *Corynebacterium ulcerans*, and rarely by *Corynebacterium pseudotuberculosis*. It is a rare infection, but potentially fatal if untreated.

Suggested on-call action

- Obtain full clinical details, travel and vaccination history.
- Liaise with both local and reference labs to ensure rapid diagnosis and toxigenicity testing.
- Prepare list of close contacts.
- If diagnosis strongly suspected, arrange for immediate swabbing, chemoprophylaxis and vaccination of close contacts.
- Ensure case is admitted to specialist unit.

Epidemiology

Diphtheria is rare in countries with well established immunisation programmes. In the EU there were 65 laboratory-confirmed cases reported in 2015, of which 40 were due to *C. diphtheriae* and 25 were due to *C. ulcerans*. The notification rate was <0.01 per 100 000 population. The highest number of cases was reported from Latvia. Many cases were mild, in vaccinated individuals. The case fatality rate is 5–10%. Indigenous cases are very rare; Latvia is the only country in Europe with sustained indigenous transmission, which has continued for several years. The number of reported cases in Europe over the last five years has increased every year. Mild infections (usually sore throat) also occur due to non-toxigenic strains of *C. diphtheriae* and *C. ulcerans*; rarely more severe disease (endocarditis) can occur. Infections due to Non-Toxigenic, Tox-Gene Bearing (NTTB) *C. diphtheriae* have recently been identified in the UK, their significance is uncertain

Clinical features

Diphtheria is rarely recognised on clinical grounds, as many cases are in vaccinated individuals. In classical respiratory diphtheria, there is sore throat, fever, enlarged cervical lymph nodes and swelling of the soft tissues of the neck – the 'bull neck' appearance. The pharyngeal membrane, which is not always present, is typically grey, thick, and difficult to remove. There may be hoarseness and stridor. Nasal diphtheria usually presents with a bloodstained nasal discharge. Cutaneous diphtheria causes small ulcers, often on the legs. The disease is caused by a toxin that particularly affects the heart and nervous system. The effects of this toxin are irreversible and so early treatment (with antitoxin) is essential.

Laboratory confirmation

It is usually the identification of a *Corynebacterium* sp. from a nose or throat swab or skin ulcer that alerts the public health physician to the possibility of diphtheria. Any isolate of a potentially toxigenic *Corynebacterium* should be referred promptly to the national reference laboratory for confirmation and toxigenicity testing. Where the diagnosis seems likely, an acute serum

specimen should be obtained before giving antitoxin, and any skin lesions should be swabbed.

Transmission

Man is the only reservoir for *C. diphtheriae* and carriers are rare in vaccinated populations, so an infectious case is the usual source. Transmission is usually by air-borne droplets or direct contact with infected respiratory discharges or skin ulcers; rarely from contact with articles contaminated by discharges from infected lesions. Diphtheria is not highly infectious, although exposed cutaneous lesions are more infectious than nasopharyngeal cases. The normal reservoir for *C. ulcerans* is cattle; human infections are usually acquired through animal contact or by eating or drinking unpasteurised dairy products; recently contact with domestic companion animals has also been recognised as a source of infection

Acquisition

The incubation period is two to five days, occasionally longer. Cases are no longer infectious after three days of antibiotic treatment. Untreated cases are infectious for up to four weeks. The infectious dose is not known. Natural immunity usually (although not always) develops after infection. A substantial proportion of adults are non-immune and the proportion increases with age.

Prevention

- Vaccinate with diphtheria toxoid (usually combined with other routine antigens). A full primary course is three doses in the first year of life. Booster doses are recommended at varying intervals; the aim is to have five doses eventually. In some countries 10-yearly boosters are recommended.
- Boosters are recommended for travellers to countries where diphtheria is endemic or epidemic, and for laboratory and clinical infectious disease staff.

Surveillance

- The disease is notifiable throughout the EU, and co-ordination of European surveillance activities is undertaken by ECDC.
- Report immediately to the public health authorities on suspicion.

Response to a case

- Secure confirmation from reference laboratory. The priority is to determine whether the strain is toxigenic; this can be done within a few hours by PCR.
- All cases must be assessed by a suitably experienced physician. Unless there is strong clinical suspicion, other control measures can await confirmation of toxigenicity.
- Obtain vaccination history and possible source of infection (travel, animal contact, raw milk consumption).
- No control measures required for infections due to non-toxigenic strains, except for NTTB *C. diphtheriae* infections which should be considered as potentially toxin-producing).
- For confirmed or probable toxigenic infections, action is outlined in the following sections for case and contacts.

Measures for the case

- Arrange strict barrier nursing until microbiological clearance demonstrated (minimum two negative nose and throat swabs, at least 24 hours apart, the first at least 24 hours after stopping antibiotics).
- Secure microbiological clearance with a seven-day course of erythromycin (or other macrolide antibiotic) or parenteral penicillin. Give a booster or primary vaccination course (depending on vaccination status).
- Rapid treatment with antitoxin is vital. It is important to know how to access supplies of diphtheria antitoxin, including out of hours.

Measures for close contacts

- Close contacts include household and kissing contacts; this may be extended further, for example to school contacts if many of these less-close contacts are unvaccinated.
- Obtain swabs for culture from nose and throat, and any skin lesions.
- Monitor for seven days from last contact with case (daily measurement of temperature and examination of throat).
- Exclude food handlers, health and social care workers and those with close contact with unvaccinated children from work until all swabs shown to be negative.
- Give a seven-day course of erythromycin (or another macrolide antibiotic).
- Obtain further nose and throat swabs after course of antibiotics and repeat course if still positive.
- Give a booster or primary vaccination course (depending on vaccination status). A booster should be given if more than 12 months have elapsed since the last dose.
- Infections due to toxigenic *C. ulcerans* should be treated the same as *C. diphtheriae*, as there is some evidence that person-to-person transmission may occur.
- No public health action required for infections due to non-toxigenic *C. diphtheriae* (except NTTB strains), although the patient should be treated with penicillin or erythromycin if symptomatic.

Investigation of a cluster

- Investigate possible common links and sources (travel, animals).

Response to an outbreak

- As for an individual case, but in addition consider the need for a community-wide vaccination programme.
- Prepare for media interest and disseminate public information widely.

Suggested case-definition for an outbreak

Laboratory evidence of infection due to toxigenic *C. diphtheriae* or *C. ulcerans*, in a patient with compatible symptoms. Sore throat only in a vaccinated individual is a compatible symptom.

3.21 Enterococci, including Glycopeptide-Resistant Enterococci (GRE)

Enterococci, including the species *Enterococcus faecalis* and *Enterococcus faecium*, are part of the normal bacterial flora of the gastrointestinal tract. They are usually harmless and more frequently cause colonisation but can cause a range of infections especially in immunocompromised and hospitalised persons. These include wound infection, urinary tract infection, intra-abdominal infection, bacteraemia and endocarditis. Enterococci have intrinsic resistance to several antibiotics and they are also capable of acquiring resistance from other organisms through transferable plasmids, transposons or mutations. By the mid-1980s resistance to commonly used antibiotics was widespread, leaving only glycopeptides (vancomycin and teicoplanin) available for treatment. In 1986, Glycopeptide Resistant Enterococci (GRE) (also known as vancomycin resistant enterococci) were reported and have since spread to many hospitals. This growing antibiotic non-susceptibility among enterococci, their ability to transfer vancomycin resistant genes to other organisms and to cause prolonged hospital outbreaks, has seen them gain increased prominence as nosocomial pathogens. Globally, the increasing trend in reports of vancomycin-resistant *E. faecium* led to its inclusion in the World Health Organization's list of priority pathogens in need of new antibiotics.

Suggested on-call action

The local public health team should be prepared to assist the hospital infection control team to investigate and control nosocomial outbreaks of enterococcal infections.

Epidemiology

In EU countries, acute care organisations take part in the Healthcare-Associated Infections Surveillance Network (HAI-Net), a European network for the surveillance of Healthcare-Associated Infections (HCAI). In 2015, the proportion of intensive care unit bacteraemias caused by *Enterococcus* spp varied from 21% in Belgium and 20% in Germany to 4.8% in the UK and 0% in Malta (only 16 isolates).

For 2015, the European Antimicrobial Resistance Surveillance Network (EARS-Net) reported that <5% of invasive *E. faecalis* isolates were non-susceptible to vancomycin, this ranged from 0% (Austria) to 4.4% (Romania). The proportion of invasive *E. faecium* isolates that were non-susceptible to vancomycin was 8.3%, this ranged from 0% (Estonia, Norway and Sweden) to 45.8% (Ireland)

In England, infections due to *Enterococcus* spp. initially fell from a peak of 7627 in 2006 to 5397 in 2010 and then increased to 6783 in 2016, which is equivalent to a rate of 12.4 per 100 000 population. Mandatory reporting of bacteraemias due to glycopeptide-resistant enterococci was discontinued in England in 2013. Data from voluntary laboratory surveillance shows that the proportion of isolates with vancomycin resistance among all *Enterococcus* spp. from bacteraemia in England and Northern Ireland increased each year from 12% in 2012 to 17% in 2015 before decreasing to 15% in 2016.

Clinical features

Enterococcal bacteraemia is a common presentation and should be suspected in any case of sepsis in critically ill hospitalised patients, particularly those with severe underlying disease. GRE bacteraemias (especially if caused by *E. faecium*) may be associated with a poorer clinical prognosis compared with non-GRE bacteraemia.

Laboratory confirmation

Appropriate microbiological investigation is essential to accurately identify enterococci and detect glycopeptide resistance. Enterococci are often detected in mixed culture where the clinical significance is unclear. Molecular methods such as PFGE can be used for typing isolates.

Transmission

- The lower gastrointestinal tract is the main reservoir: most human infection is endogenous.
- Transmission occurs through direct contact with infected or colonised patients, or indirectly via the hands of healthcare workers, contaminated equipment or environmental surfaces.
- Animal strains of GRE may colonise GI tract of humans via contaminated food.

Acquisition

- Stool carriage may persist for months or years.
- Risk factors include prior or prolonged antibiotic therapy (glycopeptides or cephalosporins), prolonged use of medical devices such as urinary or intravenous catheters, immunocompromise, prolonged hospital stay, surgery procedures such as abdominal or chest surgery, admission to intensive care or other specialist units.

Prevention

- Effective antimicrobial stewardship arrangements to ensure appropriate use of antibiotics in medical and veterinary practice.

- Heightened awareness in persons who have received medical care overseas.
- Implementation of appropriate infection control (contact precautions and source isolation).
- Targeted screening of high-risk patients such as those with prior GRE positivity and persons admitted to intensive care units, haematology/oncology and transplant units.

Surveillance

- Cases should be reported to existing national surveillance schemes and clinical isolates may be submitted to the appropriate reference microbiology unit for antibiotic susceptibility testing and typing.
- Periodic point prevalence surveys of antibiotic susceptibility.

Response to a case

- Treatment is with a combination of bactericidal antibiotics guided by sensitivity testing.
- Removal of urinary or invasive catheters and drainage of abscesses may be necessary.
- Attempted clearance of carriage by oral therapy is usually unsuccessful and is not recommended.
- Screening staff for stool carriage is not advised.
- Emphasise hand and environmental hygiene.
- Implement infection control measures based on clinical risk assessment.
- Patients with GRE (especially where there is diarrhoea or incontinence) should be isolated in single rooms or cohort nursed in bays on the open ward.
- When a patient with GRE is transferred to another institution, inform clinical and infection control staff.

Investigation of a cluster

Isolates from both infected and colonised patients should be typed: hospital outbreaks can involve a single or multiple strain types whereas community strains are usually of multiple types.

Control of an outbreak

- Reinforce measures for a single case.
- Active surveillance cultures to identify colonised patients (faecal samples are the most useful screening specimen followed by rectal swabs).

Suggested case-definition
Cases are defined microbiologically, based on the results of culture and antibiotic sensitivity

3.22 Enterovirus infections (including hand, foot and mouth disease)

Non-polio enteroviruses are a diverse group of non-enveloped RNA viruses in the family *Picornaviridae*. There are over 100 serotypes of Enteroviruses (EV) identified in humans and are classified into four species namely EV-A to EV-D. The most common enteroviruses are coxsackieviruses A and B and echovirus. Non-polio enteroviruses cause a range of clinical syndromes, including Hand-Foot-and-Mouth Disease (HFMD), aseptic meningitis, acute flaccid paralysis, myocarditis, and respiratory disease.

For poliovirus infections, see Chapter 3.56.

Suggested public health on-call action
None generally needed.

Epidemiology

Infection may be sporadic or epidemic. The incidence of non-polio enterovirus infections in EU/EEA countries is unknown. There is a lack of reliable surveillance data on HFMD in Europe in the last 20 years: a study in the Netherlands of neonates in intensive care units (1993–1995) estimated an annual incidence of 26 per 100 000 neonates. In the UK, data for the period 2015–2017 from the Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) database shows that HFMD among persons aged four years and under has been relatively stable at around 2400 per 100 000 GP consultations per year.

The epidemiological pattern observed in Europe differs from Asia. In temperate climates, enterovirus infections are seasonal with the highest incidence in summer and autumn. However, infection can occur all year with epidemic peaks at intervals of two to five years. There is evidence of spread of epidemic serotypes across Europe in certain years. Outbreaks of A9 were reported in the UK and A71 in Bulgaria and Hungary in the 1970s. A16 was epidemic in the UK in 1981 and there has been an increase in cases of severe acute neurological conditions caused by EV-D68 in North America and some European countries in 2016.

Clinical Features

Most cases are asymptomatic or experience mild febrile illness that may include rhinorrhoea, skin rash and myalgia (see Table 3.22.1). HFMD is usually due to coxsackievirus A16 and is a mild illness with fever and a vesicular rash in the mouth and on the palms, soles and buttocks. HFMD due to a closely related virus, enterovirus A71, has been known to cause widespread and severe HFMD outbreaks including one with associated neurological involvement in Catalonia in 2016.

Laboratory confirmation

Non-polio enteroviruses are diagnosed using RT-PCR. Virus isolation is labour-intensive and time-consuming and not practical for clinical decision-making. Serological tests and molecular typing are available.

Transmission

Human clinical and subclinical cases are the reservoir of infection. Spread is by direct contact with faeces, saliva, sputum and respiratory droplets or blister fluid from an infected person. Enteroviruses may also spread indirectly via environmental water and sewage.

Acquisition

The incubation period is three to ten days. Cases are infectious during the acute illness and for several weeks while the virus persists in the faeces. Non-polio enteroviruses can be shed in stool for several weeks or longer after infection. The virus can also be shed from the respiratory tract for one to three weeks or less.

Children are at highest risk of infection because they do not yet have immunity from previous exposures to these viruses.

Pregnant women infected with a non-polio enterovirus shortly before delivery may pass the virus to their baby. These babies usually have only mild illness, but in rare cases they develop severe infection.

Infection generally leads to immunity, although infection with different serotypes may occur.

Prevention

- Standard and enteric precautions, particularly hand washing and hygienic disposal of faeces, will reduce spread.

Table 3.22.1 Clinical syndromes caused by selected non-polio enteroviruses

Coxsackievirus A24	Acute haemorrhagic conjunctivitis	Subconjunctival haemorrhages and lid oedema.
Coxsackievirus B	Epidemic myalgia (Bornholm disease)	Chest or abdominal pain aggravated by movement and associated with fever and headache. Outbreaks have been reported.
Coxsackievirus A16	Hand, foot and mouth disease	A mild infection with ulcers in the mouth and a maculopapular or vesicular rash on the hands, feet and buttocks. Systemic features and lymphadenopathy are absent and recovery is uneventful.
Coxsackievirus A17	Acute Flaccid Paralysis (AFP) or Acute Flaccid Myelitis (AFM)	Prodromal fever or fever at the time of onset of paralysis is less frequently reported than poliomyelitis.
Coxsackievirus A16 and Coxsackievirus B	Herpangina	Acute febrile illness with dysphagia due to vesicles and shallow ulcers on tonsils and soft palate, abdominal pain and vomiting.
Coxsackievirus B and Echoviruses	Acute Viral Meningitis Encephalitis	Fever with signs and symptoms of meningeal involvement. Encephalitic signs may be present.
Coxsackievirus EV-B (B1-B6)	Myocarditis Pericarditis	Most often associated with heart disease. Heart muscle necrosis varies in extent and severity. Heart failure may follow. Most patients with viral myocarditis recover fully. Treatment is largely supportive.
	Skin	Rashes are common including a fine pink rubella-like rash or petechial, purpuric, vesicular, bullous or urticarial rashes. Onychomadesis (complete nail shedding) has been described
Enterovirus D68 (EV-D68)	Severe acute respiratory illness	During 2014, EV-68 caused outbreaks of severe respiratory illness among children, many whom had asthma or a history of wheezing

Surveillance

- Sporadic cases will not normally be reported to public health authorities, but clusters of cases and outbreaks should be reported.
- Use existing non-polio enterovirus surveillance system to monitor trends

Response to a case

- Children with HFMD may attend school or nursery when well enough.

Investigation of a cluster and control of an outbreak

- The local public health team may wish to alert local schools and general practitioners if an outbreak of HFMD occurs or other conditions caused by a non-polio enterovirus.

Suggested case definition
Characteristic clinical appearance with or without laboratory confirmation

3.23 Epstein–Barr Virus

Epstein–Barr Virus (EBV), also known as Human Herpesvirus 4 (HHV-4), a member of the herpesvirus family, is the main cause of infectious mononucleosis (glandular fever, kissing disease, Pfeiffer's disease). EBV is also associated with Burkitt's lymphoma in African patients, nasopharyngeal carcinoma in South-East Asia and Northern Africa, several other neoplasias, and autoimmune conditions.

Suggested on-call action
No action generally needed.

Epidemiology

In countries where there is overcrowding and poor hygiene, 90% of children have serological evidence of EBV infection by the age of two years. In developed countries, infection is delayed until adolescence (kissing age) and early adult life.

Clinical features

Most infections result in asymptomatic seroconversion. Worldwide, the clinical features of infectious mononucleosis are tiredness, fever, tonsillitis (75–90%), lymphadenopathy (80–90%), splenomegaly (50%), and hepatomegaly (12%). Up to 80% of patients have moderately elevated hepatic transaminases, but less than 10% have jaundice. Most people recover in two to four weeks but recovery can take several months. Rare complications are myocarditis, splenic rupture (0.1–0.5%), hepatitis, and neurological complications. A temporary erythematous rash occurs in cases who have received ampicillin. Young children generally have a mild non-specific illness. In the immune compromised the infection can persist (Severe Chronic EBV infection, SCEBV), and in EBV-negative transplant patients Post-Transplant Lymphoproliferative Disorder (PTLD) can occur. The possible relationship between primary infection during pregnancy and congenital abnormalities is controversial.

Laboratory confirmation

Diagnosis is confirmed by the finding of atypical mononuclear cells in the peripheral blood. Heterophile antibody tests such as the Paul–Bunnell or Monospot tests generally have low sensitivity but are often used as first line tests. Tests for IgM and IgG to EBV viral capsid antigen, and tests for EBV nuclear antigen can distinguish between primary and latent infection.

Transmission

Once infected, people shed the virus periodically without having symptoms, thereby causing most new cases as a result of contact with saliva, either directly during kissing or indirectly on hands or fomites. Attack rates may be as high as 50%. EBV can also be spread in blood transfusions, and occasionally transmission is reported through semen and organ transplantation.

Acquisition

The incubation period is four to six weeks. After acute infection the virus remains latent in B lymphocytes in the immune system and a person may remain infectious for up to 18 months because EBV is excreted in saliva. Lifelong immunity follows infection, although latent infection can reactivate, especially in the immunosuppressed.

Prevention

Health education and hygienic measures where practical may reduce exposure to saliva, especially from infected persons.

Surveillance

Reporting of cases is not generally required.

Response to a case

Exclusion of cases is not necessary. Although evidence is lacking, it is prudent to recommend that strenuous physical exercise is avoided for three to eight weeks after the onset of illness and that contact sports are avoided until there is no evidence of splenomegaly.

3.24 Giardiasis

Giardia lamblia, also known as *Giardia intestinalis* or *Giardia duodenalis*, is a protozoan parasite that causes intestinal infection throughout the world. In developed countries the illness is particularly associated with water-borne outbreaks, nurseries and other institutions, and travel abroad.

Suggested on-call action

- Exclude symptomatic cases in risk groups.
- If linked cases, consult outbreak control plan.

Epidemiology

Prevalence rates (including asymptomatic excretion) of between 2 and 7% have been demonstrated in developed countries. A study in England and Wales found only about one-fifth of cases were reported to national surveillance. The annual rate for reported cases in most of Europe is about 5 per 100 000. Cases occur at all ages, with children under five years having the highest incidence in surveillance data and an excess in males is reported. Cases occur throughout the year, with a small peak around September. Travellers abroad (particularly to lower-income countries), refugees, residents of institutions, and men who have sex with men are reported to be at higher risk.

Clinical features

Symptomatic diarrhoea may be accompanied by malaise, flatulence, foul-smelling greasy stools, abdominal cramps, bloating, nausea, anorexia and weight loss. Vomiting occurs in about a quarter and fever in about an eighth, but blood or mucus in stool is unusual. Prolonged diarrhoea, malabsorption and weight loss may occur, especially in children, and may be particularly suggestive of giardiasis. Symptoms (and excretion) may be intermittent. The duration of illness is variable, with a range of 1–90 days reported (average two to three weeks). Asymptomatic infection is also a common outcome of exposure: a prevalence of asymptomatic carriers of about 3% has been reported in two European studies.

Laboratory confirmation

Giardia infection is usually confirmed by microbiological examination of fresh stool samples for cysts, although testing for *Giardia* may not be performed unless specifically requested. A single stool sample will identify only about 60% of those infected but three samples (preferably taken on non-consecutive days) will identify over 90% (NB, excretion can be intermittent). Cysts may not yet be present at the onset of disease, so early negatives may need to be repeated later before infection can be excluded. Antigen assays are now available and are more sensitive and specific than microscopy. PCR is also available in some laboratories and is highly sensitive.

Transmission

Giardiasis results from faeco–oral transmission of *Giardia* cysts. This can occur directly or via food or water. Humans appear to be the main

source for *G. lamblia* infection in other humans, although zoonotic transmission does occur (possibly just for assemblage A strains). *Giardia* cysts are environmentally resistant and survive well in cold water. Water-borne transmission appears to be the most common route through faecal contamination of recreational or drinking water. Direct person-to-person spread is the other main route, particularly in children (both in families and nurseries) and between men who have sex with men. Outbreaks are also reported from nursing homes and day care centres. Food-borne outbreaks, often linked to infected food handlers, occur, but are not common.

Acquisition

The incubation period is usually 5–16 days (median 7–10), but extremes of 1–28 days have been reported. The pre-patent period may be longer than the incubation period, with a reported range of 10–36 days from ingestion to first excretion (this may be lower if more sensitive antigen assays used). Although average duration of excretion is about two weeks, it may persist for up to six months and may be intermittent. The exact risk from asymptomatic excretors is unclear, but as few as 10 cysts may cause infection (although 100–10 000 cysts are usually needed). Breast feeding has a protective effect; but there is increased susceptibility in those with reduced immunity or gastric acidity.

Prevention

Prevention of giardiasis is dependent on:

- Adequate treatment of water supplies; standard chlorination may not be sufficient to destroy cysts and should be supplemented by filtration, flocculation or sedimentation.
- Adequate control of infection and food hygiene practices in institutions, especially those dealing with children.
- Handwashing after toilet use and before preparing food.
- Advice to travellers abroad on safe food and water.

Surveillance

- Diagnosed cases should be reported to public health authorities: compulsory notification in many EU countries.

Response to a case

- Hygiene advice should be given.
- Cases in risk groups (Table 2.2.1) should be excluded until 48 hours after the first normal stool. Microbiological clearance is not necessary before return. Schoolchildren should ideally not attend school until they have had no diarrhoea for 24 hours. Ideally, other cases should not attend work or school until they have normal stools.
- Treatment of symptomatic cases. Metronidazole for five days or single dose tinidazole are both effective.
- Enteric precautions for cases in hospitals and care homes.
- Screening of symptomatic household contacts may identify individuals needing treatment.

Investigation of a cluster

Enquiries should include water consumption (compare to water supply zones), food sources, swimming pools or other recreational water, contact with day centres (especially for children) or other institutions, travel and (if cases mainly adult men) sexual contact.

Control of an outbreak

- Water-borne outbreaks are usually due to use of untreated surface water, inadequate water treatment (e.g. ineffective filtration) or sewage contamination. Geographic mapping of cases can help the local water company identify areas for further investigation.
- Outbreaks in nurseries and other institutions are controlled by enhanced infection control, especially supervised handwashing for

all children, and exclusion and treatment of all symptomatic children. Some would also recommend treatment of asymptomatic carriers: while this will help control the outbreak and prevent spread to community and family contacts, the benefit to the asymptomatic individual is unclear.

Possible case definition for an outbreak

Demonstration of cysts plus one of:
- Diarrhoea
- *or* 3 from bloating/flatulence, abdominal cramps, weight loss, nausea, smelly stools and fatigue.
- *or* Common exposure with acute cases (outside of family).

3.25 Gram-negative bacteraemia (including carbapenem-resistant enterobacteriaceae)

Gram-negative bacteria consist of a wide group of organisms that are capable of causing gastrointestinal infections, pneumonia, bloodstream infections (bacteraemia), and wound or surgical site infections in community and healthcare settings. These bacteria are resistant to several available antibiotics (multi-drug resistance) and have extensive mechanisms for acquiring new antibiotic resistance and transferring resistance genetic materials that allow other bacteria to develop antimicrobial resistance.

We focus on three Gram-negative bacteria of clinical and epidemiological importance namely *Escherichia coli* (*E. coli*), *Klebsiella* spp. and *Pseudomonas aeruginosa,* together with the associated problem of multi-drug resistant Gram-negative bacteraemia especially carbapenem-resistant enterobacteriaceae.

Suggested on-call action

The local public health team should be prepared to assist the hospital infection control teams to investigate and control nosocomial outbreaks of Gram-negative bacteraemia.

Epidemiology

Blood Stream Infections (BSI) caused by Gram-negative bacteria have increased considerably over the past decades across EU/EEA countries and are considered a healthcare safety issue. These bacteraemias are also increasingly multi-drug resistant, and in particular, there is a rising incidence of carbapenem resistance (for example in Southern Europe).

In England, *E. coli, P. aeruginosa and Klebsiella* spp. account for 72% of all Gram-negative BSIs; mandatory reporting of bacteraemias due to *E. coli* was introduced in 2011 in response to a growing incidence and reporting was expanded to include *P. aeruginosa and Klebsiella* spp. in 2017.

In 2016, the incidence of *E. coli* bacteraemia was 63.6 per 100 000 population, this represents a considerable increase compared to 2009 (43.7 per 100 000). The incidence of *Klebsiella* spp. bacteraemia has also increased slightly while that of *P. aeruginosa* bacteraemia has been relatively stable over a similar period. Some key epidemiological features of the various Gram-negative organisms are given in Table 3.25.1.

Laboratory confirmation

Appropriate microbiological investigation is essential to accurately identify Gram-negative organisms and antibiotic resistance mechanisms like carbapenemase enzymes. Typing of strains is available via molecular methods including whole genome sequencing.

Table 3.25.1 Key features of infection with specific Gram negative organisms

Disease/Organism	Epidemiology	Incubation period	Mode of transmission	Clinical features	Other features
Acinetobacter spp. (*Acinetobacter baumannii*)	Acinetobacter species can all cause human disease, but *A. baumannii* accounts for about 80% of reported infections. These infections commonly occur in healthcare settings (particularly intensive care units) and are rarely reported in the non-healthcare settings.	Varies depending on the site of infection.	Person-to-person spread usually on the hands of healthcare workers. Exposure to contaminated environments	It may cause colonisation (asymptomatic), pneumonia, wound infections and bloodstream infections.	Risk of infection is high among persons who are immunocompromised, have pre-existing health conditions, are hospitalised (particularly ventilated patients on ITU), prolonged hospital stay and patients with invasive devices like urinary catheters and intravascular cannula.
Escherichia coli	Majority (around 75%) of cases have their onset in the community and the main primary focus of infection is the urinary tract. *E. coli* BSI occurs all year round but has a seasonal peak in the summer months.	Few hours to two days	Person-to-person spread usually on the hands of healthcare workers. Contaminated water and food	Colonisation (asymptomatic), gastroenteritis, Urinary Tract Infections (UTIs), haemolytic uremic syndrome and bloodstream infections.	
Klebsiella spp. *(Klebsiella pneumoniae)*	*Klebsiella* bacteria are a normal part of the human gut flora (colonisation) and do not normally cause infection in healthy people. However, they are capable of causing a range of healthcare associated infections including pneumonia, bloodstream infections, surgical site infections and meningitis. Carbapenem resistance through production of carbapenemase enzyme (KPC-producing organisms) is a growing problem with some strains expressing the KPC gene.	Unclear but likely to be few days.	Person-to-person spread usually on the hands of healthcare workers. Exposure to contaminated environments	Pneumonia, UTIs, wound infections, infections of intravascular and other invasive devices, liver abscess, biliary tract infections, peritonitis, meningitis and blood stream infections.	

(*Continued*)

Table 3.25.1 (*Continued*)

Disease/Organism	Epidemiology	Incubation period	Mode of transmission	Clinical features	Other features
Pseudomonas spp. *(Pseudomonas aeruginosa)*	*Pseudomonas* spp. are ubiquitous in the environment. *P. aeruginosa* is the commonest type that causes human infection, usually in immunocompromised or hospitalised persons. However, healthy people can also develop mild illnesses especially after exposure to contaminated water.	Varies depending on the site of infection.	Endogenous acquisition in colonised persons and person-to-person spread usually on the hands of healthcare workers. Other common sources include environmental reservoirs/fomites such as contaminated recreational water, contaminated endoscopes and mechanical ventilation devices, sinks and shower heads. Contaminated food products may also be a source in community and nosocomial settings.	Colonisation, pneumonia, meningitis, bone and joint infections and bloodstream infections.	Risk is high in the immunocompromised, surgical and burns patients, prior hospitalisation, previous antimicrobial exposure, the elderly and invasive devices.

Carbapenem -resistant Enterobacteriaceae	Carbapenem-Resistant Enterobacteriaceae (CRE) are multi-drug resistant Gram-negative organisms. Enterobacteriaceae are a normal part of the human gut flora and CRE usually affects people in hospitals, long-term care facilities and other healthcare settings. In England, the number of carbapenemase producing enterobacteriaceae (CPE) isolates reported by the laboratory for Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) increased from 450 in 2010 to 2600 in 2016.	Varies depending on organism and the site of infection.	Transmission may occur in both healthcare and community settings. Transmission mode is dependent on the organism.	Varies depending on organism	Risk of infection is high in patients who with a history of previous hospitalisation (particularly in endemic countries), prolonged hospitalisation, catheterisation (urinary and/or vascular), ventilated, and/or on prolonged antibiotic courses (specific antibiotics).

Transmission

- The lower gastrointestinal tract is the main reservoir
- Spread can occur from infected or colonised patients, either directly or indirectly via the hands of medical and nursing staff, contaminated equipment or environmental surfaces.
- Animal strains of GRE may colonise the GI tract of humans via contaminated food.

Acquisition

- Most infection is endogenous.
- Stool carriage may persist for months or years
- Risk factors for healthcare associated infections include (not exhaustive): antimicrobial therapy within the previous 28 days, hospital admission within the previous 28 days, use of indwelling vascular access devices, urinary catheterisation, and invasive procedures (e.g. surgery including, but not restricted to, gastrointestinal tract surgery).

Prevention

- Prudent use of antibiotics in medical and veterinary practice.
- Heightened awareness in those who have received medical care overseas.
- Microbiology laboratory may consider routine active screening for carbapenem resistance among clinical isolates from high risk patients/settings. This may include intensive care units, patients with a history of having received medical care/transferred from healthcare settings or countries known to be endemic.
- Implementation of standard infection prevention/control measures and source isolation.

Surveillance

- Cases should be reported to national surveillance systems and isolates may be submitted to the appropriate reference microbiology units.
- Periodic in-hospital point prevalence surveys may be required.

Response to a case

- Treatment is with a combination of antibiotics guided by sensitivity testing (colonisation is more frequent than infection).
- Removal of urinary and intravascular catheters and drainage of abscesses may be necessary.
- Attempted clearance of carriage by oral therapy is usually unsuccessful and is not recommended.
- Screening staff for stool carriage is of no value.
- Emphasise hand hygiene and ward cleaning.
- Implement infection control measures based on clinical risk assessment.
- Patients should be isolated in single rooms or cohort nursed in bays on the open ward.
- When a patient is transferred to another institution, inform clinical and infection control staff.

Investigation of a cluster

- Isolates from both infected and colonised patients should be typed: hospital outbreaks can involve a single strain whereas community strains are usually of multiple types.

Control of an outbreak

- Reinforce measures for a single case.
- Institute screening for carriage in persons at risk (faecal sample most useful screening specimen).
- Undertake terminal disinfection of vacated areas

Suggested case-definition

A laboratory-confirmed Gram-negative BSI is defined as one or more positive blood cultures for a Gram-negative pathogen.

A BSI is defined as a positive blood culture of a recognised pathogen OR the

combination of clinical symptoms (fever >38 °C, hypotension, etc.) and two positive blood cultures of a common skin contaminant from two separate blood samples drawn within 48 hours.

3.26 Gonorrhoea, syphilis and other acute STIs

Sexually Transmitted Infections (STIs) are defined by their predominant route of transmission: they are transmitted by direct sexual contact. Some viral STIs are also included in the group of blood-borne infections (e.g. HBV, HCV, HIV, see Chapters 3.31, 3.32, 3.37 and 4.9). Most STIs can also be transmitted at birth from mother to child. In fact, all direct human-to-human transmissible pathogens are transmitted by close contact, hence also in sexual contact, but these are discussed separately in the respective chapters (e.g. HAV, HCV, shigellosis). For HIV infection and AIDS, see Chapter 3.37 and for anogenital chlamydia infections, see Chapter 3.10.

Suggested on-call action

On-call action is rarely required; however the public health team may be alerted to clusters of cases of STI (e.g. HIV infections, syphilis or gonorrhoea) and should be prepared to initiate or assist with an investigation.

Epidemiology

Data on the epidemiology of STI is heavily biased by the heterogeneity of surveillance systems and testing strategies per country. It is estimated that each year 146 million persons acquire *Chlamydia trachomatis* infection, 51 million get gonorrhoea, and 5 million contract syphilis worldwide. These ongoing epidemics affect different subpopulations: *C. trachomatis* infection is reported more frequently in young women, while gonorrhoea and syphilis are reported more often among men, related to the high proportion of cases among MSM. Greater exposure of women to screening and more testing of MSM, even when asymptomatic, contribute to these differences. Syphilis is reported in MSM of higher average age than gonorrhoea. More detail is given in Table 3.26.1 and in Chapter 10 on *C. trachomatis* in Table 3.10.1.

Clinical features

Although all STIs also cause genital symptoms, clinical features are distinct (see Table 3.26.2). Syphilis is most famous for its ability to cause all possible symptoms in medicine ('La grande simulatrice').

Laboratory confirmation

See Table 3.26.3

Transmission

STIs are spread by direct, usually sexual, contact with infectious discharges or lesions. During viremia or bacteremia all infections can be transmitted by blood transfusion. Syphilis, HBV, HCV, HIV and HSV may also be spread in utero.

Acquisition

Incubation periods vary. See Table 3.26.2

Prevention

The prevention of STIs depends on:

- Health and sex education promoting correct and consistent use of barrier methods (condoms, dental dams) and safer sex play techniques.
- Early detection of cases and prompt effective treatment, including routine Chlamydia screening in the UK.
- Identification, examination and treatment of the sexual partners of cases.

Table 3.26.1 Epidemiology of acute STIs in Europe and the UK[a]

Gonorrhoea	The WHO estimates 51 million new cases of gonorrhoea occur each year. In 2013, 52995 cases of gonorrhoea were reported in 25 EU/EEA Member States (no data from Germany, Italy and Liechtenstein) – an overall notification rate of 16.9 per 100000 population. MSM accounted for 43% of reported cases. Since 2008, the rate of gonorrhoea cases has increased by 79%, with most EU/EEA countries reporting increasing trends. The notification rate varies widely among European countries, but variations in surveillance systems prevent meaningful comparisons. In the UK, gonorrhoea incidence has increased since 2008 from 14985 to 41193 in 2015. There is a disproportionately high incidence of gonorrhoea in young men and women, homosexual and bisexual men, those of black-Caribbean ethnic origin and those living in urban areas. The recent sharp rise, together with the rise in syphilis, especially seen among MSM, suggests increased unsafe sex practices in this risk group. There is widespread resistance of gonococci to antimicrobial agents including ciprofloxacin, penicillin, tetracycline and azithromycin, particularly in isolates from MSM and persons who have acquired infections abroad. Cefixime or ceftriaxone are the treatment of choice for gonorrhoea. In Europe resistance to cefixime is stable and recently even decreased to 2% in 2014 (except for Belgium where it increased to 12% in 2014). Resistance to ceftriaxone is still extremely rare (of an average of 2000 annual European samples, 10 isolates in 2011, 3 in 2012 and 7 in 2013). In 2014, in the UK none of the 231 tested gonococcal isolates demonstrated decreased susceptibility to cefixime and none to ceftriaxone. In 2015, no isolates were resistant to spectinomycin.
Infectious Syphilis	Syphilis is an ubiquitous STI with an estimated 5–6 million new cases annually. Syphilis still is a leading cause for genital ulcers, particularly in developing countries. In China syphilis has spread rapidly in the last decade, related to social upheaval. In Europe (and the USA) incidence declined after World War II, but started increasing in the late twentieth century, stabilising in the general population, but with a continued increase among MSM. In 2014, 23541 cases were reported in 29 EU/EEA countries (incidence 5.1 per 100000, compared to 4.1 in 2010). Two-thirds of all diagnoses are in MSM. Central and eastern Europe experienced the highest rates of syphilis in the late 1990s (incidence 177 per 100000). There are wide variations in syphilis notification rates in Europe due to differences in national surveillance systems. Although relatively rare in the UK, syphilis continues to increase in the twenty-first century to 5288 new cases in 2015 (primary, secondary and early latent cases), a 76% increase since 2012 (3001). The increase coincides with a similar increase in gonorrhoea and LGV, related to MSM. There has been a steady increase in diagnoses of STIs since 2009, especially in HIV-positive MSM. In 2015, 40% (1653/4141) of syphilis diagnoses in MSM were in HIV-positive men. There is evidence that this relates to condomless sex associated with HIV seroadaptive behaviours, occurring in dense sexual networks of HIV-positive MSM.

Genital Herpes Simplex Virus Infection	Genital herpes is the most prevalent ulcerative STI in the world with an estimated 417 million HSV-2 infected individuals. In the developing world the prevalence ranges from 2 to 74%. In the USA 40–60 million individuals are infected and 1–2 million new infections occur each year, resulting in 600 000–800 000 clinical cases annually. An increase in incidence has been reported in the last decades across the world. In the UK, cases of genital herpes have been rising gradually for many years, but in the last 3 years a levelling off has been seen, at 35 000 first episodes per year at GUM clinics and non-specialist and community services combined. As infection is more commonly symptomatic in women, they consistently have a higher incidence than males.
Genital Warts	The last decades show an increase in the prevalence of anogenital warts. The prevalence is consistently higher in males compared to females. Most cases are seen in age group 15–29 years. It is estimated that 50–80% of sexually active adults have ever been infected with one or more HPV types. Most of these infections were asymptomatic; only 1% develop anogenital warts.In the UK the number of new cases has recently decreased from over 91 000 in 2008 to 68 310 in 2015. Most of this is explained by a reduction in diagnoses in 15–19 year old females (38.9% reduction) associated with Human Papillomavirus vaccination. Reductions were greatest among 15-year-old females (83.2%), an age cohort largely offered the quadrivalent vaccine.
Trichomoniasis*Trichomonas vaginalis* a flagellate protozoan	Although 80% of *T. vaginalis* (TV) infections are asymptomatic, TV infections have increased risk for HIV transmission, preterm labour, and pelvic inflammatory disease (PID). TV infection is not reportable in any country, and epidemiologic data are scarce. WHO estimates that 250 million new infections occur annually, equally in males and females, but 90% of all diagnosed cases are in women. Prevalence in sub-Sahara Africa and SE Asia is higher than in Europe. Treatment with metronidazole is effective in 90% of symptomatic cases.

[a] For Chlamydia and LGV see Table 3.10.1.

Table 3.26.2 Clinical features of acute sexually transmitted infections (STIs)

Infection	Clinical features and sequelae
Bacterial vaginosis	Presents with vaginal discharge and itching. There is debate about the importance of sexual transmission
Chancroid	A painful ulcerating genital papule appears 4–10 days after exposure. If untreated, suppurating lymphadenopathy follows
Genital candidiasis	Presents with vaginitis with irritation and discharge. *Candida albicans* is a vaginal commensal and infection is often endogenous although sexual spread may occur. In males, infection is often asymptomatic but irritation and a rash on the glans penis may occur
Genital HSV	Incubation period 2–10 days. Primary infection produces painful vesicles or ulcers on the penis, labia, cervix and adjacent genital areas. There may be fever and malaise. Healing occurs within 17 days. In the majority of cases, recurrent secondary episodes, usually less severe, occur as often as once a month due to HSV latency in local nerve ganglia. Precipitating factors for recurrence include menstruation, sexual intercourse and stress Subclinical attacks are common and are important in transmission. Serious HSV infection of the neonate may be acquired during delivery
Genital warts, HPV	Incubation period is from 1 month to several months. Sessile warts are 1–2 mm in diameter and affect dry areas of skin. Condylomata acuminata are large fleshy soft growths and occur particularly when cellular immunity is depressed. Genital warts are often multiple and may occur anywhere on the external genitalia and within the vagina. Subclinical HPV infections of the genitalia are common. Certain HPV types are associated with genital tract neoplasia. Possible sequelae are carcinoma of anus, cervix, penis and vulva.
Gonorrhoea	Incubation period 2–5 days. Causes cervicitis in females and urethritis in males, with purulent discharge. Anorectal and oropharyngeal infection can occur. Subclinical infection is common and an important source of transmission. Salpingitis is a complication in 10–15% of females, local complications in males are uncommon
Non-chlamydial, non-gonococcal urethritis	*Ureaplasma urealyticum* and *Mycoplasma hominis* are causes of urethritis and pelvic inflammatory disease. Possible sequelae are infertility and ectopic pregnancy
Granuloma inguinale	Destructive ulcerating genital papules appear 1–12 weeks after exposure. Possible sequelae are genital lymphoedema, urethral stricture
HTLV	Leukaemia, lymphoma, tropical spastic paraparesis
Lymphogranuloma venereum	Starts with a painless penile vesicle 1–4 weeks after exposure. This heals but is followed 1–2 weeks later by fever and regional lymphadenopathy, which leads to suppuration and fibrosis
Syphilis	The clinical manifestations of syphilis are varied. The primary and secondary stages are characterised by mucocutaneous lesions. The primary chancre occurs on average 21 days after exposure. A variable secondary rash follows after six to eight weeks, often with fever and malaise. Gummata (tertiary lesions) appear after several years. Almost any organ of the body can be affected. Transplacental spread of *Treponema pallidum* may result in foetal death, prematurity, or congenital syphilis. Possible sequelae are foetal and neonatal infection, neurological and cardiovascular disease
Trichomoniasis	Vaginitis with offensive discharge. Asymptomatic urethral infection or colonisation common in males. The incubation period for urethritis in males is 10 days, clearing spontaneously in 10 days. In women vaginitis occurs after 4–28 days and can persist for years.

Table 3.26.3 Laboratory diagnosis of acute STIs

Infection and infectious agent	Diagnosis
Bacterial vaginosis, *Gardnerella vaginalis*, other anaerobes	Wet mount (10% potassium hydrochloride) of the discharge reveals vaginal epithelial cells studded with *clue cells* and produces amine odour (whiff test) Culture possible but not advised (predictive value <50%) PCR in research settings
Chancroid, *Haemophilus ducreyi*	Swab of ulcer base for culture on special media is gold standard. Gram-stain less sensitive Direct antigen detection and PCR in development
Genital candidiasis, *Candida albicans*	Wet mount (normal saline), Gram stain or culture PCR in research settings
Genital HSV. Usually HSV-2 but HSV-1 causes 20% of cases	Genital herpes may have an atypical appearance so diagnosis should be confirmed by demonstrating HSV in the genital lesions by NAAT HSV-1/HSV 2 (samples from bladder, ulcer, crust) or culture
Genital warts, condylomata acuminata HPV	Visible warts: clinical diagnosis Diagnosis may be confirmed histologically on biopsy NAAT HPV on cervical cytology specimens is capable of distinguishing between the 40 different HPV types that affect the genital tract
Gonorrhoea, *Neisseria gonorrhoeae*	NAAT Ng: Females urethral and cervical self-taken swab; males urethral swab. NAAT first pass urine less sensitive Culture and antibiotic sensitivity testing Microscopy: Gram-stain of smear showing Gram-negative diplococci
Non-chlamydial, non-gonococcal urethritis	Specific diagnostic tests for these organisms are not usually clinically indicated
Granuloma inguinale *Klebsiella granulomatis*, a Gram-negative coccobacillus	Biopsy of the edge of the ulcer shows Donovan bodies (bi-polar staining) on appropriate staining Smear of ulcer showing Donovan bodies (bi-polar staining) using Giemsa stain
HTLV	Serology: HTLV-specific antibodies
Syphilis, *Treponema pallidum*	NAAT Tp Direct fluorescence test Serology: TPHA/TPPA or EIA followed by FTA-abs or IgG Western blot; if positive VDRL/RPR
Trichomoniasis, *Trichomonas vaginalis*	Wet mount (normal saline) shows motile organisms on microscopy (sensitivity 50–70%) Culture advised if suspicion is high and wet mount negative Direct antigen test ('dipstick' immunochromatographic test) and DNA probe have better sensitivity (>80%) and specificity (90%) than wet mount microscopy PCR in research settings is promising

EIA, Enzyme Immunoassay; FTA-abs, Fluorescent Treponemal Antibody-Absorption test; GUM, Genito-urinary Medicine; HPV, Human Papillomavirus; HSV, Herpes Simplex Virus; HTLV, Human T-Cell Lymphotropic Virus; NAAT, Nucleic Acid Amplification Test; PRP, Rapid Plasma Reagin; TPHA/TPPA, *T. pallidum* Hemagglutination/*T. pallidum* Particle Agglutination Assay; VDRL, Venereal Disease Research Laboratory.

Table 3.26.4 Some specific UK STI surveillance schemes

Surveillance type	Comment
Genitourinary Medicine Clinic Activity Dataset (GUMCADv2)	A mandatory reporting system providing data on sexual health services and STI diagnoses from all commissioned Level 3 and Level 2 sexual health services in England. It is an electronic, pseudo-anonymised patient-level dataset reported by over 600 services. It includes data on area of residence, age, sexual orientation, ethnic group and country of birth in addition to clinical and risk factor data.
Routine laboratory reporting of STIs to PHE	Voluntary laboratory reports to PHE from diagnostic laboratories.
Chlamydia Testing Activity Dataset (CTAD)	CTAD collects data on all chlamydia tests undertaken in England from Local Authority (LA) and National Health Service (NHS) commissioned laboratories, to measure screening activity. Provides data at national and local level, on screening coverage, the proportion of chlamydia tests that are positive and the chlamydia diagnosis rate.
Gonococcal Resistance to Antimicrobial Surveillance Programme (GRASP)	A national sentinel surveillance programme was established in 2000 to monitor trends in susceptibility to antimicrobial agents used for the treatment of gonorrhoea in England and Wales. GRASP collects *N. gonorrhoeae* isolates from consecutive patients attending a network of Genitourinary Medicine (GUM) clinics across England and Wales between July and September annually. Clinicians are asked to provide detailed demographic and behavioural data including age group, sex, ethnic group, sexual orientation, previous infection, sexual lifestyle and antimicrobial susceptibility.
Enhanced syphilis surveillance scheme *(now only operates in some geographical areas)*	Clinicians are asked to provide enhanced patient data including gender, age, ethnic background, sexual orientation, stage of infection, HIV status, location where infection was likely to have been acquired and connection with sexual networks such as saunas and bars.

- Opportunistic or routine screening and treatment of certain subgroups of the population who may be at increased risk of STIs or their complications. Examples are the routine use of syphilis serological tests in pregnancy, to prevent congenital syphilis; and regular re-testing for STIs and HIV in MSM.
- See also Chapters 4.8 and 3.37.

Surveillance

As with any infectious disease, control of STIs depends on good surveillance. Most European countries have STI surveillance systems (data can be accessed on national centre or ECDC websites), but there are major variations in terms of coverage, completeness and representativeness, and this prevents useful international comparisons. UK surveillance is one the most comprehensive: in European epidemiological reports UK data dominate, but this is likely to be the result of a substantial ascertainment bias. Some specific sources of data in England are given in Table 3.26.4: outputs from these surveillance sources are published regularly by PHE on its website.

Response to a case

- Individual cases of STIs are not generally reported to the local health protection team.
- The case should receive prompt effective treatment and should refrain from sexual

intercourse until non-infectious after treatment.
- Sexual contacts should be identified, examined and treated as appropriate.

Investigation of a cluster and control of an outbreak

An STI incident has been defined as:
- observed number of cases greater than expected over a defined time period in a particular setting,
- linked cases of STIs,
- the need for additional resources to manage the cases,
- any case of congenitally acquired infection.

The underlying principles of outbreak investigation can be applied to outbreaks of STIs, but there are some differences. STIs are often associated with a degree of stigma; confidentiality issues may restrict the availability of patient data and although patients and sexual contacts may be identified and treated relatively easily, effective control may require sustained behavioural change to reduce spread in sexual networks. In addition, compared with other outbreaks, STI outbreaks will usually take longer to investigate and control.

The management of STI outbreaks requires a multi-agency approach involving the STI diagnosing physician (e.g. GUM clinic physician), sexual health advisers, health protection team, microbiologist, director of public health, and sexual health lead at the local commissioning organisation. Ideally these participants should meet at least annually and should draw up an STI outbreak contingency plan. Guidelines on investigating STI outbreaks have been published at https://www.gov.uk/government/publications/sexually-transmitted-infections-stis-managing-outbreaks (Table 3.26.5).

Table 3.26.5 Managing STI outbreaks at local level

Identification	• Increase in number of cases in local area • Recognise potential outbreak • Review local surveillance data • Compare with national disease trends • Confirm local increase • Identify cases and contacts • Descriptive epidemiology • Describe those affected and possible source
Response	• Discuss with colleagues • Establish Outbreak Control Group • Case finding • Introduce enhanced surveillance to obtain further descriptive and risk-factor data. • Analytical epidemiology • Microbiological investigation • Further research
Secondary prevention	• Partner notification • Investigate networks • Publicity campaigns to encourage those at risk to come forward for screening • Alert local practitioners (GUM and general practice) • Additional clinic sessions
Primary prevention	• General health promotion campaigns • Targeted health promotion campaigns • Outreach work
Evaluate control measures	• Monitor surveillance data • Outbreak report • Key lessons

3.27 Hantavirus infection

Hantavirus infection is an acute zoonotic viral disease.

Suggested on-call action
None usually required.

Epidemiology

Hantavirus infections are found where there is close contact between people and infected rodents. Regions especially affected include China, the Korean peninsula, Russia and Northern and Western Europe. In Europe, foci are recognised in the Balkans, the Ardennes, and the Nordic countries. Since 2005 the number of reported cases in Europe has increased and a slow spread of the affected geographical area has been observed. In Europe 3752 cases were reported in 2014. Most cases were reported in Finland (2089), Germany (571), Sweden (418), Croatia (209) and France (105). Cases are mainly seen in autumn and winter when rodents (bank vole, *Myodes glareolus*) are entering houses, and again in spring when people start cleaning summer houses and barns that were uninhabited during winter.

Clinical features

The clinical picture depends upon the subtype causing the infection (90% of Puumala infections are asymptomatic) and is characterised by nephritis (NE), Haemorrhagic Fever with Renal Syndrome (HFRS), or Acute Hantavirus Pulmonary Syndrome (HPS). All three syndromes generally have the same start: after the incubation period, acute fever, headache, general malaise occurs, frequently followed after three to four days by nausea, vomiting, abdominal pains and low back ache (toxic phase). Nephritis is a self-limiting renal insufficiency with proteinuria, oliguria, and severe pain in the kidney area (oedema). HFRS manifests as fever, thrombocytopenia and acute renal failure, and HPS as fever with respiratory difficulty. A number of different subtypes exist, each of which is associated with a particular rodent species. Of the two main European subtypes, Puumala tends to cause milder disease (Nephropathia Epidemica, NE) and rarely HFRS, while Dobrava HFRS is often severe (Table 3.27.1).

Laboratory confirmation

Specific antibodies (IgM or IgG) can be identified by ELISA or Indirect immunofluorescent antibody test (IFA). IgM is often present on hospitalisation. PCR for specific RNA may be available.

Transmission

Aerosol transmission from rodent excreta is common. Human to human transmission has been reported in South American (Andes virus) HPS.

Acquisition

The incubation period is one to six weeks, mostly two to three weeks.

The infectious period for HPS is unclear.

Prevention

- In areas that are known to be endemic, rodents should be excluded from living quarters. To avoid contact all potential entry sites should be closed. Food should be kept in sealed containers and garbage should be kept in closed bins.
- Cross-ventilation at least 30 minutes and 'wet' cleaning of nest material, rodent urine and faeces to prevent aerosolisation.

Table 3.27.1 Main hantavirus serotypes

Syndrome	Serotype	Geography
HFRS	Dobrava	Balkans
	Saarema	Balkans, South East Europe
	Hantaan	Asia
	Seoul	Worldwide
NE/HFRS	Puumala	(Northern) Europe
HPS	Sin Nombre	North America
	Various other serotypes	North and South America

Response to a case

- HFRS is not transmitted from person to person and there is generally no need for urgent public health action.
- The first cases in a hitherto hanta-free area should be investigated. Similarly, the first cases in a new season should induce preventative seasonal action, such as alerting GPs and re-informing the public on preventive measures concerning contact with rodent excreta.
- In view of the possibility of person-to-person spread in HPS, suspected cases should be nursed in isolation.

Suggested case-definition
HFRS or HPS confirmed by IgM or PCR.

3.28 Head lice

Head lice (*Pediculus humanus capitis*) are wingless insects that live close to the scalp where they feed on blood. Head lice infestation is associated with little morbidity but causes high levels of anxiety amongst parents.

Suggested on-call action
Not generally applicable

Epidemiology

Anecdotal evidence suggests that prevalence has increased worldwide, mainly in resource-rich countries. Data from surveys amongst children in Europe suggest a wide range of prevalence from 2 to 9%. Incidence in preschool children in Germany (five to six years) was 600 per 10 000 year^{-1}. Anyone with head hair can get head lice but children and teenagers are particularly affected.

Clinical features

Many early infestations are asymptomatic. Itching and scratching of the scalp may occur after four–six weeks due to sensitisation to head lice excretions and secondary bacterial infection may occur.

The female head louse lives for approximately one month and lays 50–150 eggs during her lifetime. The eggs are tear-shaped, 1 mm in length and are securely glued to the hair shaft close to the scalp. The eggs hatch after 7–12 days and the emerging nymphs moult three times before reaching maturity in 9–12 days when mating occurs. The full-grown louse is 2–3 mm long. Empty egg sacks (nits) are white and shiny, and may be found some distance from the scalp as the hair grows out. Although there may be a large number of lice on an affected head, the average number is about 10.

Laboratory confirmation

Diagnosis depends on finding live lice on the head. Empty eggshells (nits) are not proof of active infestation. Lice move rapidly away from any disturbance, and examination of dry hair is unreliable. Lice can only be reliably detected by combing wet lubricated hair with a 'detector' comb. If lice are present they fall out or are stuck to the comb. If necessary, lice and nymphs can be examined with a magnifying glass or low-power microscope to confirm their presence.

Transmission and acquisition

Transmission is by direct contact with the head of an affected person. Lice cannot jump or fly, but move readily through dry hair and cross from person to person when heads touch. Transmission occurs in schools, at home, and in the wider community. The fashion of taking 'selfies' with friends in close proximity and the modern full embracing greetings might contribute to the increased spread. Indirect spread when personal items are shared is possible, but negligible in practice. Head lice do not survive for more than 48 hours away from the scalp. A person will remain infectious for as long as there are adult lice on the head and re-infestation may occur. Humans are the only source of head lice, which are host-specific and do not spread from or to animals.

Prevention

- It is probably impossible to completely prevent head lice infestation.
- A number of preventative measures have been promoted including repellents such as piperonal, regular brushing and electronic combs, but evidence for their effectiveness is lacking.
- Reducing head lice infestation depends on case finding by weekly diagnostic wet combing, followed by prompt treatment of cases if active infestation is found.
- Contacts of cases must also be examined and treated if appropriate.

Surveillance

- Pharmaceutical data may provide some insights into pediculocide prescribing patterns.
- If head lice are causing particular problems in community settings such as schools, the local public health team should be informed.

Response to a case

- There are four main methods of treatment (Box 3.28.1).
- The role of other agents such as 'natural' products and flammable or toxic substances is unclear.
- No treatment method is 100% effective.
- Treatment may fail because of misdiagnosis, non-compliance, re-infestation, pediculocide resistance or use of an ineffective preparation.
- Resistance to topical chemical pediculocides is increasing (see Box 3.28.1).
- Contacts of a case should be examined for head lice by wet combing and treated if necessary.
- It is not necessary to exclude children with head lice from school or nursery.

Investigation of a cluster

- Clusters of cases of head lice may be reported from schools or other institutional settings.
- The school health nurse is usually the most appropriate person to investigate and advise on control measures (Table 3.28.1).

Control of an outbreak

- Organise parents to carry out case finding by wet combing at daily sessions in classrooms.
- Parents are strongly advised to treat their child promptly if live lice are discovered, using one of the treatment options.
- Accurate information, explanation and sympathetic reassurance will be required.

Box 3.28.1 Treatment of head lice

Mechanical removal	Lice and larvae as they hatch can be mechanically removed by wet combing well lubricated hair with a detector comb every day for two weeks. This process which must be carried out meticulously breaks the life cycle of the head louse. Complete shaving generally eliminates infestation and prevents re-infestation, but is rarely appropriate.
Occlusive agents	These agents suffocate lice by obstructing their respiratory spiracles. In trials 92% dimeticone lotion has proved highly effective. If 4% dimeticone is combined with 96% cyclomethicone cure rates are 70–77%. Cure rates of all silicone oils range from 63 to 100%.
Topical chemical pediculocides	A number of chemical pediculocides are available including carbaryl, malathion and the pyrethroids (permethrin and phenothrin). Lotions and liquids are preferred and contact time should be 12 hours. A single application may not kill unhatched eggs and a second application is advised according to the package leaflet. After treatment, wet combing should be carried out to check for lice. Pediculocides should only be used if live lice are confirmed, and should never be used prophylactically. Pediculicide resistance is increasing and varies in Europe from country to country. Before resistance is accepted as cause of therapeutic failure, other possibilities of failure should be ruled out (inappropriate application; no subsequent wet combing; re-infestation and so on).
Oral drugs	Some antihelminths (thiabendazole, levamisole, albendazole, ivermectin) have been tested against headlice: ivermectin has shown best results with little adverse events. In poor resource communities with high nematode and ectoparasite infestations, ivermectine is an excellent option for mass treatment.

3.29 Helicobacter pylori

Helicobacter pylori causes a chronic infection associated with chronic upper gastrointestinal disease.

Epidemiology

Infection occurs worldwide. Prevalence in developed countries is 20–50% in adults (up to 75% in socially deprived areas) and, in general, increases with age, with acquisition rates higher in children. However, there is also a cohort effect of decreasing incidence with time.

Diagnosis

Most infection is asymptomatic, but it may cause gastritis and both gastric and duodenal ulceration. The annual incidence of peptic ulcer disease is 0.2% and over 90% of these patients have *H. pylori* infection. Infection is also associated with gastric adenocarcinoma. Diagnosis is by serology, breath testing with urea, culture from gastric biopsy/aspirate, or antigen testing of faeces. Treatment is with a mix of antibiotics and anti-secretory drugs.

Transmission and acquisition

Transmission is unclear but probably by ingestion of organisms, most likely faeco-oral, but perhaps by oral–oral or gastro–oral routes. Spread via contaminated gastric tubes and endoscopes is recorded and endoscopists have an increased risk. Infectivity is assumed to be lifelong and higher in those with achlorhydria.

Control

Other than routine hygiene and disinfection, there is insufficient evidence to

Table 3.28.1 Head lice: suggested responsibilities

Parents	Brush or comb their children's hair each day for two weeks, and weekly thereafter. Use detector comb to detect infestation.
	Ensure recommended treatment and informing (parents of) contacts has been carried out properly.
Health visitors and school health nurses	Education of parents about head lice, treatment options and the importance of contact tracing and informing parents of possible contacts in other groups (sports club, musical training, and so on).
	In case of outbreaks in schools and nurseries ensure policy is being correctly followed.
	Advise families with recurrent problems and consider further measures.
Head teacher	Agree a written policy on the management of head lice with the school nurse and public health team.
	Publicise this policy to parents, pupils, staff and others.
	Children who are found to have head lice should be managed confidentially by the school health nurse (if available).
	Creating treatment facilities if no school health nurses are available.
	There is no need to exclude children from school because of head lice.
	Letters to parent alerting them to head lice in school may be used.
Specialist health protection staff and Community Infection Control Nurses	Receive reports of particular head lice problems in community settings and advise on management.
	Involve other carers, such as community nurses, GPs and teachers as appropriate.
	Form a head lice project team at the affected institute to co-ordinate the measures.
	Make available information on head lice for the public and professionals.
General practitioners and practice staff	Explain the use of a detection comb and wet combing to confirm active infestation.
	Discuss treatment options.
	Make available patient information leaflet.
	Prescribe pediculocides when appropriate: only those with confirmed infestations should be treated.
Drug stores and pharmacists	Explain the use of a detection comb and wet combing to confirm active infestation.
	Discuss treatment options.
	Offer for sale wet combing materials including detector combs or pediculocides as appropriate.
	Pediculocide formulated as shampoos should not be offered for sale.
	Patient information leaflet should be provided with all prescriptions and sales of head lice treatment

recommend further preventative interventions. Eradication of infection is associated with remission of gastritis and peptic ulceration and may also be helpful for those with gastric tumours, but eradication of infection in asymptomatic cases is not usually recommended.

3.30 Hepatitis A

Hepatitis A Virus (HAV) causes an acute infection of the liver and six HAV genotypes (I to VI) have been identified. Genotypes I, II and III, divided into subtypes A and B, infect

Table 3.30.1 General patterns of HAV infection in European countries

Endemicity	Countries	Age of Cases	Most common transmission
Very low	Scandinavia	over 20	Travel abroad
Low	Germany Netherlands U.K Southwestern Europe	5–40	Common source outbreaks, travel abroad.
Intermediate	Balkan countries Baltic states Eastern Europe Turkey	5–24	Person to person, common source outbreaks, contaminated food/water, travel abroad.

Based on 2014 data

humans. Genotype I is the most prevalent worldwide, with IA being reported more frequently than IB.

Suggested on-call action

- If a case is in a risk group for further transmission (Box 2.2.1), exclude from work or nursery.
- Exclude any contacts in risk groups who are known to be unwell.
- Arrange for household contacts to be offered vaccination if appropriate.

If you, or the referring clinician/microbiologist, are aware of potentially linked cases, consult the local outbreak plan.

Epidemiology

The incidence of hepatitis A has been decreasing in high-income countries over the last 50 years and most of the EU/EEA is considered to have very low hepatitis A endemicity. About 13 000 cases are reported each year in EU/EEA countries (3.0 per 100 000) with a seasonal peak in the autumn. Incidence of HAV is lowest in Scandinavia, higher in Mediterranean countries and highest in Eastern Europe (Table 3.30.1). The decreased incidence in Europe has led to increased susceptibility in younger people. Cases are more common in under 45s and in men.

High prevalence areas include most of Asia, Africa and Latin America and many cases in Europe result from travel to these countries. Other groups at increased risk include those in contact with a case of HAV (e.g. household or nursery), MSM, Intravenous Drug Users (IDU), ethnic minorities with links to high prevalence countries, haemophiliacs and residents and workers in institutions for those with mental disability.

Clinical features

The clinical picture may range from no symptoms to fulminant hepatitis and is greatly influenced by age. Less than 10% of those aged under six years develop jaundice, but 40% have fever and dark urine and 60% develop nausea/vomiting, malaise and diarrhoea. Around half of older children and three-quarters of adults develop jaundice after a two- to three-day prodrome of malaise, anorexia, nausea, fever and dark urine. Overall case fatality is around 0.1% but may increase to around 1.8% in those aged over 65. Prolonged, relapsing hepatitis for up to one year occurs in 15% of cases. No chronic infection is known to occur and infection confers lifelong immunity.

Laboratory confirmation

Confirmation of acute HAV is dependent upon demonstration of specific IgM antibodies (Anti-HAV IgM), which are usually present at onset of symptoms and persist for around three months. IgG antibody persists for life and so in the absence of IgM, a fourfold rise in titres in paired samples is required for diagnosis. Persistent IgG is taken as evidence of immunity due to past infection (or vaccination). Blood samples are usually used, but salivary IgM (and IgG) testing is available at specialist laboratories and may be useful in outbreak investigations. HAV-RNA can be detected in blood and stool early in the infection. Subtyping may also be available.

Transmission

HAV infection is spread primarily by the faeco-oral route from other humans. Up to 10^8 infectious units per millilitre are excreted in faeces during the late incubation period and the first week of symptoms. Viraemia also occurs during the prodromal phase of the illness but the viral load is at much lower levels than in stool. Saliva and urine are of low infectivity.

Faeco-oral spread is likely to be responsible for secondary transmission to household and nursery (secondary attack rate of between 2 and 26%) and institutional contacts, perhaps aided by transmission via fomites. HAV can spread rapidly, but silently among mobile, faecally incontinent children in nurseries and then cause illness in their contacts.

Infection among IDUs has been reported in several European countries and is likely to be due to poor hygiene, although contamination of drugs and needle sharing may contribute. Travellers to endemic countries risk exposure via contaminated food or water. HAV can survive for 3–10 months in water, suggesting that even in Europe, shellfish harvested from sewage contaminated waters are a potential source; shellfish concentrate viruses by filtering large quantities of water and are often eaten raw or after gentle steaming which is inadequate to inactivate HAV. Infected food handlers with poor personal hygiene may also contaminate food. Imported fruit and salad vegetables have also caused outbreaks.

Transmission among MSM does occur and there have been outbreaks of hepatitis A among the MSM population.

Many cases of HAV do not have a recognised risk factor: it is likely that many of these contracted their infection from an undiagnosed or asymptomatic child case in their household. Such cases may be a factor in community outbreaks that evolve slowly over several months.

Acquisition

The incubation period is reported as 15–50 days (mean 28 days) and appears to be dose-dependent. The infectious period is from two weeks before onset of symptoms until one week after, although some, particularly children, may excrete a week longer. Infectivity is maximal during the prodromal period.

Immunity to previous infection is lifelong, but because of the decreasing incidence in EU countries over the last half-century, the majority of those under 50 years of age are susceptible. Those at increased risk of severe disease include those with chronic liver disease or chronic hepatitis B or C infection and older people.

Prevention

- Personal hygiene: including hand washing; ensuring toilet hygiene in nurseries and schools; care with food and water during travel to low- and middle-income countries; condom use and careful hygiene after anal sex.
- Sanitary disposal of sewage and treatment of water supplies.
- Vaccination of travellers (over one year of age) to countries outside Northern or Western Europe, North America, Australasia or

Japan, preferably at least two weeks before the date of departure (but can be given up to day of departure if necessary). This includes ethnic minority residents who are visiting relatives or friends in their family's country of origin. If time permits those over 50 years of age or born in high endemicity areas or with a history of jaundice can be tested for immunity before vaccination. Human Normal Immunoglobulin G (HNIG) may be available for immunocompromised travellers.
- Vaccination of other risk groups, including patients with chronic liver disease or haemophilia, those with chronic hepatitis B or C, sexually active MSM, IDU, certain laboratory staff, staff and residents of certain institutions where good hygiene standards cannot be achieved, sewage workers and people who work with primates.
- Shellfish should be steamed for at least 90 seconds or heated at 85–90 °C for four minutes before eating.
- Sodium hypochlorite, 2% glutaraldehyde, and quaternary ammonia compound with 23% HCI are effective for decontaminating surfaces.

Surveillance

- Confirmed or suspected cases of acute infectious hepatitis should be reported to local public health authorities.
- All laboratory confirmed acute cases (e.g. IgM positive) of hepatitis A should be reported to local public health authorities and national surveillance systems.

Response to a case

- Enteric precautions until seven days after onset of jaundice (if no jaundice, precautions until seven days after onset of compatible symptoms). Case should not prepare food for 14 days after onset.
- Exclude all cases from work, school or nursery until seven days after onset of jaundice or compatible symptoms, irrespective of whether they are in groups with increased risk of further transmission (Box 2.2.1).
- Exclude household and sexual contacts with compatible symptoms as for cases.
- Personal hygiene advice to cases and contacts, particularly handwashing. Asymptomatic contacts that attend nursery or infant school should have hand washing supervised.
- Close contacts who are food handlers should be offered hepatitis A vaccine and advised to restrict activities to those which do not involve preparing and handling unwrapped ready-to-eat-food until 30 days post exposure unless demonstrated to be immune.
- Vaccination should be offered to relevant household, sexual, and other close contacts (see national policy). In England and Wales, healthy close contacts identified within 14 days of exposure to a case should be offered hepatitis A vaccine if aged two months to one year and attends childcare or is aged 1–59 years; and hepatitis A vaccine and HNIG if aged over 60 years. Close contacts who are food handlers should be offered hepatitis A vaccine.
- Offer HNIG plus hepatitis A vaccine to close contacts with pre-exiting chronic liver disease, chronic HBV or HCV, HIV infection or immunosuppression. Some authorities (e.g. PHE) would offer vaccine up to eight weeks after exposure to prevent tertiary infection and offer immunoglobulin plus vaccine up to four weeks after exposure to those with chronic pre-existing liver disease or HBV/HCV infection to attempt to ameliorate the severity of infection.
- If the case has attended pre-school childcare whilst potentially infectious, consider extending vaccination to close contacts. If case is a food handler or in primary school, a risk assessment will be required to assess risk of transmission and the need for post-exposure prophylaxis of workplace contacts.
- Collect risk-factor data for eight weeks before onset: contact with case, travel abroad, mental disability, or other institution, seafood, meals out of household, blood transfusion, sexual history, occupation.

Investigation of a cluster

- Confirm that cases are acute (clinical jaundice and/or IgM positive).
- Describe by person, place, and time. Does epidemic curve suggest a point source, ongoing person-to-person transmission (or both) or a continuing source? Are there cases in neighbouring areas?
- Collect risk-factor data as for individual case and interview cases sensitively regarding sexuality and sexual activity, illicit drug use and imprisonment. Obtain full occupational and recreational history, for example exposure to faeces, nappies, sewage, untreated water, and so on. Obtain as full a food history as patient recall allows for eight weeks before onset.
- Discuss with microbiologist use of salivary testing for case finding and availability of genotyping to confirm cases are linked.

Control of an outbreak

- Try to define population at risk suitable for immunisation, for example staff and pupils at a nursery.
- Hygiene advice to cases, contacts and any implicated institution. Ensure that toilet and hygiene facilities are adequate.
- For community outbreaks, re-inforce hygiene measures in nurseries and schools and vaccinate contacts of cases.
- For prolonged community outbreaks, consult with relevant experts on appropriateness of mass vaccination of affected population.
- Pre-exposure vaccination: Hepatitis A vaccine is highly effective in preventing infection if given prior to exposure. In England, it is recommended that all MSMs attending GUM and HIV clinics should be opportunistically offered a single dose of adult monovalent hepatitis A vaccine unless they have documented evidence of two doses of hepatitis A vaccine or of previous hepatitis A illness.

Suggested case-definition for an outbreak

Suspected (clinical case): acute illness with compatible symptoms AND jaundice or raised serum aminotransferase levels (confirmation important in groups at risk of other hepatitis viruses, e.g. drug users).

Probable case: clinical case definition and an epidemiological link to a confirmed hepatitis A case OR clinical case definition AND detection of IgM antibody to hepatitis A (anti-HAV IgM).

Confirmed case: clinical case definition AND demonstration of specific IgM and IgG antibodies to hepatitis A in serum or saliva.

OR

Case with hepatitis A RNA (HAV RNA) detected regardless of clinical features.

OR

An asymptomatic person with no recent history of immunisation with anti-HAV IgM from oral fluid or serum AND an epidemiological link to a confirmed hepatitis A case.

3.31 Hepatitis B

Hepatitis B is a viral infection of the liver. Its public health importance lies in the severity of disease, its ability to cause long-term carriage leading eventually to cirrhosis and hepatocellular cancer, its transmissibility by the blood-borne route and the availability of vaccines and specific immunoglobulin.

Suggested action (next working day)

- Arrange for laboratory confirmation.
- Identify likely source of infection for acute cases.
- Arrange for testing and vaccination of close household/sexual contacts.

Epidemiology

The incidence of acute hepatitis B varies considerably across Europe, but has been steadily declining across Europe for many years, mainly due to the implementation of vaccination programmes. The overall notification rate in 2015 was 0.6 per 100 000, ranging from 0 (Luxemburg) to 3.4 (Latvia), although comparisons between countries should be made with caution due to a large variability in surveillance systems. The true incidence is higher, as about 70% of infections are subclinical and may not be detected. Most cases are in adults at high risk of infection (see Table 3.31.1). The carriage rate is below 1% in most European countries, although there is considerable geographical variation within countries, with higher rates in inner cities amongst those of minority ethnic origin (especially from South-East Asia and the Far East).

In contrast to acute infections, the rate of chronic infections in Europe has increased in recent years, and the reported rates are highest in Northern Europe, whereas the rates of acute disease are highest in Eastern Europe.

Table 3.31.1 Risk groups for hepatitis B in Europe

Injecting drug users
Individuals who frequently change sex partners
Close family and sexual contacts of cases and carriers
Individuals who receive regular blood or blood products
Patients with chronic renal failure and chronic liver disease
Healthcare workers and laboratory staff
Foster carers and people who adopt children from medium- and high-prevalence countries
Staff and residents of institutions for those with learning difficulties
Morticians and embalmers
Prisoners and prison staff
Long-term travellers to high prevalence countries
Babies born to acutely infected or carrier mothers

The most likely explanation for the trend in chronic infections is the impact of recent migration from medium and high endemicity countries.

Clinical features

Hepatitis B is clinically indistinguishable from other causes of viral hepatitis. After a non-specific prodromal illness with fever and malaise, jaundice appears and the fever stops. The course of the disease is very variable and jaundice may persist for months. Liver failure is an important early complication.

Laboratory confirmation

Laboratory diagnosis of hepatitis B involves serological testing for several hepatitis B specific antigens and antibodies. Different serological 'markers' or combination of markers are used to identify phases of hepatitis B virus (HBV) infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination or is susceptible to infection. Specialist advice from the reference laboratory should be sought in their interpretation. The hepatitis B markers are:

- hepatitis B surface antigen (HBsAg)
- total antibody to hepatitis B core antigen (anti-HBc total)
- antibody to hepatitis B surface antigen (anti-HBs)
- antibody to hepatitis B core antigen immunoglobulin M (anti-HBc IgM)
- hepatitis B e antigen (HBeAg)
- antibody to hepatitis B e antigen (anti-HBe)

Additional tests for hepatitis B include quantification of HBV DNA and HBV core avidity testing.

Patients with detectable hepatitis B antigen at six months (surface antigen [HBsAg] and/or e antigen [HBeAg]) are considered to be carriers.

Transmission

Humans are the only reservoir. Transmission is from person to person by a number of blood-borne routes, including sharing of drug injecting equipment, transfusions of blood and blood products, needlestick injuries, skin piercing with inadequately sterilised equipment, mother to baby transmission during or soon after childbirth, and sexual intercourse.

In low-prevalence countries transmission occurs mainly through shared syringes, needlestick injuries, sexual contact, bites and scratches. In high prevalence countries, perinatal transmission is the most important route; ulcerating skin disease and biting insects also play a role in developing countries.

Acquisition

The incubation period ranges from 40 to 160 days, with an average of 12 weeks. Carriers of hepatitis B surface antigen who are also e antigen positive and/or e antibody negative are much more infectious than those who are e antibody positive. Patients who do not become carriers and develop natural immunity are immune for life.

Approximately 10% of patients with acute hepatitis B become chronic carriers. Long-term complications of being a carrier include cirrhosis and hepatocellular carcinoma.

Prevention

- Hepatitis B vaccination of infants and/or older children, is recommended in nearly all EU countries. Vaccines are available as monovalent preparations, or in combination with Hepatitis A. There are many different schedules; however a primary course usually consists of three doses with or without a fourth dose. An accelerated schedule may be used when rapid protection is required, for example for travellers. The vaccine should not be given in the buttock as efficacy may be reduced. Higher dose formulations are available for patients with chronic renal failure.
- Protection is probably lifelong in a healthy adult who responds to the primary course. Healthcare workers and babies born to hepatitis B carrier mothers should, however, have their antibody status checked four to six months after immunisation. Poor responders (anti-HBs 10–100 miu ml^{-1}) should receive a booster dose and in non-responders (anti-HBs< 10 miu ml^{-1}) a repeat course should be considered. Adults over 40 years of age and those with immunodeficiency are more likely to be non-responders.
- Ensure that all blood and blood products are screened and not derived from donors at risk of infection.
- Adopt universal procedures for the prevention of blood-borne virus transmission in hospitals and all other situations where needles and other skin-piercing equipment are used (e.g. acupuncture clinics, tattoo parlours, ear/body-piercing).
- Prevent infected healthcare workers from performing exposure-prone procedures.
- Promote condom use.
- The above general measures for the prevention of blood-borne virus infections are covered in more detail in Chapter 4.9.
- Screen all women in pregnancy. Babies born to mothers who are HBsAg-positive and anti-HBe-positive (i.e. low infectivity) should receive an accelerated course of vaccine. Babies whose mothers are e antigen-positive, or who have had acute hepatitis B in pregnancy, or who have no e markers, or whose e markers are not known, should in addition to a course of vaccine receive hepatitis B-specific immunoglobulin (HBIG) 200 IU intramuscularly as soon as possible after birth.
- Offer post-exposure prophylaxis with HBIG and vaccine (if needed) for significant exposures to a known or suspected HBsAg source. The need for vaccine will depend on prior vaccination status and local recommendations. A significant exposure is

one in which HBV transmission may occur. This may be an injury involving a contaminated needle, blade or other sharp object or blood contaminating non-intact skin or eyes. HBV does not cross intact skin. Exposure to vomit, faeces, and sterile or uncontaminated sharp objects poses no risk. Transmission is not known to have occurred as a result of spitting or urine splashing.
- The dose of HBIG is 200 IU for children aged 0–4 years, 300 IU for children aged 5–9 years and 500 IU for adults and children aged 10 years or more.

Surveillance

- Acute hepatitis B is notifiable in most European countries.
- Surveillance should ideally be based on laboratory reports, as the disease is clinically indistinguishable from other causes of viral hepatitis. IgM and e-antigen/antibody results should be included with notifications to facilitate public health action.

Response to a case

- Obtain laboratory confirmation, assess whether acute (IgM and/or clinical history) and how infectious (HBeAg, anti-HBe, HbsAg).
- If acute, determine possible source of infection.
- If infectious, give advice to case to limit infectivity to others and identify sexual and close household contacts. Arrange to have their hepatitis B markers checked to see if they have already been infected before vaccinating them. Contacts who are HBsAg, anti-HBs, or anti-HBc positive do not need to be vaccinated, although for sexual partners the first dose of vaccine should be given while awaiting test results and the use of condoms advised until immunity is established.

Investigation of a cluster and response to an outbreak

- Look for a common source and take appropriate action.
- If an infected healthcare worker (HCW) is the source, a look-back investigation should be conducted to identify other cases associated with the HCW (see Chapter 4.6).

Suggested case-definition for an outbreak
Jaundice plus presence in serum of HBsAg, or HBeAg, or anti-HBc IgM.

3.32 Hepatitis C

Hepatitis C Virus (HCV) is a small, enveloped, single-stranded RNA virus, causing hepatitis. Hepatitis C poses a significant threat to global public health. With approximately 2.5% or 177.5 million adults worldwide ever infected with HCV, and 67% of them (i.e. 118.9 million) chronically infected. A substantial proportion of those chronically infected are at increased risk for developing chronic liver disease in the future.

Suggested on-call action
Action rarely needed outside of office hours.

Epidemiology

HCV was first identified in 1989 and a reliable antibody test became available in 1991. Surveillance of HCV infection is influenced by the availability and extent of testing and reporting of results. Current antibody tests do not differentiate between present and past infection and since most acute infections are asymptomatic it is not possible to distinguish

incident from prevalent cases, except when someone has detectable HCV-RNA but no antibodies (yet). A rule of thumb is that two-thirds of people with antibodies are chronically infected. The most prominent risk group is people who inject drugs (PWID). HCV prevalence is also expected to be higher among first-generation migrants from endemic countries, HIV-infected MSM and people who received blood and blood products before 1992.

From 2006 to 2014, the overall number of diagnosed and reported cases across 28 reporting EU/EEA Member states increased by 28.7% to 8.8 cases per 100 000 population, varying from 0.1 in Italy to 74.5 in Latvia. The majority of the reported HCV infections are classified as chronic or 'unknown'; the latter probably representing mainly chronic infections.

Clinical features

Acute hepatitis C virus infection is often asymptomatic. The incubation period for clinical disease is variable (two weeks to six months). Liver enzymes (e.g. ALT) may be elevated, but jaundice is uncommon and fulminant hepatitis is rare. Following infection, 20–25% will clear the virus within six months. Of those that are chronically infected, 75% will have some degree of active liver disease and of these 25% may develop fibrosis and ultimately cirrhosis over a period of 20 years. A patient with liver cirrhosis has an annual risk of hepatocellular carcinoma and hepatic decompensation, of respectively 1–5% and 3–6%.

Laboratory confirmation

Anti-HCV IgG antibody tests are usually positive within three months of infection, but this may be delayed when one is co-infected with HIV or with other causes of immunosuppression. Quantitative and qualitative PCR tests for HCV RNA are used in the second step to differentiate between chronic infection and cleared infection. HCV genotypes and subtypes have different geographical distributions and may predict (partly) response to treatment. In the EU, genotype 1a is the most prevalent genotype. Depending on the risk group, genotype 3a, 1b, 4d, 4a, and to a lesser extent genotype 2, are also prevalent in the EU. Genotypes 5, 6 and 7 are predominantly seen in South Africa, Southeast Asia and Central Africa, respectively. To distinguish between the seven main HCV genotypes (and the many sub-types that are currently known), sequence analysis is possible. Alternatively, a commercial line probe assay (LiPA) and a real-time HCV genotype assay are available.

Transmission

HCV is mainly spread by contact with the blood of an infected person (blood–blood contact), for example through needle sharing (or other injecting equipment) among PWID. Other, less efficient routes of transmission are unprotected anal sex with an infected partner (especially when one is already infected with HIV); vertical spread from mother to infant, unsafe medical and dental procedures; tattooing or skin piercing with blood-contaminated equipment; and horizontal spread in households as a result of sharing contaminated toothbrushes or razors.

Nosocomial and vertical transmission is uncommon. Sexual transmission among serodiscordant heterosexual couples is inefficient.

Prevention

Unlike hepatitis A and hepatitis B, no vaccine is available yet for hepatitis C. Control of HCV infection therefore depends on the following (see Table 3.32.1):

- improved surveillance,
- raising public and professional awareness
- case finding by more testing of defined risk groups,
- better treatment and care,

Table 3.32.1 Target groups for particular HCV prevention measures

People who inject drugs (PWID)	Needle exchange schemes. Supply of other injecting equipment such as spoons, filters, water and tourniquets. Methadone and other maintenance programmes. Health education targeted at younger drug injectors and people injecting drugs for the first time. Promote hygienic injecting practices. Encourage other drug administration routes such as smoking and snorting. Consider alcohol and hepatitis B (co-factors in development of liver disease). Established PWIDs and ex-PWIDs should have access to appropriate services.
People with HCV infection, their sexual partners and household contacts	Access to information, counselling, testing and referral. Adopt measures to reduce the risk of further transmission (see Chapter 1.3, universal precautions for blood-borne infections). Advise on alcohol use to reduce risk of liver damage. Develop clinical networks for diagnosis and treatment.
Health and social care workers including staff of alcohol and drug agencies	Ensure good knowledge of HCV and other blood-borne viral infections. Implement infection control measures, including universal precautions. National guidelines on occupational aspects of HCV have been published. Guidelines are available for staff in drugs services and renal dialysis centres.
Prisoners, prison staff and Probation Service staff	Access to information and professional advice, including counselling, testing and referral. Supply injecting equipment in prisons.
General population, particularly young people	Ensure awareness of HCV and transmission. Implement universal precautions to manage bleeding and blood spillages in the community. Follow infection control guidelines for skin piercing, tattooing, and so on.
Blood, organ and tissue donation	People with HCV and those who may have been exposed to HCV should not donate blood or carry a donor card. Screening and heat treatment should be used where appropriate.
HCV infection in mothers and infants	Universal antenatal screening for HCV is not recommended. Pregnant women at risk of HCV infection should be offered hepatitis C testing. Breast feeding should be discouraged only if the mother is viraemic.

- preventing transmission among injecting drug users, young people and in prisons by needle exchanges and targeted education,
- promoting infection control measures in community and health care settings.

Surveillance

- Hepatitis C is a statutory notifiable disease in all 28 EU countries; 14 using the same case definition. In four countries, only acute hepatitis C is notifiable.
- Cases of chronic HCV infection, detected as a result of serological testing should be reported to national laboratory surveillance schemes where appropriate.
- Acute cases should be reported to the local health authorities for investigation.

Response to a case

- Cases should receive information about the infection and advice on preventing further spread. Patient advice leaflets are available.
- For acute cases, enquire about the circumstances of exposure and the possibility of infection as a result of condomless (anal) sex, unsafe medical procedures, acupuncture, other alternative therapy and blood transfusion.
- The case should be referred for further investigation and possible treatment if indicated and longer-term support and counselling.

- HCV is increasingly being treated with a relatively short course (12 weeks) of direct-acting antiviral (DAA) therapy. The use of these DAAs is replacing therapy with pegylated interferon and ribavarin, which was given for 24–48 weeks (depending on the genotype of infection). International and national treatment guidelines are available. The preferred regimen may vary by HCV genotype, fibrosis stage, and previous treatment outcome. Drug interactions with HIV medication need to be addressed before commencing treatment. Sustained virological response (SVR) is regarded as a cure, and is defined as having no detectable HCV-RNA 12 weeks after cessation of treatment. SVR may be achieved after DAA treatment in ≥95% of cases.

Investigation of an HCV incident or outbreak

- All those who have potentially been exposed should be identified and offered testing. Those with evidence of infection will need counselling and follow-up by a liver specialist who can advise on treatment options.
- If a healthcare worker who has performed exposure prone procedures is found to have HCV infection, a look back exercise may be required (see Chapter 4.6).

Suggested case definition for an outbreak

An acute illness with:
(a) discrete onset of symptoms (such as nausea, vomiting, abdominal pain and diarrhoea) AND
(b) jaundice or abnormal serum aminotransferase levels.

Laboratory criteria for diagnosis:
(a) Elevated serum AST/ALT level and anti-HAV IgM negative, AND
(b) Anti-HBc IgM negative, or if not done, HBsAg negative, AND
(c) Anti-HCV screening-test-positive verified by an additional more specific assay (e.g. HCV RNA).

3.33 Hepatitis, delta

Delta hepatitis (HDV) is caused by a satellite virus that only infects patients during the antigen-positive stages of acute hepatitis B (HBV) or long-term HBsAg carriers.

The epidemiology is thus similar to that of HBV (see Chapter 3.31), although it is much less common; worldwide about 15–20 million people are infected with HDV. In Europe, prevalence rates are highest in Romania and the Mediterranean countries.

Clinically HDV infection leads more frequently to fulminant hepatitis, compared with HBV alone. Chronic HDV causes also more morbidity and complications than chronic HBV alone.

Transmission is by the same routes as HBV, but HDV is rarely transmitted sexually or horizontally; in Europe transmission is most commonly by intravenous drug misuse.

The incubation period is two to eight weeks.

General control measures for blood-borne viruses (Chapter 4.9) will prevent spread of HDV.

There is no specific vaccine or immunoglobulin, but vaccination against HBV prevents infection, as immunity to HBV prevents HDV infection.

3.34 Hepatitis E

Hepatitis E virus (HEV) is the main cause of enterically transmitted non-A non-B viral hepatitis worldwide. The epidemiology varies considerably depending on which of the four HEV genotypes (HEV1 to HEV4) is circulating (HEV1 Asia and Latin America; HEV2 Africa and Mexico; HEV3 world wide; HEV4 Eastern Asia and Central Europe). HEV1 and HEV2 are found in humans, cause sporadic and epidemic hepatitis and are spread via the faecal–oral route, mainly via contaminated drinking water. HEV3 and HEV 4 are enzootic in a number of animals (domesticated pigs, wild boars and deer mainly) and can cause infections in humans.

Suggested on-call action
• None usually required

Epidemiology

Although rare in Europe, HEV should be considered an emerging infectious disease. Although not notifiable in most EU countries, reported cases increased from 514 in 2005 to 5617 cases in 2015, with 21 000 cases reported from 22 countries between 2005 and 2015. In England and Wales, reports have increased from 274 cases in 2010 to 848 in 2015. Seroprevalence increases with age and in Europe, the majority of cases (>60%) are males aged >55 years. HEV is responsible for around half of acute sporadic hepatitis in many developing countries and is hyper-endemic in southern Asia (HEV1, HEV4), northern and western Africa and Central America (HEV2). Most clinically reported cases in hyper-endemic areas occur in young or middle-aged adults.

Diagnosis

HEV causes a mild, self-limiting illness with clinical features that range from asymptomatic infection to fulminant hepatitis without carriage. Symptoms are similar to hepatitis A (abdominal pain, anorexia, dark urine, fever, hepatomegaly, jaundice, malaise, nausea and vomiting). The severity of hepatitis is agent, age and dose-dependent. Case-fatality is low (around 1% for HEV3 and HEV4), except in women infected in the third trimester of pregnancy, when it may reach 25–30%, although this has only been observed in hyper-endemic regions for HEV1 and HEV2.

Chronic HEV infection has been observed in immunocompromised persons infected with HEV3 or 4.

Diagnosis is based on serology to detect IgM and IgG anti-HEV antibodies and/or molecular tests (RT-PCR) to detect HEV RNA.

Groups at greater risk of severe disease following HEV infection include:

- pregnant women (risk highest during the third trimester);
- Persons with pre-existing chronic liver disease, liver injury or heavy alcohol consumption;
- Immunocompromised persons (example: HIV-infected persons, solid organ transplant recipients, and so on).

Transmission and acquisition

HEV is transmitted faeco–orally, with most outbreaks in hyper-endemic regions linked to contaminated drinking water. In the EU/EEA, non-travel related HEV infections (indigenous cases) are mostly zoonotic and occur via food-borne transmission, with HEV 3 identified as the predominant genotype (associated with consumption of processed pork products). Person-to-person spread is uncommon (1–2% secondary attack rate), but vertical transmission can occur resulting in poor foetal outcomes. Nosocomial spread is described and transfusion-related HEV infection has been reported in the UK, France and Japan. Virus excretion in stools probably occurs before clinical onset and lasts up to 14 days afterwards. The incubation period is reported as 15–60 days (mean 40 days).

Prevention

- Prevention relies primarily on provision of safe water supplies.
- European travellers to hyper-endemic countries, particularly if pregnant, should take care to avoid consuming contaminated food (e.g. undercooked meat and shellfish) and water.
- Confirmed or suspected cases in Europe should be notified to local public health authorities.
- There is currently no licensed vaccine available in Europe, but two effective vaccines have been developed with one licensed for use in China protecting against HEV4.

- Severely immunocompromised persons (solid organ transplant, haematological malignancy, and so on) should avoid eating pork meat and related products.

Surveillance

Acute infectious hepatitis is notifiable in the UK. However, HEV infection is not notifiable in most European countries.

Response to a case

- Supportive care
- Ribavirin may be considered in severe cases and chronic HEV

Suggested definitions for acute and chronic hepatitis E infection

Acute HEV infection is confirmed by one of the following virology laboratory markers:
- HEV IgM and IgG positive;
- HEV RNA positive (with or without detectable HEV antibodies).

Chronic HEV infection is confirmed by HEV RNA persisting for at least six months (with or without detectable HEV antibodies).

3.35 Herpes simplex

Infection with herpes simplex viruses (HSV) is characterised by a localised primary infection, latency, and recurrence. HSV-1 is typically associated with gingivostomatitis and pharyngitis with recurrent 'cold sore', and HSV-2 with genital infection (see Chapter 3.26). However, either may affect the genital tract and HSV-2 can also cause primary infection of the mouth.

Suggested on-call action

Usually none required.

Epidemiology

Seroprevalence increases with age. Worldwide, by the fifth decade of life the seroprevalence of HSV-1 and HSV-2 combined is around 90%, with higher prevalence in populations with low socio-economic status. The WHO estimated that in 2012 over 3.7 billion people aged 15-49 were living with HSV-1 infection and 417 million with HSV-2. The global incidence is estimated at 23 million new cases per year. In Europe the seroprevalence of HSV-1 has been decreasing over the last decades, and of HSV-2 increasing (to 65.6 and 22% respectively in 2015), although HSV-2 incidence seems to have levelled off in recent years. In Europe, the prevalence of HSV-1 and HSV-2 demonstrates a geographical gradient from east to west and south to north. The incidence of HSV-1 infection peaks in preschool-aged children, with a second lower peak in young adults; it is rare in infancy because of passive maternal antibody. HSV-2 is generally acquired sexually and seroprevalence increases in puberty with initiation of sexual activity. Higher prevalences are seen in people with previous STI, more sexual partners, MSM, and HIV+MSM. Generally HSV prevalence is higher in females, older age groups, persons with low socio-economic status, certain immigrant groups (HSV-1 Turkey and Morocco; HSV-2 Caribbean America). UK General Practitioners report a 10-year mean weekly incidence of herpes simplex of around 6 per 100 000 population. Neonatal herpes is rare in Europe with a range of 1.6–3.2 per 100 000 deliveries, but can be higher in other parts of the world (Israel 8 per 100 000, USA 5–33 per 100 000)

Clinical features

Most infections are asymptomatic. Primary infection is symptomatic in 67% of HSV-1 and 37% of HSV-2. Following a short prodromal period of fever, muscle pains and weakness, localised symptoms appear, which depending on site of inoculation may include painful gingivostomatitis, keratitis, ulcerating skin

vesicles, urethritis, proctitis, ulcerating genital vesicles, vaginal discharge. As a result of autoinoculation lesions may affect other sites such as the eye and finger (herpetic whitlow). The illness resolves after 7–28 days. Complications include eczema herpeticum (in patients with pre-existing constitutional eczema), Bell's palsy, encephalitis, meningitis, ocular herpes and erythema multiforme. Following primary infection, HSV persists in the dorsal root ganglia of the spinal cord, reactivating after a range of trigger factors (e.g. upper respiratory tract infections, fatigue, emotional stress, physical trauma, exposure to sun, dental extraction, menstruation, and drugs such as corticosteroids). Frequency of reactivation varies widely, depending on locus of infection and virus type. HSV-2 reactivation is four times more frequent (0.34 per month after first episode) than in HSV-1, and is most seen in the first year after primary infection. Asymptomatic viral shedding over one to four days is demonstrated to occur periodically in 20% of the days in a year. Some dental procedures (i.e. trigeminal nerve root decompression/dental extractions) are associated with a higher risk of reactivation.

In persons with impaired cellular immunity (e.g. HIV infections with CD4<200 cellsmm^3; bone marrow transplant recipients) the disease is more serious and dissemination can occur leading to pneumonia, colitis, oesophagitis, meningo-encephalitis with high mortality rates.

Laboratory confirmation

HSV is a large DNA herpes virus with a typical appearance on electron microscopy. The diagnosis of mucocutaneous HSV infection is often made clinically, but PCR for HSV-1 and HSV-2 DNA in vesicle fluid or scrapings can assist in case of doubt to confirm diagnosis. PCR has replaced electron microscopy and viral culture as the preferred method of diagnosis.

Transmission

Humans are the only reservoir of infection and spread is by contact with oral secretions during kissing, skin contact (during contact sports: herpes gladiatorum) and during sexual intercourse. Neonates may be infected vertically (5%), at the time of delivery (90%), or in the week after delivery (5%). The risk for neonatal herpes is greatest when a mother acquires HSV infection for the first time in late pregnancy. Parents or carers can transmit the virus in the first week by hugging and kissing. The virus does not survive for long periods in the environment and cannot penetrate intact skin. HSV is highly infectious, especially in young children and attack rates approach 80% in non-immune subjects.

Acquisition

The incubation period is 2–20 days (mean 6 days). The virus may be shed in saliva for 2–20 days (mean 7 days) in primary infection and 1–4 days in recurrent infection. At any one time, 20% of young children may be shedding virus. HSV infection is lifelong and patients with impaired cellular immunity, skin disorders and burns are at risk of severe and persistent infections.

Prevention

- Health education and attention to personal hygiene (hand washing) and barrier methods (condom use) may reduce exposure.
- Condom use is included in all STI health education programmes and is targeted at groups with highest risk, for example MSM, HIV+ persons, and people with multiple sex partners.
- Gloves should be available for health and social care staff in contact with potential infection.
- Patients and health care workers (HCW) with active HSV infection should avoid direct contact with high-risk patients (i.e. infants less than one month, burns patients and people with eczema or impaired immunity): cover lesions (cold sore) with a mouth mask and maintain meticulous hand hygiene.

- Caesarean section is indicated (according the Royal College of Obstetricians and Gynaecologists) in patients with primary genital herpes infections with lesions within six weeks of estimated delivery.
- In primary infected patients with amenorrhoea >34 weeks consider acyclovir until delivery, and if vaginal delivery consider acyclovir i.v. during labour.
- Sunscreen and oral antivirals may be considered to prevent reactivation.

Response to a case/cluster/outbreak

- Treatment is symptomatic and supportive.
- Oral antivirals may be considered for primary infection and reactivation particularly when there is severe disease. Nucleoside analogues (acyclovir, valacyclovir, famciclovir) reduce viral shedding and transmission.
- Topical antivirals may be used for reactivation.
- Ocular herpes simplex disease is the commonest cause of corneal blindness in high-income countries and should be treated as an ophthalmic emergency.
- Patients with extensive infection should be nursed with source isolation.
- Children, nursery and school staff with cold sores do not need to be excluded from day-care centres or school.

Suggested case definition for an outbreak

Characteristic lesions with or without laboratory confirmation by PCR, electron microscopy or viral culture.

3.36 *Haemophilus influenzae* type b (Hib)

Haemophilus influenzae type b (Hib) is a bacterial infection of young children that causes meningitis and other bacteraemic diseases including pneumonia, epiglottitis, facial cellulitis and bone and joint infections. Its importance lies in the high rate of disease complications and the availability of a vaccine.

Suggested on-call action

- Seek laboratory confirmation.
- Obtain vaccination history.
- Arrange for chemoprophylaxis and vaccination of contacts for confirmed type b cases (see 'Response to case' section)

Epidemiology

The disease is commonest in children under five. Before vaccination was introduced, Hib was the second most common cause of bacterial meningitis overall, and the commonest in young children. In Europe the incidence in children under 5 was 42 per 100 000, this has dropped to less than 0.1 per 100 000. The case fatality rate is 4–5% (higher in infants) and up to 30% of survivors have permanent neurological sequelae, including deafness, convulsions and mental impairment. There is a seasonal trend, with more cases reported in winter months.

With the widespread introduction of vaccination against type b strains, non-capsulated strains of *H. influenzae* are now the most common cause of invasive disease. Other capsulated serotypes of *H. influenzae* (especially type f) also cause invasive disease and are now as common as type b cases. Non-capsulated *H. influenzae* also causes ear infections or acute exacerbations of chronic bronchitis.

The overall notification rate for invasive *H. influenzae disease* in 2015 for Europe was 0.7 per 100 000 with highest rates in infants (4.5 per 100 000) and the elderly (1.9 per 100 000). For the 2015 cases with a known serotyping result, 82% (n = 1647) were non-capsulated. The majority of invasive non-capsulated strains were 65 years of age or over. Serotype b (Hib) caused only 4% (n = 90) of cases in 2015.

Clinical features

Hib meningitis typically has a slower onset than meningococcal meningitis, with symptoms developing over three or four days. There is progressive headache, drowsiness, and vomiting with intermittent fever. Photophobia may be present. A haemorrhagic rash can be present, but is unusual. In soft tissue, bone and joint infections there is swelling of the affected area. Hib epiglottitis presents with acute respiratory obstruction.

For the cases of *H. influenzae* (all serotypes) reported in Europe in 2015, the clinical presentation was known for 1633. Septicaemia was reported in 854 cases (52%), pneumonia in 486 (30%), and meningitis in 160 (10%). Fifteen cases presented with both septicaemia and meningitis. Five cases of epiglottitis, five cases of cellulitis, and ten cases of septic arthritis/osteomyelitis were reported. For 98 cases, the clinical presentation was reported as 'other'.

Laboratory confirmation

This is important, as the clinical features are variable and non-specific; it is also useful to ascertain vaccine failures. A positive culture may be obtained from blood or CSF. Alternatively, Hib antigen can be demonstrated by latex agglutination or PCR. All strains should be sent to the national reference laboratory for confirmation and typing.

Transmission

Man is the only reservoir. Transmission is by droplet infection and direct contact with nose and throat secretions. In unvaccinated populations carriage is common in young children; about 4–5% of unvaccinated three-year-olds are carriers. Vaccination prevents carriage.

Acquisition

The incubation period is not known, but is probably only two to four days. Cases are non-infectious within 48 hours of starting effective antibiotic treatment. Disease usually results in lifetime immunity, although repeat infections have been described. Immunity is also derived from carriage, from infection with cross-protective antigens such as *Escherichia coli*, and from vaccination.

Prevention

Routine vaccination of infants with protein–polysaccharide conjugate vaccines has been implemented throughout Europe. Three doses are required in infants; children over 12 months require only a single dose. A booster dose is required in the second year of life.

Surveillance

- Report cases of invasive Hib disease to local health protection team. Some countries also operate an enhanced surveillance scheme.
- Report any case in a vaccinated child to the national surveillance unit. Notifications should always be based on laboratory reports.
- Hib surveillance in Europe is co-ordinated by ECDC through The European Surveillance System (TESSy).

Response to a case

- Laboratory confirmation must be sought. Most cases (especially in neonates) are due to non-encapsulated strains, for which no public health action is required. If serotyping is likely to take more than 48 hours, public health action should be considered.
- Check vaccination status of the case and of household contacts.
- If there are any unvaccinated children under 10 years in the household, they should be vaccinated.
- Irrespective of vaccination status of other children in the household, all household members (including adults, who may be the source of infection) should be given chemoprophylaxis (Box 3.36.1). The case

Box 3.36.1 Chemoprophylaxis for invasive Hib disease

Rifampicin, orally, 20 mg kg^{-1} daily for four days (maximum 600 mg daily).

should also receive chemoprophylaxis and vaccine.

- Warn patients of the adverse effects of rifampicin (red staining of urine, sputum, tears and contact lenses, interference with the oral contraceptive pill).
- Cases should be excluded from school/nursery until antibiotic treatment has started; there is no need to exclude siblings or other close contacts of cases.
- Inform families of other children at nursery or school, if index under 10 years of age, to seek medical advice if child becomes unwell and to ensure that immunisations are up to date. For settings where a group of children who have levels of contact approaching those in the household can be defined – for example, a small number of children attending the same child-minder for several hours each day – offering prophylaxis to the close-contact group should be considered.
- Index cases aged under 10 years should receive rifampicin prophylaxis before discharge from hospital and if vaccination history incomplete, should receive any missing Hib vaccine doses. Those who have been previously fully vaccinated may benefit from antibody testing and/or a further booster. National vaccination recommendations should be followed.

Investigation and control of a cluster

- Give chemoprophylaxis (and vaccine, if unvaccinated) to nursery contacts if there are two or more cases within 120 days.
- In addition to the measures described for a case, there may be a need to conduct a local vaccination programme if coverage is low.

Suggested case-definition for an outbreak

Confirmed: clinically compatible illness with an isolate or antigen detection of Hib from a normally sterile site.
Clinical: meningitis or epiglottitis with no other cause in:
an unvaccinated child under five years of age; *or*
an unvaccinated individual with links to confirmed case(s).

3.37 HIV

Acquired immune deficiency syndrome (AIDS) is the result of advanced infection with human immunodeficiency virus (HIV-1). There is a second human immunodeficiency virus, HIV-2, which is endemic in western Africa: it causes a spectrum of disease similar to that produced by HIV-1.

Suggested on-call action

- Most cases do not require an on-call response
- Advise on the management of HIV-related incidents, particularly exposure incidents (see Box 3.37.1).

Epidemiology

About 36.7 million people worldwide were estimated to be living with HIV infection in 2016, of which 25.6 million were living in Africa. About 1.8 million new cases were diagnosed in 2016 and there were about 1 million HIV-related deaths.

About 30 000 new cases of HIV infection a year are reported in the 31 EU/EEA countries, a rate of about 6 per 100 000: rates have remained relatively stable for the past 10 years, after a substantial increase in the previous 10 years, particularly in eastern and central Europe. The highest incidence rates within

Box 3.37.1 Action following an HIV exposure

- The risk of acquiring HIV from a patient with HIV infection following a needle stick injury is 3 per 1000 injuries and is less than 1 per 1000 following mucous membrane exposure. Risks are greater with hollow needles, needles that are visibly blood-stained or which have been in an artery or vein, deep injuries and injuries from source patients who are terminally ill. Risk of infection can be reduced by 80% by post-exposure prophylaxis (PEP) with antiretroviral drug combinations.
- Follow national or local guidelines where available.
- Following an exposure, the wound should be washed liberally with soap and water and free bleeding should be encouraged. Exposed mucous membranes including conjunctivae should be irrigated and contact lenses should be removed. The injury should be reported promptly.
- All healthcare employers should provide staff with 24-hour access to appropriate advice (e.g. via Occupational Health departments in working hours and hospital emergency departments out of hours). The designated doctor should assess the risk of transmission of HIV (and HBV+HCV) and the need for post-exposure management. The risk assessment is based on the type of body fluid involved and the route and severity of the exposure. Injuries from sharp objects that break the skin, exposure of broken skin and exposure of mucous membranes including the eye are significant injuries. Most body fluids pose a risk of transmission. The exceptions are urine, vomit, faeces and saliva, unless visibly bloodstained. Saliva associated with dentistry is considered blood-stained.
- As a routine, the designated doctor or member of the clinical team (not the exposed worker) should approach the source patient (if known) and obtain informed consent, after pre-test discussion, to test for HIV antibodies plus antigen, HIV RNA, HBsAg, anti-HCV and HCV RNA. Testing of the source patients should be completed within 8-24 hours.
- If there is an HIV risk, PEP should be started within one hour. Subsequently PEP may be discontinued if it is established that the source patient is HIV negative or is confirmed to have a sustained undetectable viral load.
- PEP should be started as soon as possible after exposure, preferably within 24 hours (and certainly within 72 hours) and continued for 28 days. If the exposed healthcare worker (HCW) is pregnant, has an existing medical condition, is taking other medication or if there is the possibility of viral resistance, then expert advice should be obtained. The HCW should be followed up during the period of PEP, to monitor treatment side effects and ensure compliance.
- In addition, the HBV immunity of the HCW should be assessed and if necessary blood should be taken for urgent anti-HBs testing. An accelerated course of vaccine, a booster dose of vaccine and/or HBIG may be given according to published algorithms. For HCV no immunisation or prophylaxis is available. A baseline blood sample should be obtained from the exposed worker and stored for two years. If the source is HIV infected, the worker should be tested for anti-HIV at least 12 weeks after the exposure or after HIV PEP was stopped whichever is the later. Testing for anti-HIV at six weeks and six months is no longer recommended. Also if the source is HCV infected, the worker should be tested for HCV RNA at 6 and 12 weeks and for anti-HCV at 12 and 24 weeks.
- In the absence of seroconversion, restriction of working practices is not necessary, but infection control measures, safer sex practices, and avoiding blood donation should be observed during the follow-up period. Generally management of workers exposed to a potential blood-borne virus source whose status is unknown, or a source that is unavailable for testing, will depend upon a risk assessment and a discussion of the benefits of intervention.
- Exposure outside the healthcare setting including sexual exposure and sharing drug-injecting equipment may give rise to a request for PEP or the need to consider it. A similar process of risk assessment should be followed and national guidelines may be available. PEP is not usually advised for needlestick exposure in the community from an unknown source. For sexual exposure, the risk varies by type of sexual act (anal/vaginal/oral; receptive/insertive), and knowledge of the HIV status of the contact (known positive? Viral load? Known higher risk group?).

the EU/EEA were reported from Latvia, Estonia and Malta (up-to-date country-specific rates can be found on the ECDC website), although rates are higher in eastern non-EU/EEA countries such as Russia, Ukraine, Belarus and Moldova. Rates were three times higher in men than women; and the most commonly reported route of transmission was sex between men (MSM, 40%), followed by heterosexual transmission (32%), intravenous drug use (IDU, 4%), and vertical transmission (1%), although the transmission route was not stated for 23% of reports. An average of 40% of cases originated from outside the country of diagnosis, although this varied considerably by country. Late diagnosis remains common (about half of cases across EU/EEA have a CD4 cell count below 350 cells mm^{-3}) and over 3600 cases of AIDS (0.7 per 100 000) were reported in 2016, although AIDS incidence has fallen in recent years. HIV prevalence is much higher than the reported annual incidence and has increased in recent years, due to improvements in treatment, leading to prolonged survival after diagnosis (in England, 5164 new infections were reported in 2016, but overall incidence was estimated as 89 400). Many infected individuals will be undiagnosed: in the EU/EEA, it is estimated that 15% are unaware of their infection, but this will be considerably higher in some countries.

Clinical features

The clinical manifestations of HIV infection range from the initial acute retroviral syndrome, via latent infection to full-blown AIDS. About one to six weeks after exposure to HIV, an acute retroviral syndrome may result, in which there is a period of viraemia during which the individual is very infectious and may experience fever and rash. Antibodies to HIV then develop and the infection may then remain dormant for many years, although the presence of certain 'HIV indicator' symptoms (e.g. unexplained fatigue, diarrhoea, weight loss, lymphadenopathy, anaemia, thrombocytopenia, fever, polyneuropathy) or illnesses (e.g. oropharyngeal candidiasis, herpes zoster, severe seborrhoeic eczema and hepatitis B, C and other STIs) may lead to testing for HIV infection (amongst other potential causes).

HIV-1 binds to CD4 receptors on lymphocytes or macrophages. The virus is internalised and integrated into the host cell genome leading to permanent infection. Virions may bud from the cell surface to infect another cell or infection may be spread when cells divide. Eventually the infected cells are killed by the virus. The CD4 count is normally 600–1200 cells mm^{-3}, but in untreated HIV infection it may fall to less than 200 cells mm^{-3} leading to severe immunosuppression which is associated with opportunistic infections, neoplasia and AIDS.

Laboratory confirmation

Diagnosis has traditionally been made with an ELISA test that detects both anti-HIV-1 and anti-HIV-2: ELISA sensitivity is high and negative tests are considered reliable (although may need to be repeated if exposure recent – NB, this 'window period' is longer in fourth-generation ELISA tests). A positive test should be confirmed by a more specific test, such as a western blot antibody test. Combined antigen–antibody tests are now available and are used in many laboratories as first line tests. Rapid Antibody Tests are qualitative immunoassays that can be used as point-of-care tests on blood or oral fluid. Nucleic acid based tests identify certain target sequences located in specific HIV genes and can detect disease soon after infection. They can be used to screen blood donations when, because of expense, 8–24 samples are usually pooled before testing. 'Do It Yourself' tests available on the internet vary in sensitivity and specificity: testing in accredited laboratories is preferred. Quantification of plasma HIV-1 RNA ('viral load') is used to predict disease progression, monitor response to anti-viral treatment and assess infectivity. A CD4 cell count shows the level of immunosuppression. Genetic analysis can identify

subtypes of HIV suggesting connections between individuals sharing the same strain. Anti-viral resistance testing is also available.

Transmission

HIV is spread from person to person as a result of exposure to infected blood or tissues, usually as a result of sexual contact, sharing needles or syringes or transfusion of infected blood or blood components. Normal social or domestic contact carries no risk of transmission. Transmission is especially efficient between male homosexuals in whom receptive anal intercourse and multiple sexual partners are particular risk factors (it is estimated that the average infection risk after sexual contact with an infected person is between 0.1–3% for receptive anal and 0.06–0.62% for insertive anal contact). In countries where heterosexual spread is common, sexually transmitted infections causing genital ulceration and contact with multiple partners are associated with the highest rates of transmission (the average infection risk for one unsafe heterosexual contact with an infected person is estimated to be 0.014% for insertive vaginal contact and 0.2% for receptive vaginal contact). HIV is present in saliva, tears and urine, but transmission as a result of contact with these secretions is uncommon. HIV infection is not thought to be transmitted by biting insects. Between 15 and 30% of infants born to HIV-infected mothers are infected with HIV (without intervention) as a result of vertical transmission before, during or shortly after birth due to breast-feeding.

Acquisition

Following exposure, HIV nucleic acid sequences may be detected in the blood within 1–4 weeks and HIV antibodies can be detected within 4–12 weeks. Untreated, half of those with HIV infection will develop AIDS within 7–10 years and of these 80–90% will die within 3–5 years of this. Combination antiretroviral therapy (cART) dramatically reduces disease progression. A person with HIV infection will be infectious to others from shortly after the onset of the HIV infection throughout the rest of his or her life. Infectiousness increases with the degree of immunosuppression, viral load and the presence of sexually transmitted infections (however, HIV positive people under treatment with undetectable viral load have been demonstrated not to transmit the virus during sexual intercourse). Susceptibility to HIV infection is near universal, although a very small percentage of the population (<1%) is less susceptible to infection due to mutations in the gene coding for chemokine receptor, CCR5: heterozygote mutation may lead to delayed disease progression; in homozygote individuals infection is rarely seen.

Prevention

- Reduction of sexual transmission in the general population through health promotion activities to promote safer sex practices, including consistent condom use, which can reduce the risk of transmission by about 85%.
- Specific health promotion activities with higher risk groups, such as commercial sex workers, MSM and ethnic groups with links to high-prevalence countries (e.g. those in sub-Saharan Africa). General measures to reduce stigmatisation and discrimination against risk groups and HIV-positive individuals is also likely to benefit control efforts.
- Transmission between intravenous drug users can be reduced via harm reduction programmes, including by using sterile injecting equipment (e.g. from needle-exchange schemes), not sharing drugs or injecting paraphernalia, reducing injecting (through treatment services and/or oral opioid substitution) and testing and treating intravenous drug users for HIV.
- Vertical transmission from mother to child can be reduced by about 95% by screening all pregnant women, treating those who are HIV-positive with antiviral drugs, and avoiding breastfeeding.

- Blood-borne spread can be reduced by universal precautions in the healthcare environment; good infection control practice for practices such as tattooing and body piercing; and screening of blood donations, tissues for transplant and donations of other body fluids.
- Testing for HIV in:
  - sexual contacts of cases;
  - those attending specific health services (e.g. STI clinics, other sexual health services, antenatal clinics, dialysis patients and patients presenting with STIs, hepatitis B or C, TB or lymphoma);
  - specific high risk groups (e.g. IDUs, MSM, those with links to sub-Saharan Africa); and
  - wider screening of patients presenting to primary or secondary care services in geographical areas with high HIV prevalence (defined in UK as a prevalence of diagnosed HIV infections is 2 per 1000 population).
- Diagnosis and treatment of all HIV infected cases has public (as well as individual) health benefits by reducing transmission from existing cases by about 95%: UNAIDS 90 : 90 : 90 targets are that 90% of people living with HIV infection should be diagnosed, 90% of people diagnosed should be receiving treatment and 90% of people receiving treatment should be virally suppressed.
- Pre-exposure prophylaxis (PrEP) with antiretroviral drugs can reduce the risk of infection in HIV-seronegative individuals who are at substantial risk and is approved for this use in the EU.
- Post-exposure prophylaxis (PEP) can be used after a high-risk event to reduce the risk of seroconversion: this needs to be started within 72 hours of the exposure and continued for a month.
- Voluntary male circumcision has been shown to reduce the risk of heterosexually transmitted HIV in men by 60% in sub-Saharan Africa, but its effectiveness for women, MSM and in developed countries is unclear.
- There is no routinely available effective vaccine at present.

Surveillance

Most EU countries have national voluntary reporting systems for HIV infection and/or AIDS cases.

A comprehensive picture of the pattern of HIV infection can be obtained from a combination of the following types of surveillance:

- Ongoing case-based reporting from clinicians and laboratories of new diagnoses of HIV infection and AIDS,
- Regular cross-sectional survey of all persons who attend for HIV-related care,
- Laboratory testing for CD4 counts, HIV viral load and antiretroviral drug resistance to help monitor late diagnoses and treatment effectiveness,
- Monitoring of incidence in routine voluntary patient testing in specific groups (e.g. antenatal patients and blood donors),
- Specially designed unlinked anonymous HIV prevalence surveys in specific groups, such as intravenous drug users and STI clinic attenders, to help estimate the level of undiagnosed infection.

Response to a case

- Hospital patients with HIV infection should be nursed with infection control precautions for blood-borne viral infections (see Chapter 4.9).
- Offer advice on preventing further spread and encourage identification of sexual and needle sharing contacts so that counselling and HIV testing can be arranged: this may be undertaken by specialist confidential sexual health services.
- Early treatment with combination antiretroviral drugs dramatically limits disease progression and reduces infectivity: refer immediately to appropriate specialist for treatment in line with national guidelines.

Investigation and control of a HIV incident or cluster

- Clusters of cases of HIV infection may be detected when contact tracing is carried

out in sexual or drug-using networks. Occasionally a local increase in the incidence of HIV infection may occur. Standard outbreak investigation methods should be adopted. Particular care is needed to preserve patient confidentiality. Colleagues in the local sexual health clinic or drug team should be able to assist with case finding, interviews and blood tests.

- HIV-related incidents occur more commonly and may include: a healthcare worker with HIV infection, a percutaneous injury involving exposure to material from an HIV-infected person (Box 3.37.1) or a person with HIV infection who will not reliably follow advice to prevent further spread. Guidelines on how to respond to many of these incidents are available (see Appendix and/or national centre website). Generally public health legislation has not proved to be helpful in controlling spread from a person with HIV infection.

Suggested case-definition

HIV infection is defined by positive laboratory tests for HIV.

AIDS is defined by the development of one or more of the specific 'AIDS-defining' marker infections or neoplasms.

3.38 Influenza

Influenza virus (or 'flu') is a highly infectious cause of acute respiratory infection. It is a major cause of morbidity during epidemics and can be life threatening in the elderly and chronically unwell. It also has the potential to cause devastating pandemics.

Suggested on-call action

- Suggest case limits contact with non-vaccinated individuals who are at risk of severe disease.
- If linked to other cases in an institution, activate outbreak control plan or SOP.

Epidemiology

Influenza causes both annual winter epidemics of varying size and severity, and occasional more severe pandemics. All age-groups are affected, with highest incidence in children, but most hospitalisations and deaths are in the elderly. Between 3000 and 30000 excess winter deaths per year are attributed to influenza in the UK, depending on the size of the epidemic. Community outbreaks occur at variable times between November and March and tend to last 6–10 weeks, peaking at around the fourth week of the outbreak.

Influenza A and B viruses may alter gradually by 'antigenic drift': every few years this will result in a significant epidemic with rapid spread and a 10–20% attack rate. Influenza A may also change abruptly by 'antigenic shift' leading to the circulation of a new subtype to which there is little existing population immunity and causing a major pandemic, usually with severe disease in all ages: in the last century, these have occurred in 1918 (causing 20–40 million deaths worldwide), 1957, 1968 and 2009. Despite the huge impact of pandemics, more deaths result from the steady accumulation associated with yearly non-pandemic influenza activity.

Clinical features

About half of cases will have the classic flu picture of a sudden onset of fever, chills, headache, myalgia, malaise, and anorexia. There may also be a dry cough, sore throat, or runny nose. Up to 25% of children may also have nausea, vomiting or diarrhoea if infected by influenza B or A (H_1 N_1). The illness lasts two to seven days and may include marked prostration. Up to 10% of these cases progress to tracheobronchitis or pneumonia; some will develop non-pulmonary complications including cardiac and CNS features. Those at particular risk of complications are those with underlying chronic chest, heart or kidney disease, diabetes or immunosuppression, smokers, the obese and pregnant women.

About 20% of infections are asymptomatic (varies with strain) and 30% have upper respiratory symptoms but no fever. Influenza A may cause more severe disease than Influenza B, particularly in the elderly.

Laboratory confirmation

Confirmation of diagnosis is usually not required for uncomplicated sporadic infection in lower risk patients, once the virus has been shown to be circulating. If confirmation required for surveillance, outbreak investigation or use of antivirals, rapid diagnosis can be obtained by antigen detection tests or molecular assays (e.g. PCR), with the latter usually having higher sensitivity (specificity varies with background incidence of flu). The virus may be detected from nasopharyngeal aspirates, nasal swabs or throat swabs: these must be collected early in the disease and require special transport media. Typing results can be obtained by culture or from some PCR tests. Serology, which requires two specimens, 10–21 days apart, is about 80% sensitive: it can be useful for retrospective diagnosis.

Influenza virus has three types (A, B, C) of which influenza C produces only sporadic infections. Subtyping of influenza A is based on a combination of H antigen (15 subtypes) and N antigen (9 subtypes), for example HIN1 or H3N2. All recent common human pathogens are combinations of H1, H2 or H3 with N1 or N2. Strains may be further differentiated by serology and named after the place and years of their identification (e.g. A/Sydney/97): these can be compared to current vaccine strains.

Transmission

Influenza in humans is transmitted via the respiratory secretions of cases by air-borne droplet spread and via small particle aerosols. Coughing and sneezing particularly promote spread. Transmission is facilitated by overcrowding and enclosed spaces, particularly by the number of susceptibles sharing the same room as the case. Spread in such circumstances is usually rapid and attack rates high.

Transmission may also occur via direct or indirect contact: this may occasionally cause a slowly evolving outbreak with low attack rates. Many outbreaks have occurred in hospitals.

The reservoir for influenza A is zoonotic, particularly aquatic fowl: transmission to humans is rare but new strains may be spread directly or via intermediaries such as pigs. Humans may occasionally be exposed to avian influenza, although the risk from most strains is low (Box 3.38.1). Influenza B only affects humans.

Acquisition

The incubation period is short, usually 7–67 hours, with a median of 34 hours for type A and 14 hours for type B. The infectious period starts one day before onset of symptoms, peaks after one to two days of symptoms and then declines, so that infectivity is very low after seven days in adults. Shedding is higher in children and may be earlier and longer. Immunocompromised and other chronically ill patients may also excrete for a longer period. The infectious dose is low.

Immunity develops and protects against clinical illness with the same strain for many years. Cross immunity to related strains occurs. It is not clear why outbreaks often cease before exhausting the pool of susceptibles.

Prevention

- Basic personal hygiene to reduce transmission by coughing, sneezing or contaminated hands.
- Immunisation reduces the risk of severe disease, hospital admission and death and has a good safety record. Annual immunisation with WHO-recommended vaccines should be offered to all those with an increased risk of serious illness from influenza ('at risk'). All European countries

Box 3.38.1 Avian influenza

In recent years there has been much international concern over reports of human infection with avian influenza strains such as H_5N_1, H_9N_2, and H_7N_7. Some avian viruses cause serious infections in humans (Human HPAI H_5N_1 disease has a reported 60% mortality), but fortunately they do not spread easily, if at all, between humans. However, influenza viruses have the ability to undergo genetic reassortment, and co-infection with both avian and human influenza strains in humans or pigs could produce a new strain with the increased virulence of the avian strain and the ability to spread easily from person to person like human influenza. Transmission of this highly pathogenic virus could then occur to a population with no existing immunity and, as yet, no vaccine to protect them. Although such a virus is most likely to arise in China or South-East Asia, one modelling study suggested that it might only take two to four weeks for a suitably transmissible strain to spread from Hong Kong to the UK (and presumably to the rest of Europe) because of modern patterns of international travel. Rapid containment of incidents where avian strains infect humans is therefore essential to reducing the risk of future pandemics.

Although most containment activities will take place in the source area, European countries can limit the risk to their population by measures aimed at early detection of cases and minimising their contact with others.

European residents may occasionally be exposed to infected birds that have migrated from an infected area or to other birds that have been exposed to them (e.g. at poultry farms). Government animal health agencies will have plans to respond to cases in birds, but the public health professional may have to undertake a risk assessment of those potentially exposed, taking into account the known/apparent pathogenicity and transmissibility of the specific influenza strain. Depending on the result of the risk assessment, action may include use of post-exposure antiviral prophylaxis for those already exposed; use of pre-exposure prophylaxis and PPE for those involved in control of the animal outbreak; administration of seasonal flu vaccine (to prevent co-infection with transmissible human strains); and surveillance of those exposed and their close contacts.

recommend vaccination of older adults (most commonly defined as aged 65 or greater) and most recommend vaccination of people with chronic medical conditions, such as chronic respiratory, cardiac, renal, hepatic or neurological disease, and those with immunosuppression, asplenism or diabetes mellitus. Pregnant women and the morbidly obese are also at higher risk and may be offered vaccination.

- In addition, people in long-stay residential care homes should also be vaccinated because of the risk of rapid spread and the potentially severe consequences of infection. As efficacy in elderly people may be lower than the 70–90% in younger adults, indirect protection in this group may also be valuable.
- Immunisation is offered to healthcare workers in most European countries, both to protect patients and to maintain staffing levels, and it is recommended that residential care providers for elderly/unwell clients should also offer vaccination to their staff.
- Some European countries also immunise household contacts of 'at-risk' individuals (in line with WHO recommendations) and children on long-term aspirin.
- A few countries recommend vaccination of all children in certain age-groups: the nasally administered live virus vaccine is used in the UK. This has been shown to protect vaccinated children and reduce spread to other groups of the population, including at-risk groups.

- Uptake of immunisation in disease-based risk groups has been poor in some European countries, including the UK. Primary care staff can increase uptake by compiling an at-risk register from chronic disease, computerised patient or prescription records, or as patients are seen during the year. A letter should be sent to each of these patients, preferably from their family doctor, recommending vaccination. Education on the benefits of vaccination is required both for the target population and for healthcare workers. Local health services should appoint a co-ordinator to lead on improving influenza immunisation uptake locally.
- The antiviral drugs oseltamivir or zanamivir can be prescribed when influenza A or B virus is circulating in the community for the prevention of influenza in those who:
  - belong to an 'at-risk' group, and
  - have not received an influenza immunisation this season, or who had one within the last two weeks, or have had an influenza immunisation but the vaccine did not match the virus circulating in the community, and
  - have been in close contact with someone with influenza-like symptoms in the same household or residential setting (including care homes), and
  - can start taking oseltamivir within 48 hours (36 hours for zanamivir) of last being in contact with the person with influenza-like symptoms.
- National and local planning prior to occurrence of a pandemic (see Box 3.38.2).

Box 3.38.2 Pandemic preparedness

Influenza A viruses have the ability to exchange segments of their genome (genetic reassortment): if an animal is infected with two or more different strains of influenza A, then a novel viral strain could emerge. Should such an event produce a strain that is pathogenic to humans and is transmissible between people, but which has an antigenic profile that the human population has not been exposed to before (or not been exposed for many decades), then it could result in an influenza pandemic, with rapid spread worldwide and consequent morbidity and mortality. Many such pandemics have occurred throughout human history, with some, such as the 1918 'Spanish flu', producing unusually severe disease, with a much higher case-fatality rate. In contrast the 2009 pandemic had a much lower case-fatality rate.

The potentially devastating consequences of an influenza pandemic has made pandemic preparedness a public health priority. The WHO has updated its guidance following the 2009 pandemic and undertakes ongoing risk assessment of the global situation regarding each influenza virus with pandemic potential infecting humans. These assessments are made initially when such viruses are identified and are updated based on evolving virological, epidemiological and clinical data. This provides a high-level, global view of the evolving picture and uses the following phases:

Interpandemic phase: the period between influenza pandemics.

Alert phase: the phase when influenza caused by a new subtype has been identified in humans. Increased vigilance and careful risk assessment, at local, national and global levels, are characteristic of this phase. If the risk assessments indicate that the new virus is not developing into a pandemic strain, a de-escalation of activities towards those in the interpandemic phase may occur.

Pandemic phase: the period of global spread of human influenza caused by a new subtype based on global surveillance. Movement between the interpandemic, alert and pandemic phases may occur quickly or gradually, as indicated by the global risk assessment, principally based on virological, epidemiological and clinical data.

Box 3.38.2 (*Continued*)

Transition phase: as the assessed global risk reduces, de-escalation of global actions may occur, and reduction in response activities or movement towards recovery actions by countries may be appropriate, according to their own risk assessments.

All EU countries have developed detailed national preparedness plans; a series of planning and guidance documents, as well as indicators for self-assessments, are available on the ECDC web portal (http://www.ecdc.europa.eu). Pandemic preparedness plans typically cover the following areas:

- Preparation, planning and organisation, including:
  - Principles and strategic aims and objectives of national and local response.
  - International and national risk assessment and mechanism to declare a pandemic.
  - Scenarios of the impact of a pandemic and of interventions.
  - Roles and responsibilities of the main organisations contributing to the response, including member list of National Influenza Committee.
  - Exercising national and local plans.
- Public health response, including:
  - Surveillance requirements to detect initial cases, monitor spread and assess ongoing impact of pandemic.
  - Non-pharmacological public health measures to reduce spread, for example policies on isolation of cases, school closures, mass gatherings, public transport, border controls, and use of facemasks/respirators.
  - Antiviral prophylaxis and treatment strategies, including plans for procurement, stockpiling and delivery to patients.
  - Immunisation strategy, including procurement, distribution, and targeting of pandemic vaccines.
- Health service response, including:
  - Management of patients.
  - Infection control.
  - Organisation of health services and increasing capacity.
- Civil emergency response, including:
  - Maintaining essential services.
  - Managing deaths.
- Communications response, including:
  - Strategic communications.
  - Professional information and guidance.
  - Communications with the public and the media.
- Phased response, including escalation and recovery.

Surveillance

- Influenza activity can be monitored via a combination of clinical surveillance for 'influenza-like illness' and laboratory data.
- At the international level, WHO co-ordinates a global network covering 105 countries and publishes regularly updated information online. In Europe, weekly surveillance of seasonal influenza during the season is performed jointly by ECDC and WHO Regional Office for Europe and published on a joint platform, Flu News Europe (http://flunewseurope.org).
- At national level, data may be available from (some UK examples in brackets):
  - Telephone helplines for patients (e.g. NHS 111 diagnostic algorithms).

- General Practice consultations (e.g. Royal College of General Practitioners (RCGP) sentinel surveillance).
- Illness in schoolchildren (e.g. Medical Officers of Schools Association reports for boarding schools).
- Outbreaks of respiratory infection in institutional settings, such as hospitals, care homes and schools.
- Internet based weekly reporting from volunteer members of the public (e.g. FluSurvey in 10 European countries).
- Death certificates and excess mortality.
- Emergency admissions to hospital and/or Intensive Care Units (e.g. via UK Severe Influenza Surveillance Scheme).
- Sentinel virological surveillance using samples collected from primary care patients with influenza-like illness.
- Laboratory surveillance of routine samples of respiratory pathogens (e.g. PHE Respiratory DataMart Scheme).
- Subtyping, antigenic characterisation and antiviral susceptibility testing by reference laboratories.

UK data from these sources are available on the PHE website (www.phe.gov.uk).

- Regional or district monitoring may also be useful. Timely local feedback of interpreted data is particularly useful to local health service planners during the winter.
- Some countries set thresholds for clinical activity: these vary according to each system, but will often attempt to reflect baseline activity, normal seasonal activity, above average activity, and epidemic levels.

Response to a case

- Although spread may occur before diagnosis, symptomatic cases should ideally not attend work or school until recovered.
- Avoid contact with those at increased risk of severe illness. In hospital, isolate during acute illness.
- Handwashing and safe disposal of respiratory secretions. Droplet precautions in hospital.
- Use of antivirals in severely ill or higher-risk patients during flu season, in line with national guidelines.

Response to a cluster

- Only of concern if cases have links to institutions containing individuals at increased risk of severe disease and/or rapid spread (unless a pandemic strain).

Control of an outbreak

For outbreaks in institutions containing individuals at risk of severe disease:

- If virological diagnosis of outbreak is not confirmed, organise rapid testing (e.g. viral swabbing of the five most recent onset cases).
- Organise typing of virus to compare to vaccine.
- Immunise anyone not yet protected.
- Consider oseltamivir or zanamivir prophylaxis for 'at risk' patients for two weeks until vaccine induced protection present (influenza A or B): consult national guidelines.
- Exclude staff and visitors with respiratory illness.
- Isolate or cohort those with acute symptoms.
- Reinforce respiratory hygiene measures, including cough etiquette and handwashing. Re-inforce infection control and cleaning procedures. Use appropriate PPE.
- Close care home/ward to new admissions and avoid transfers to other homes/wards unless medically necessary.
- Treat influenza-like illness in 'at risk' patients (irrespective of vaccine status) with zanamivir or oseltamivir, unless contraindicated or symptoms have been present for over 48 hours (36 hours for zanamivir).

Suggested case-definition

Confirmed: upper or lower respiratory tract infection with laboratory evidence of influenza infection.

Clinical:

1 Managing an institutional outbreak: upper or lower respiratory tract infection without other identified cause in person epidemiologically linked to a confirmed case.

2 Monitoring a community outbreak: sudden onset of syndrome of fever, and cough occurring during a period of high influenza virus activity.

3.39 Japanese B encephalitis

This is a mosquito-borne viral encephalitis caused by a flavivirus. It occurs throughout South-East Asia and the Far East. The WHO has estimated that 67 900 clinical cases occur annually. Most infections are inapparent, although the illness can be severe with high mortality and permanent neurological sequelae in survivors. The reservoir is pigs and occasionally birds. Transmission to man is via a mosquito that lives in rice-growing areas. Transmission rates are highest in the rainy season.

Travellers to endemic countries are only at risk if they spend long periods (more than a month) in rural areas where pig farming and rice growing coexist. A vaccine is available which is licensed; the schedule is two doses 28 days apart; an accelerated schedule (0, 7 days) is licensed for adults. Adults at continuing risk (e.g. long-term travellers and laboratory personnel) should receive a booster dose at 12–24 months. The usual precautions against mosquito bites should be taken (see Chapter 4.11).

3.40 Legionellosis

Infection with *Legionella pneumophila* can cause a potentially life-threatening atypical pneumonia (Legionnaires' disease, LD) or a milder febrile illness (Pontiac fever, PF). Its public health importance lies in its ability to cause outbreaks, including large outbreaks in the community and hospital outbreaks with high case-fatality in particularly susceptible patients.

Suggested on-call action

- If linked to other cases, consult the outbreak control plan or SOP.
- If in hospital during incubation period, inform hospital infection control team.
- Otherwise, organise investigation of case on next working day.

Epidemiology

The true incidence of Legionnaires' disease is not known: estimates range from 1 to 20 per 100 000. LD has been reported to be responsible for between 0.5 and 15% of community-acquired pneumonias, with the proportion increasing with severity of disease. Approximately 7000 cases of LD are reported in the EU/EEA each year, of which about three-quarters are in males and over 90% are aged over 45 years (age-sex differences are not obvious in PF). Cases peak from June to October.

Travel is a major risk factor for LD: 20% of cases in Europe are contracted abroad (40% in UK, with a further 6% on trips within the UK), often in visits to southern Europe. About 10% of UK cases are linked to local outbreaks (predominantly due to 'wet cooling' systems or hot water systems) and about 4% are hospital acquired. Many cases are, however, sporadic and often from an unidentified source.

Clinical features

Both LD and PF commence with non-specific flu-like symptoms such as malaise, fever, myalgia, anorexia and headache, often with diarrhoea and confusion. PF is self-limiting, but LD progresses to pneumonia which, in an individual patient, is difficult to differentiate clinically from other causes of atypical pneumonia. In an outbreak, diagnostic clues might be the presence of diarrhoea (25–50% of cases), confusion, high fever, a lack of upper respiratory symptoms, and poor response to penicillins or cephalosporins. About 10% of reported LD cases die, rising to about a third of nosocomial cases. Many individuals who seroconvert to *Legionella* will be entirely asymptomatic.

Laboratory confirmation

There are 52 species of *Legionella*, comprising over 60 serogroups. Over 90% of legionellosis in immunocompetent individuals is due to *L. pneumophila*, which comprises at least 16 serogroups, of which serogroup 1 is responsible for the large majority of diagnosed infections.

Legionellae are not usually identified in routine culture of sputum or other respiratory samples, but selective media can be deployed: samples should be taken as early as possible to maximise sensitivity. Serogroup 1 antibody takes three to six weeks to rise to diagnostic levels. Serogroup 1 antigen may be detected in urine samples at a much earlier stage of the illness (approximately 75% sensitivity): local tests can be confirmed by reference laboratories, which may also be able to test for the virulent 'mAb2+ve' subgroup in urine samples. Organisms may be detected in lung tissue, sputum and other secretions by PCR (which has good sensitivity in experienced laboratories) or direct fluorescence antibody testing, (which is less sensitive). Reference laboratories may be able to diagnose infection due to other serogroups, if routine samples are negative in epidemiologically suspected Legionnaires' clusters. All suspected cases of Legionnaires' disease should have urine antigen testing (for rapid diagnosis of Serogroup 1) *and* culture of appropriate respiratory secretions on selective media to exclude other species (e.g. *Legionella longbeachae*) and serogroups and to allow subtyping to be performed (and preferably PCR if culture negative): this may require a respiratory sample to be sent to a reference laboratory (such reference testing is free in the UK).

Legionellae are common contaminants of water and so routine environmental testing is not helpful. However, culturing is useful in investigating suspected water sources for identified cases: five litres of water is necessary for culture. Biofilms are also worth culturing in outbreaks. Although some positive samples can be detected in two to three days, it may take ten days to confirm a sample as negative. If cultures are available from both patient and suspected source, then subtyping is available for comparison of the organisms (direct sequence based typing of samples may also be able to do this).

Transmission

The reservoir for the organism is environmental water, in which it occurs in low concentrations. Transmission to humans occurs via inhalation of aerosols or droplet nuclei containing an infective dose of the organism. Legionellae grow at temperatures between 25 and 45 °C (preferably 30–40 °C) and so the highest risk occurs with water systems which lead to the aerosolisation of water which has been stored at these temperatures. Such systems include hot water systems (especially showers), wet cooling systems (e.g. cooling towers and evaporative condensers), plastics factories, whirlpool spas, indoor and outdoor fountain/sprinkler systems, humidifiers, respiratory therapy equipment and industrial grinders. Wet cooling systems may contaminate air outside the building up to 6 km away, depending on conditions.

Legionellae can survive in water stored between 0 and 60 °C. They survive normal levels of chlorination and are aided by sediment accumulation and commensal microflora in the water (e.g. in biofilms). Temperatures above 63 °C are bactericidal, as are many common disinfectants (e.g. phenol, glutaraldehyde and hypochlorite).

Acquisition

The incubation period for Legionnaires' disease is usually two to ten days (median six to seven days), but may occasionally be longer, and for Pontiac fever is 5–66 hours (average 36 hours). *Legionella* is not communicable from person to person.

The infectious dose is unknown, but certainly low. Attack rates are higher in PF (>90%) than LD (<5%). Risk of disease may be related to amount of time exposed to the source. Cigarette smoking, advanced age, diabetes, chronic lung or kidney disease, haematological malignancy, immunosuppression and excess alcohol intake are risk factors for identified infection.

Prevention

- Design, maintenance and monitoring of water systems: store hot water above 60 °C

and deliver above 50 °C; store and deliver cold water below 20 °C. Eliminate stagnant water.
- New air-conditioning systems to be air-cooled.
- Maintenance and hygiene of wet cooling systems in line with national recommendations (e.g. Health and Safety Executive guidance in UK). Drain when not in use.
- Disinfection, regular cleaning, and changing of water in indoor fountains and whirlpool spas.
- Use sterile water for respiratory therapy devices.

Surveillance

- Mandatory notifiable in all EU countries.
- Cases of laboratory confirmed legionellosis should be reported to local public health authorities on the day of diagnosis.
- Clusters of respiratory infection should be reported without waiting for confirmation.
- Confirmed cases should also be reported to the relevant national surveillance scheme: some countries (e.g. UK) have a national enhanced surveillance scheme, with standard case-definitions and enhanced surveillance questionnaires.
- Legionellosis should be included in hospital infection surveillance schemes, especially for higher risk patients. Nosocomial pneumonia cases should be tested for *Legionella*.
- Cases associated with travel to other European countries are reported to the European Legionnaires' Disease Surveillance Network (ELDSNet) at ECDC.

Response to a case

- Ensure appropriate laboratory confirmatory tests undertaken, including a respiratory sample for selective culture as soon as possible.
- Report to local public health authority and national surveillance centre.
- Obtain risk factor history for 2–14 days (LD) or 0–3 days (PF) before onset of symptoms, preferably using a standard surveillance questionnaire (e.g. PHE enhanced surveillance questionnaire): details of places of residence and work; visits for occupational or leisure reasons; exposure to industrial sites, hotels, hospitals, leisure/sport/garden centres; air conditioning, showers, whirlpools/jacuzzis, fountains, humidifiers, nebulisers, and similar.
- If recognised risk factor identified, discuss inspection of possible source, examination of maintenance records and sampling with environmental health and microbiology colleagues. Enquire about respiratory illness in others exposed to potential source.
- Report travel outside district to relevant public health authority and travel outside country to national surveillance centre.
- If case reports exposure at healthcare premises, undertake a risk assessment in conjunction with infection control team responsible for the premises.
- Compare exposure data (and any typing data) to any other cases reported in the last six months who reside or work within 6 km of the new case.

Investigation of a cluster

- Undertake a hypothesis-generation exercise of risk factors as identified for individual cases including day-by-day analysis of movements in 14 days before onset. Adapt standard questionnaire to include any specific higher-risk site identified by a case (e.g. spa pool, hospital) and any site mentioned by two or more cases to ensure that all cases have been specifically questioned on exposure to these sites, re-interviewing earlier cases as necessary.
- Further case-finding: ensure all cases of community or hospital acquired pneumonia are tested for legionellosis. If serogroup 1 disease, encourage urine antigen testing for rapid diagnosis. Also encourage culture, so that typing may be performed and submission of samples to reference laboratory. Alert colleagues in other areas to check whether cases visited your locality (outliers are particularly helpful in investigating the source of outbreaks).

- Use geographical analysis of home, work and places visited of cases to look for links. Geographical information systems can be used to see if cases have been near each other and can also use weather data.
- If cases have been to same area, identify all potential sources. Undertake risk assessment for all cooling towers in area.
- In nosocomial outbreaks, test all water sources (hot and cold) and relevant environmental samples (e.g. showerheads) in suspect wards. Obtain specialist engineering advice on plumbing and heating systems.
- Compare typing results from cases and suspected source.
- An outbreak investigation toolbox is available from the ECDC website: https://legionnaires.ecdc.europa.eu

Control of an outbreak

- Shutdown of suspected source whilst expert engineering advice obtained.
- Drainage, cleaning, disinfection, maintenance and re-evaluation of suspected source. Occasionally major redesign or closure necessary.
- Warn clinicians of increase and of appropriate antibiotics.
- Rarely, temporary chemoprophylaxis in high-risk populations during a severe nosocomial outbreak may be considered.

Suggested case-definition for an outbreak

Confirmed: Case of pneumonia (LD) or flu-like illness (PF) with *Legionella* infection diagnosed by
- isolation (culture) of *Legionella* species from a respiratory specimen; *or*
- the presence of *L. pneumophila* antigen in a urine specimen; *or*
- detection of *Legionella spp*. nucleic acid (e.g. by PCR) in a lower respiratory tract specimen (e.g. sputum, bronchoalveolar lavage [BAL]) (this is classified as probable in some countries); *or*
- a positive direct fluorescence (DFA) on a respiratory specimen using *L. pneumophila* monoclonal antibodies, also referred to as a positive result by direct immunofluorescence (DIF) (this is classified as probable in some countries); *or*
- a fourfold rise in serum antibody titres.

Suspected: Case of pneumonia epidemiologically linked to confirmed LD *or* a case of flu-like illness linked to confirmed PF, awaiting final confirmation.

3.41 Leprosy

Leprosy is a curable chronic inflammatory disease caused by *Mycobacterium leprae*.

Suggested on-call action

No urgent action is required

Epidemiology

Leprosy occurs in tropical and warm temperate regions. It is associated with overcrowding and becomes less common as living standards rise. In 2015, 211 973 new cases were reported globally. The majority of cases were seen in South and East Asia, while no cases were reported from Europe where leprosy is rare and mostly imported.

Clinical features

The organism has a predilection for the skin and nerves. Nerve involvement results in an area of anaesthesia and or muscle weakness/wasting; tissue damage occurs secondarily to the anaesthesia.

The clinical appearance of the disease depends upon the degree of Cell Mediated Immunity (CMI). In Tuberculoid (TT) disease there is a high degree of CMI, and disease is localised; in Lepromatous (LL) there is little CMI, skin and nerves are heavily infiltrated with bacilli.

Immunologically mediated reactions which include reversal reactions and Erythema Nodosum Leprosum may occur as CMI returns during treatment.

Laboratory confirmation

The diagnosis can usually be made following a careful clinical examination. Confirmation is by identifying mycobacteria in slit skin smears or histological preparations. In LL, the patient's nodules should be biopsied and the nasal mucosa scraped. In tuberculoid patients the edge of a lesion should be biopsied.

Transmission

The major source of infection is patients with LL who shed large numbers of bacilli in their nasal secretions. The portal of entry is probably the respiratory tract.

Acquisition

Incubation: from a few months to many years.

Infectious period: lepromatous patients may be infectious for several years

Prevention

Identification and treatment of lepromatous patients is the mainstay of prevention.

Surveillance

Leprosy is a notifiable disease in most countries. In England, a National Leprosy Surveillance Database is maintained on all reported cases.

Response to a case

Cases should be referred to a specialist unit for treatment. There is scientific consensus that isolation is unnecessary, but some countries continue to recommend isolation of untreated lepromatous until treatment has been initiated (e.g. Australia).

Investigation of a cluster

A cluster should be investigated for misdiagnosis or laboratory contamination.

Suggested case-definition for an outbreak

A clinically compatible case that is laboratory confirmed by demonstration of acid-fast bacilli in skin or dermal nerve.

3.42 Leptospirosis

A rare cause of septicaemia caused by the zoonotic genus *Leptospira*, which occurs worldwide.

Suggested on-call action

- Person-to-person spread is very rare, so no urgent on-call action is required.
- In the event of an apparent outbreak associated with flooding/recreational activity, ensure early circulation of guidance to the public and health workers.

Epidemiology

Leptospirosis is an occupational hazard to farmers and sewage workers and a recreational hazard of outdoor water sports. Epidemics may be seen in areas of poverty. In (western) Europe, the most commonly identified serovars belong to serogroups Icterohaemorrhagiae (Icterohaemorrhagiae and Copenhageni, associated with rats), Sejroe (Hardjo type bovis, cattle), Canicola (Canicola, dogs), Australis, Ballum, Grippotyphosa, Pomona (Pigs),

Tarassovi and Javanica (rodents and other mammals). In 2012, incidence in Europe varied from 0 to 0.72 per 100 000 population per year. In tropical areas the incidence can reach up to 95 per 100 000 inhabitants per year.

Clinical features

The signs and symptoms of leptospirosis are protean: infection is often mild or subclinical. When symptomatic, the onset is characteristically abrupt with severe headache, myalgia, conjunctival suffusion and fever, that usually resolves after three to seven days. In biphasic disease, which may follow a transient remission, meningitic, renal, hepatic and vasculitic manifestations can occur. Leptospirosis with jaundice and uraemia is sometimes known as Weil's disease. The case fatality rate is 1–5%, (Weil's disease 2–40%). Death is usually associated with renal failure, or may result from myocarditis or massive blood loss.

Laboratory confirmation

Currently, *Leptospira interrogans s.l.* comprises over 250 serovars in 24 serogroups; by molecular speciation 22 species are recognised. However, there is little correlation between the serological and the molecular classification systems. During the first phase organisms may be visualised in (under dark field illumination), and cultured from, blood, CSF, or urine. PCR techniques are useful to detect leptospiral DNA in the early stage of disease. PFGE is additionally required for epidemiological and public health purposes. The organism may persist in urine. The Microscopic Agglutination Test (MAT) is the reference method for serological diagnosis. Antibodies may be detected using ELISA.

During the first phase of the illness there may be leucopenia. Jaundice may be associated with neutrophilia. About one-quarter of cases will have an elevated urea.

Transmission

Infection results from contact with the urine of infected animals (especially rodents; other mammals in specific settings) or contaminated material, such as water and soil. Leptospires can survive in the environment for a long time, depending on favourable, that is warm and wet, conditions. The organism probably enters through mucosa or broken skin.

Acquisition

The incubation period is usually 7–13 days (range 2–30 days). Patients may excrete leptospires for many months, but person-to-person spread is rare (sex, breast milk and transplacentally). Previous infection protects against re-infection with the same serovars, but may not protect against other serovars.

Prevention

- Control rodents.
- Education to avoid contaminated areas and cover broken skin.
- Providing alert/information cards to those likely to be exposed.
- Protective clothing in line with occupational health and safety recommendations.
- Pre-exposure chemoprophylaxis with doxycycline for unavoidable high-risk short-term exposure may be considered (e.g. the military), and also post-exposure has been found to reduce the incidence of symptomatic cases.
- Immunisation against occupational exposure to specific serovars has been tried in some countries.

Surveillance

Report cases to authorities so that areas of risk can be identified. Leptospirosis is notifiable in many countries.

Response to a case

- Treatment with intravenous antibiotics (e.g. benzyl penicillin) in the first four days probably reduces severity of disease.
- Obtain risk factor information.

Investigation of a cluster

- Investigate to determine areas of risk – such as water sports locations so that the public can be informed.
- Laboratory typing may help identify risk factors.

Control of an outbreak

- Outbreaks usually occur in areas of poverty, particularly following flooding and disasters that increase the rodent population. Rodent control is the main activity.
- Outbreaks resulting from occupational exposure (for example to cattle) should be reported to the veterinary authorities.
- If outbreak associated with flooding or recreational exposure, ensure early circulation of guidance to the public to reduce exposure and to professionals to ensure early recognition.
- Antibiotic prophylaxis (e.g. doxycycline) may be considered.

Suggested case definition

Clinical: Presence of fever plus at least two clinically compatible features, particularly in the presence of known risk factor(s).

Confirmed: Isolation of *Leptospira* sp. from clinical specimen or fourfold or greater rise in antibody titre or demonstration of *Leptospira* sp. in a clinical specimen by immunofluorescence, silver staining or PCR.

3.43 Listeriosis

Infection by *Listeria monocytogenes* is usually food-borne, but often presents as septicaemia or meningitis. Although rare, infection in vulnerable groups has a high case-fatality with foetuses, neonates, the elderly, and the immunocompromised particularly at risk.

Suggested on-call action

If you or reporting clinician/microbiologist know of associated cases consult the outbreak control plan or SOP.

Epidemiology

The incidence of reported cases is Europe is 0.6 per 100 000 population, although the true incidence is likely to be substantially higher. Reported rates are highest in Scandinavian countries. The incidence of reported cases is highest in infants (2.8 per 100 000, amounting to 5% of total cases), followed by those over 65 years of age, with the latter accounting for 62% of total cases. Rates are particularly high in pregnant women and neonates: in the UK, about 12% of cases are associated with pregnancy. The high case-fatality rate means that listeriosis is one of the main causes of fatal food-borne illness.

Clinical features

Listeriosis may present in a variety of ways, including:

- Acute gastroenteritis: This often affects previously well non-pregnant individuals. The most common symptoms are headache, fever, abdominal pain, sleepiness, nausea and diarrhoea. Fatigue, myalgia, arthralgia, vomiting or sore throat may also be reported.
- Systemic illness, which may include septicaemia or meningitis: these manifestations

more often affect individuals with immunosuppression, malignancy or chronic disease and the elderly. Case-fatality rates are high in those with underlying disease. Other features can include encephalitis, abscess, endocarditis and septic arthritis.
- Infection in pregnancy or neonates: although infection in pregnant women usually causes mild infection in the mother, it may lead to miscarriage, premature delivery or stillbirth; or neonatal infection (up to 10 days after delivery), particularly meningitis, with high mortality.
- Asymptomatic infection, with excretion in the stools, or a mild flu-like infection may also occur.

Laboratory confirmation

Diagnosis is usually by blood or cerebrospinal fluid (CSF) culture, which usually takes 48 hours, plus another 24 hours for confirmation. In *Listeria* meningitis, less than half of cases have organisms demonstrable on CSF microscopy, which also shows polymorphs or lymphocytes, increased protein and normal or decreased glucose. *Listeria* may also be identified from other sterile sites and in faecal, food and environmental samples, particularly after 'cold enrichment' in the laboratory. PCR testing may also be available in some laboratories.

Typing is helpful in the investigation of outbreaks. There are at least 12 serovars of *L. monocytogenes*, of which 4b, 1/2a and 1/2b cause 90% of clinical cases in Europe. Phage typing is also obtainable on 80% of serovar 4 and 37% of serovar 1/2 strains. Genotyping is available in many countries, with whole genome sequencing (WGS) more discriminatory than pulsed-field gel electrophoresis (PFGE).

Transmission

L. monocytogenes is widespread in the environment and can be found in soil, surface water, vegetation and a wide range of wild and domestic animals. It is extremely hardy and survives drying and freezing, remaining viable in soil or silage for long periods.

The main route of infection for humans is consumption of contaminated food. The organism can grow at temperatures as low as 0 °C (although optimum growth is 30–37 °C), is relatively tolerant of salt and nitrates, resulting in an ability to survive in processed, preserved and refrigerated foods. *Listeria* contamination does not 'spoil' or affect the taste of food even at high levels of contamination. *Listeria* is killed by thorough cooking and by pasteurisation.

Many foods have been associated with transmission of infection but most have some or all of the following features: highly processed, refrigerated, long shelf life, near-neutral pH and consumed without further cooking. Regularly implicated vehicles include processed meat/fish products, dairy products, especially if unpasteurised, and pre-prepared meals (see 'Response to Cluster' section). Some outbreaks have been explained by long-term colonisation of difficult to clean sites in food processing facilities. Infected cattle can contaminate milk.

Other sources of infection include direct transmission from animals, which may cause cutaneous infection often with obvious occupational exposure; direct contact with a contaminated environment; transplacental transmission in pregnant women; exposure to vaginal carriage during birth (early-onset) or hospital cross-infection (late-onset) for neonatal sepsis; and nosocomial transmission in hospital nurseries and renal transplant units.

Acquisition

Reported incubation periods vary widely from about 10 hours to months. Outbreaks of *Listeria* gastroenteritis and/or flu-like illness have a median incubation period of about 24 hours (range 6–240 hours). Longer incubations are reported for bacteraemia (range 1–12 days, median 2), meningitis (1–14 days, median 9) and infection in pregnant women (range 17–67 days, median 27.5).

Human excreters with normal hygiene are unlikely to be an important source of infection, except for neonates. The infectious dose is uncertain (possibly 100–1000 g^{-1} food) and it is unclear what level is 'safe' for immunocompromised patients or pregnant women, leading many to suggest a 'zero tolerance' policy for food.

In addition to foetuses, neonates and the elderly, those at risk of severe infection include patients with malignancy, chronic disease and impaired immunity. Low gastric acidity increases susceptibility.

Prevention

- Hazard analysis and control in food processing to reduce the risk of contamination and multiplication.
- Pasteurisation of dairy produce effectively kills *Listeria*. Post-pasteurisation hygiene is also important.
- Limiting the length of storage of at risk refrigerated food, for example cook-chill and ready-to-eat meals.
- Advice to pregnant women and immunosuppressed to avoid unpasteurised soft cheeses, refrigerated paté, refrigerated smoked fish and pre-packed salads.
- Thorough reheating of cook-chill/microwave foods, especially if served to vulnerable populations (e.g. hospital patients).
- Pregnant women to avoid contact with pregnant or newborn animals or silage.
- Thoroughly wash raw vegetables, fruit and salad before eating.
- Adequate infection control in delivery rooms and neonatal units.

Surveillance

- Listeriosis should be reported to local public health authorities: compulsory notification in many EU countries. Some countries (e.g. UK) may have a national enhanced surveillance scheme.
- Laboratories should report all clinically significant infections to regional and national surveillance: these may detect outbreaks not apparent at a local level. Refer samples/isolates to reference laboratory in line with national protocols for typing: in UK isolates are routinely genotyped.
- Consider as a cause of two or more cases of 'late onset' neonatal meningitis/septicaemia.

Response to a case

- Report to local and national/regional public health authorities to aid detection of clusters.
- Collect data on consumption of risk foods in last month in pre-prepared standard questionnaire: there may be a standard national questionnaire available (e.g. PHE website).
- No exclusion required, although enteric precautions sensible for hospitalised patients.
- Send isolate to reference laboratory for typing.

Response to a cluster

- Discuss with microbiologist further investigation, such as serotyping, phagetyping or genotyping.
- Institute case-finding with microbiologists and relevant clinicians to ensure adequate microbiological investigation of meningitis/septicaemia in neonates and the elderly.
- Undertake a hypothesis-generating study to include all foods consumed, particularly those at increased risk of high level *Listeria* contamination, for example processed meat/fish products, such as paté/rillettes, cold meats, hot dogs and processed fish; dairy products, such as soft cheese, butter and milk, especially if unpasteurised; and pre-prepared meals, such as 'cook-chill' meals, sandwiches and salads. The prolonged incubation will make accurate recall difficult: 'food preference' questions may also be useful, as are questions on cafes/restaurants visited, food shops and travel. Consider direct exposure to animals (e.g. farms).

- If cases predominantly neonatal, look at age in days at onset: could this be nosocomial?

Control of an outbreak

- Product withdrawal of any implicated food.
- Obtain specialist Environmental Health advice to investigate and modify suspect food processes.

Suggested case-definition for an outbreak
Flu-like illness, gastroenteritis, septicaemia or CNS infection, associated with isolate of the outbreak strain of *L. monocytogenes* from blood or CSF

3.44 Lyme disease

Lyme disease (Lyme Borreliosis [LB], erythema migrans, acrodermatitis chronica atroficans, Bannwarth's syndrome) is a multisystem illness, which can affect a range of tissues including skin, heart, nervous system and to a lesser extent eyes, kidneys or liver. The illness is caused by infection with a spirochaete (*Borrelia burgdorferi*), transmitted by *Ixodes* ticks: the deer tick (*Ixodes scapularis and pacificus*) in North America and the castor bean tick (*Ixodes ricinus*) in Europe and *Ixodes persulcatus* in Asia. *B. burgdorferi* can be divided into at least 15 genospecies, of which several are pathogenic. Another spirochaete, *Borrelia miyamotoi* is found in European ticks, but disease reports are rare.

Suggested on-call action
None required.

Epidemiology

Lyme disease is common in North America (*B. burgdorferi* sensu stricto) and Western Eurasia (all pathogenic genospecies) in areas of humid heathland, affecting ramblers and campers from March to November. The highest incidence is reported in children 5–14 years. Geographical distribution of disease in Europe is associated with the known range of *I. ricinus*. Central Europe is the region with the highest tick infection rates (nymphs >10%; adult ticks >20%) in Europe, specifically in Austria, the Czech Republic, southern Germany, Switzerland, Slovakia, and Slovenia. The true incidence of disease is unknown, as reporting is incomplete. Estimates of incidence range from 155 in Slovenia to 0.6 in Ireland, England and Wales per 100 000 population. The prevalence of LB appears to be increasing all over Europe.

Clinical features

Infection can be asymptomatic, or have a range of clinical presentations, depending on host factors and the pathogen (genospecies). Clinical presentation is divided into three stages: early localised LB, early disseminated LB, and late (chronic) LB. Many features of LB, especially later infection, are nonspecific.

Early localised: 2–30 days after a tick bite, which may be inapparent, a rash (erythema migrans) develops; the appearance is of an expanding erythematous circle with central clearing, up to 30 in. in diameter. The patient may also report 'flu-like' symptoms. Early localised LB resolves without antibiotics. Borrelia lymphocytoma is a rare early localised LB. *Early disseminated LB* occurs if the pathogen spreads to other tissues where it can remain active for over a year. Clinical symptoms include more severe 'flu-like' illness, multiple erythema migrans (5%), neuroborreliosis (5–15%: facial palsy, other cranial nerve lesions, aseptic meningitis, mild encephalitis), oligo- or mono-arthritis (5–8%), and carditis with AV block (<1%). Progression to late LB can occur in inadequately

treated patients. The classical presentation is Lyme arthritis (the knee). Other presentations are Acrodermatitis Chronica Atrophicans (ACA), and rarely chronic Lyme meningoencephalitis. The clinical manifestations seen in Europe and North America differ, with milder disease often reported in Europe. Most infections are asymptomatic or self-limiting. The rationale for antibiotic treatment is to prevent possible progression of the disease. Selection and use of antibiotics (tetracyclines, penicillin, cephalosporins, etc.) vary by country. Occasionally symptoms persist after adequate antibiotic treatment, adding substantially to the total burden of disease. There is debate if 'chronic Lyme' exists. Clinicians agree that there is 'post-Lyme disease syndrome' without any evidence of active infection, which might be an immune-mediated phenomenon. Prolonged antibiotic treatment has no use.

Laboratory confirmation

Lyme Borreliosis is a clinical diagnosis, based on symptoms and tick exposure. Serological testing may be helpful. However, as infection can occur subclinically and on average 10–15% of individuals in endemic areas are seropositive, serology is not conclusive for diagnosing disease. Positive or equivocal results on an ELISA or Indirect Immunofluorescent Antibody (IFA) assay require confirmatory testing with a Western blot test. Negative serology may indicate early infection (repeat after four to eight weeks) or chronic infection. Solitary IgM positivity can be false positive. PCR (skin biopsy or synovial fluid) is available, as is culture of *Borrelia* species, but this is of low sensitivity and only available in specialist centres.

Transmission

Borrelia burgdorferi is transmitted by the bite of *Ixodes* ticks. Deer are the preferred host for adult ticks in the USA; sheep in Europe. Other mammals (e.g. dogs) can be incidental hosts and may develop Lyme disease. Lyme disease is not transmissible from person to person.

Acquisition

Erythema migrans, the best clinical indicator of Lyme disease, develops between 3 and 32 days after a tick bite. Tick bites may go unnoticed.

Prevention

The main method of prevention is avoidance of tick bites by avoiding entering the humid tick habitat, and if inevitable wearing long trousers and sleeves and using an insecticide (e.g. DEET). Transmission of *B. burgdorferi* does not usually occur until the tick has been in place for 36–48 hours; thus, screening and removing ticks after exposure is an effective prevention for infection. Transmission occurs especially by nymphs (1.3–1.5 mm long) that are easily overlooked. Disinfection of the wound is advised, more to prevent wound infection, than to prevent LB. Post-exposure prophylaxis within 72 hours after the tick bite with 200 mg doxycycline was proven effective in high-risk areas in the USA. A vaccine, producing antibodies to the spirochaete while in the ticks gut, provided protection (78%) of short duration (<1 year). It was withdrawn from the market in 2002. Other vaccines, expressing Outer Surface Proteins (Osp) are in development in phase I and II trials.

Surveillance

Cases should be reported to the public health authorities so that assessments of risk can be made.

Response to a case

No public health response.

Investigation of a cluster and control of an outbreak

Clusters should be investigated to determine areas of high risk, so that those who might be exposed can be informed.

Suggested case-definition
Clinical diagnosis of erythema migrans in a person who has been exposed to ticks.

3.45 Malaria

Malaria is a potentially fatal plasmodial infection. Almost all patients presenting to healthcare in Europe will have travelled to places where they have been exposed to malaria. There is also a risk of airport and transfusion malaria.

Suggested on-call action
None unless the case is thought to be transfusion related in which case other units from the same donor need to be identified and withdrawn urgently.

Epidemiology

Malaria is endemic in more than 100 countries throughout Africa, Central and South America, Asia and Oceania; more than two billion people are exposed to the risk of malaria infection. *Plasmodium falciparum* and *Plasmodium vivax* are the most common species. *P. falciparum* is the predominant species in Africa and Papua New Guinea. *P. vivax* dominates in South America and Asia; *Plasmodium malariae* is widely distributed but is much less common. *Plasmodium ovale* is mainly found in Africa. Between 2012 and 2016, 31966 cases of malaria were reported in the EU/EEA countries (notification rate around 1 per 100000). Most cases are usually reported from France, the UK, Germany, Italy and Spain. Patterns of importation reflect travel destinations. The commonest source of imported falciparum malaria is West Africa, followed by East and Central Africa. In Greece, 95 locally acquired *P. vivax* cases were reported between 2009 and 2017. The case fatality rate in Europe is low (about 0.5% in England and Wales).

Clinical features

Malaria may present with almost any clinical pattern. The most classical symptom is the malarial rigour; the periodic nature of the attacks of fever may give a clue as to the diagnosis. The disease must be considered in anyone who has been exposed to the parasite, by travel, blood transfusion or the rare airport malaria.

Complications are associated with high parasitaemia and are therefore more common in non-immunes and children. The course may be rapid: delay in diagnosis of *P. falciparum* malaria is associated with increased mortality (e.g. due to cerebral malaria).

Laboratory confirmation

Diagnosis is by demonstrating parasites in the peripheral blood. A minimum of three specimens should be taken at the height of fever. Thick films are of particular value when the parasitaemia is low; the technique requires experience. A thin film enables a parasite count (number of parasites per 100 RBC) to be performed and the parasite species to be more clearly identified. Slides should be reviewed by an expert so that a species diagnosis, essential to guide chemotherapy, can be made.

Rapid Diagnostic Tests (RDTs) can help in the diagnosis of malaria by detecting antigens in human blood. RDTs permit a detection of malaria infections, particularly in remote areas with limited access to good

quality microscopy services; however, antigen detection methods have lower sensitivity and specificity than microscopy. New molecular diagnosis is more reliable than microscopy, but expensive and requiring specialised laboratories.

Transmission

Malaria is normally transmitted by the bite of the female *Anopheles* mosquito. Rare cases of 'airport malaria' happen when an infected mosquito introduced to Europe bites a host before dying. There are also rare transmissions through blood donation, needlestick injuries, or poor hospital infection control.

Acquisition

The incubation period time (from infection to appearance of parasites in blood) varies with infecting species, and is typically:

- *P. falciparum* five to seven days;
- *P. vivax* six to eight days;
- *P. malariae* 12–16 days;
- *P. ovale* eight to nine days.

In transfusion-associated malaria the incubation period is much shorter.

In *P. vivax* and *P. ovale* some parasites remain dormant in the liver (hypnozoites): these can take up to a year before becoming active.

Prevention

- Good advice to those travelling is essential. The risk of those visiting relatives in their country of origin is often underestimated by travellers and those providing advice to them: pre-existing partial immunity will probably have waned.
- Prevention of mosquito bites (the mosquitoes bite mainly at night):
- Sleep in fully air-conditioned or screened accommodation and use knockdown insecticide in room each evening.
- If the room cannot be made safe, sleep under bed nets; impregnation with pyrethrum enhances the efficacy of nets.
- Electrical pyrethroid vapouriser in room may also be useful.
- Wear light long-sleeved garments and long trousers between dusk and dawn.
- Use mosquito repellents.
- Suppression of the malaria parasite with chemoprophylaxis. Regular antimalarial prophylaxis should generally begin before travel to an endemic area and sometime after return, depending on the product. Changing patterns of resistance mean that specialist advice should be consulted.

Surveillance

- Malaria is a notifiable disease in the EU.
- Cases should be reported to national authorities so that advice on prophylaxis can be based upon observed patterns of risk.

Response to a case

- The travel history should be taken.
- If there is no travel history, information about transfusions or injections (including drug misuse) and proximity to airports should be sought.
- Patients should be reviewed 28 days after treatment to confirm parasitological and clinical cure. Patients who have splenic enlargement should avoid body contact sports and strenuous exercise due to a risk of splenic rupture.

Investigation of a cluster and control of an outbreak

- Notifiable in most countries: malaria is a notifiable disease in the EU.
- If clusters arise from areas where malaria has not previously been recognised, the national authorities should be informed. Travel advice should be reviewed.
- If cases occur in people who have not been abroad, consider blood, nosocomial and airport exposures.

Suggested case-definitions for an outbreak

Clinical: Fever and/or compatible illness in a person who has travelled to an area in which malaria is endemic.

Confirmed: Fever or a history of fever, and the presence of parasites detected in a blood film or the detection of *Plasmodium* nucleic acid or *Plasmodium* antigens in blood.

World Health Organization categories:

- *Autochthonous*:

indigenous: malaria acquired by mosquito transmission in an area where malaria is a regular occurrence;

introduced: malaria acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence.

- *Imported*: malaria acquired outside a specific area.
- *Induced*: malaria acquired through artificial means (e.g. blood transfusion, common syringes, or malariotherapy).
- *Relapsing*: renewed manifestation (i.e. of clinical symptoms and/or parasitaemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than any interval resulting from the normal periodicity of the paroxysms.
- *Cryptic*: an isolated case of malaria that cannot be epidemiologically linked to additional cases.

3.46 Measles

Measles is a systemic viral infection caused by a paramyxovirus. Its main features are fever, rash and respiratory disease. The public health significance of measles is that it is highly infectious and can be prevented by vaccination.

Suggested on-call action

Obtain history of: immunisation, contact with suspected or confirmed cases and travel

If diagnosis likely: identify vulnerable contacts and assess susceptibility.

Epidemiology

In the pre-vaccination era, measles circulated widely and most people were infected in childhood. The epidemiology of measles in the post-vaccination era varies across Europe, depending on the evolution of vaccine strategies and vaccine coverage. In countries where coverage has been high for many years, the disease has been virtually eliminated. Measles has made a resurgence in many countries due to suboptimal vaccine coverage. In 2017, cases were reported from every country in Europe except Malta and Latvia; rates below one per million were reported from only five countries (Estonia, Denmark, Slovakia, Lithuania and Norway) (Table 3.46.1). The highest rates were in Romania (28.37 per million), Greece (89.67 per million), Italy (82.49 per million), and Belgium (32.53 per million). Several countries have reported large outbreaks in recent years. Thirty deaths due to measles were reported during the 12-month period; with 19 in Romania, 4 in Italy, 2 in Greece and 1 each in Bulgaria, France, Germany, Portugal and Spain. Vaccine coverage has improved in some countries but remains below the WHO target of 95% for two doses.

Clinical features

In an unvaccinated child, there is a prodromal illness with a high fever and a coryzal respiratory infection. There is cough, conjunctivitis and runny nose. Koplik's spots appear during the early part of the illness – these look like

Table 3.46.1 Measles cases and notification rate in Europe December 2016–November 2017

Country	Total cases	Cases per million	Lab positive cases
Austria	95	10.93	83
Belgium	368	32.53	244
Bulgaria	166	23.2	86
Croatia	7	1.67	7
Cyprus	3	3.54	3
Czech Republic	146	13.83	140
Denmark	4	0.7	4
Estonia	1	0.76	1
Finland	10	1.82	10
France	518	7.76	339
Germany	929	11.31	640
Greece	967	89.67	568
Hungary	36	3.66	36
Iceland	3	9.02	3
Ireland	21	4.44	21
Italy	5004	82.49	3954
Latvia	0	0	0
Lithuania	2	0.69	2
Luxembourg	4	6.94	4
Malta	0	0	0
Netherlands	16	0.95	15
Norway	1	0.19	1
Poland	62	1.63	41
Portugal	34	3.29	29
Romania	5560	281.37	2071
Slovakia	6	1.11	6
Slovenia	7	3.59	7
Spain	160	3.54	150
Sweden	41	3.05	41
UK	280	4.28	280
Total	**14451**	**28**	**8786**

grains of salt on a red inflamed background and are found on the mucosa of the cheek next to the upper premolars and molars. The rash of measles starts on day three or four, initially in the hairline, but spreads rapidly to cover the face, trunk and limbs. It is maculopapular but not itchy. Koplik's spots fade as the rash appears. The rash fades over a week to 10 days.

In a vaccinated person, the illness is usually mild with a low-grade fever, transient rash and absent respiratory features.

Complications of measles include pneumonitis, secondary bacterial infection, especially acute otitis media and pneumonia, and encephalitis. Complication rates are higher in malnourished or immunosuppressed children. Subacute sclerosing panencephalitis is a late, slow-onset, progressive complication that occurs in about one per million cases. It is always fatal.

Laboratory confirmation

The most reliable method for diagnosis of measles is demonstration of IgM, IgG, or measles RNA in oral fluid (positive up to six weeks after the onset of symptoms). IgG and IgM can also be detected in serum. Other samples (throat swab, NPA, CSF, urine) may also be used for diagnosis, but are less reliable as they only remain positive for a few days after disease onset.

Transmission

Man is the only reservoir. Carriers are unknown. Spread is from person to person by direct contact with nose and throat secretions or respiratory droplets; less commonly indirectly by articles freshly soiled with nose and throat secretions.

Acquisition

The incubation period ranges from 7 to 18 days, usually about 10 days. The period of communicability starts just before the onset of the prodrome and lasts until four days after the rash appears. Measles is highly infectious, with a reproduction rate of 15–17, that is between 15 and 17 secondary cases in a susceptible population for every index case. Natural infection provides lifelong immunity. Vaccine-induced immunity is lower, but is also usually lifelong and can be boosted by exposure to circulating wild virus. In developed countries, maternal antibody persists for up to 12 months; this period may be shorter when the maternal immunity is vaccine-induced.

Prevention

- Vaccinate with a combined Measles/Mumps/Rubella (MMR) or Measles/Mumps/Rubella/Varicella (MMRV) vaccine. Two doses are required; the first at 12–18 months of age; the timing of the second dose varies from 2 to 13 years of age. The only contraindications to measles vaccine are immunosuppression, allergy to neomycin or kanamycin and a severe reaction to a previous dose. Measles vaccine can be safely given to children with egg anaphylaxis.
- Vaccination should not be given within three weeks of another live vaccine (except OPV) or within three months of an injection of immunoglobulin.

Surveillance

Measles is notifiable in all countries in Europe, and surveillance is co-ordinated on a monthly basis by ECDC. Data are collected on laboratory confirmation, age, immunisation status, travel history and deaths (see: https://ecdc.europa.eu/en/measles for latest data).

Response to a Case

- Obtain laboratory confirmation.
- Determine source of infection (including travel history).
- Identify vulnerable contacts (immunocompromised, pregnant, infants); assess their exposure risk and susceptibility and give HNIG.
- Consider vaccine for other contacts (effective if given within 72 hours of exposure).
- Exclude confirmed and likely cases from school, nursery, college or work until five days from the onset of rash.
- Exclude health care workers from work who have been contact with a case, if there is no evidence of protection, from the fifth day of exposure to the twenty-first day after last exposure, or until immunity can be provided (vaccine) or demonstrated (IgG).
- Comprehensive guidelines on the public health management of cases are available on the PHE website.

Response to a cluster and investigation of an outbreak

- As per case investigation, but also convene an outbreak team and consider the need for a community-vaccination programme.

Suggested case-definition

Suspected case:
fever (>38 °C if measured);
plus rash
plus one of: conjunctivitis, cough, coryza.

Confirmed case:
Confirmed wild measles virus or RNA in any clinical specimen; *or*
measles IgM in blood or saliva; *or*
fourfold or greater rise in measles IgG in blood

3.47 Meningococcal infection

Meningococcal infection is the spectrum of disease caused by the bacterium *Neisseria meningitidis*. The infection may present as meningitis, septicaemia, or a combination of both. The public health significance of meningococcal infection lies in the severity of the disease, the potential for prevention by vaccination, the ability of the infection to cause unpredictable clusters, and the intense public anxiety that accompanies a case or cluster.

Suggested on-call action

- Ensure rapid admission to hospital and administration of pre-admission benzyl penicillin.
- Initiate lab investigations to confirm diagnosis.
- Arrange chemoprophylaxis for close contacts of confirmed or probable cases.

Epidemiology

In 2015, 3121 cases of meningococcal infection were reported by 30 countries to ECDC, an incidence of 0.6 per 100000. The rate of infection has declined over the past 15 years, due to the introduction of vaccines and a general decline in serogroup B disease. The highest rates in 2015 were in Ireland (1.5 per 100000) and the UK (1.4 per 100000).

There are 13 serogroups of *N. meningitidis*. In Europe, serogroups B and C accounted for 61 and 14% of cases respectively in 2015. There has been an increase in serogroup W cases in recent years in a number of countries.

The incidence is highest in infants (10 per 100000 in 2015), with a peak incidence at about six months of age, which coincides with the loss of maternally derived immunity. Children aged one to five years are the second most commonly affected; there is a smaller peak in teenagers.

Most cases arise sporadically, although clusters do occur from time to time. These are unpredictable, although they often occur in educational establishments or in the military. Serogroup C disease tends to cause clusters more than serogroup B.

The infection is seasonal, with a higher incidence in the winter months. There are geographical variations in the disease, although these are not consistent over time. Local increases are often associated with the arrival of a strain not previously seen in that community.

There are a number of factors that predispose to meningococcal infection. These include passive smoking, crowding, recent influenza type A infection, absence of a spleen and complement deficiency. Travellers to the meningitis belt of Africa (where outbreaks of serogroup A disease are common) may be at risk of disease. Cases (serogroup A and W135) among pilgrims to the Hajj in Mecca have prompted a requirement for a certificate of meningococcal vaccination from visitors.

Clinical features

The early symptoms are non-specific and are often mistaken for a viral infection. In infants there is fever, floppiness, high-pitched crying and sometimes vomiting. Older children and adults have a fever, malaise, increasing headache, nausea and often vomiting. The illness usually progresses rapidly, although sometimes there is a slower onset, which causes diagnostic difficulty. In infants there is progressive irritability, altered consciousness, and sometimes convulsions. Older children and adults develop photophobia and neck stiffness with a positive Kernig's sign, although these features are sometimes absent.

An important feature is the appearance of a petechial rash, which indicates that there is septicaemia. The rash is not always present, or there may be only a few petechiae, so a careful search for petechiae is important in

suspected cases. The 'glass test' can be used to distinguish a haemorrhagic rash from other types of rash.

Patients with rapidly advancing disease may develop hypotension, circulatory collapse, pulmonary oedema, confusion and coma. The overall case fatality rate is about 10%, although for patients without septicaemia the outlook is better. Approximately 15% of survivors have permanent sequelae, including deafness, convulsions, mental impairment, and limb loss.

Laboratory confirmation

Obtaining laboratory confirmation in suspected cases is essential for public health management. Specimens should be taken as soon as a suspected case is seen in hospital (see Box 3.47.1). The most useful specimens are blood and CSF for culture and PCR diagnosis. CSF should not be taken if a lumbar puncture is contraindicated due to increased intracranial pressure. Meningococcal DNA can be found in the CSF up to 96 hours after commencing antibiotics. A throat swab should also be obtained for culture (the yield from cases is about 50% and is unaffected by prior administration of antibiotic). Aspirates from other normally sterile sites (e.g. joint fluid) may also be helpful. A throat swab from family members before chemoprophylaxis may also help to identify the causative organism, although counselling is advised before swabbing to prevent feelings of guilt should a household member be found to be the potential source of infection. Acute and convalescent serology can also provide a diagnosis, although the result is often obtained too late to affect either clinical or public health management; it may however be useful in the investigation of a potential cluster as it provides serogroup information.

It is important to determine the serogroup of the infecting organism, to inform decisions about vaccination. PCR diagnosis is serogroup-specific and a result is available within a few hours. Latex agglutination tests are also available as a rapid screening method when there is a positive culture, although the national reference laboratory should ideally confirm the result. Genotyping methods such as *porA* sequencing, factor H binding protein sequencing, Pulsed Field Gel Electrophoresis (PFGE) and Multi-Locus Sequence Typing (MLST) provide a much more precise typing than phenotype-based methods.

Transmission

The infection is spread from person to person through respiratory droplets and direct

Box 3.47.1 The following specimens should be collected on, or soon after, admission to hospital from all patients when meningococcal infection is included in the differential diagnosis

- Blood for culture
- Blood for PCR (EDTA or other unclotted blood specimen)
- Serum (on admission and two to six weeks later)
- CSF for microscopy, culture, PCR
- Aspirate from other sterile sites suspected of being infected (e.g. joints) for microscopy, culture, PCR
- Nasopharyngeal (throat) swab normally taken through the mouth

NB Lumbar puncture should not be done where contraindicated and should be delayed until the patient's condition has been stabilised and assessment made to rule out raised intracranial pressure.

Where appropriate, specimens should be taken to check for alternative diagnoses, for example nasopharyngeal swabs and stool for viral culture.

contact with nose and throat secretions. Infectivity is relatively low, and transmission usually requires prolonged close contact such as occurs in the household setting or through 'wet' mouth kissing.

Humans are the only reservoir, and the organism dies quickly outside the host. Approximately 10% of the population carries the organism harmlessly in the nasopharynx. Carriage confers natural immunity. During outbreaks, carriage rates of the outbreak strain may rise sharply, to high as high as 50%. There is however, no consistent relationship between carriage rates and disease, and some outbreaks occur in the absence of normal carriage. Increased rates of carriage have been observed in smokers, in crowded conditions, and among military recruits.

The most common setting for transmission to occur is within households, where a member of the household (usually an adult) has recently become a carrier and infects a susceptible household member (usually a child). The absolute risk, in the absence of chemoprophylaxis, of a second case in the same household in the month following an index case is about one in 300. In comparison, transmission in other settings is rare; the estimated risks of a second case in the month following an index case in a pre-school group, primary and secondary school are respectively 1 in 1500, 1 in 18 000 and 1 in 33 000 respectively. Transmission from patients to healthcare workers has been documented, but is also rare; occurring where there has been direct exposure to nasopharyngeal secretions.

Acquisition

There is no true incubation period, as the organism may be carried in the nasopharynx for a variable time before invasive disease. Investigations of clusters suggest an incubation period of three to five days, although it may occasionally be up to 10 days. Patients are usually no longer infectious within 24 hours of starting antibiotic treatment, although it should be noted that some antibiotics used in treatment (e.g. penicillin) will only temporarily suppress carriage. For this reason, a chemoprophylactic antibiotic should be given before hospital discharge.

Maternal immunity to meningococcal infection is passed across the placenta to the neonate, but only lasts for a few months. Subsequent carriage of pathogenic and non-pathogenic meningococci confers serogroup-specific natural immunity, which usually develops within seven days of acquisition. In unvaccinated populations, carriage of pathogenic meningococci is unusual in infancy and early childhood, rises progressively to peak at 25% in 15–19-year-olds and then slowly declines through adult life. Vaccination significantly reduces carriage.

Prevention

- Polysaccharide vaccines have been superseded by polysaccharide-protein conjugate vaccines against serogroups A, C, W135, and Y. They induce immunological memory, which is likely to be lifelong. Routine group C vaccination has been introduced in a number of countries in Europe, with dramatic impact. In some countries quadrivalent ACWY conjugates vaccines are replacing or supplementing monovalent group C vaccines. Schedules vary, most countries have opted for a single dose in the second year of life; vaccination of teenagers and older adults is being increasingly implemented.
- Two serogroup B vaccines have recently become available in Europe. The UK was the first country to introduce mass infant group B vaccination, and results to date indicate high effectiveness of the programme.

Surveillance

- Both acute meningitis and meningococcal septicaemia are notifiable in most European countries, and surveillance is co-ordinated by ECDC. An enhanced surveillance scheme may be operated in some countries, for example England.

- Laboratory reports are another important source of data in most countries, although increasing use of pre-admission antibiotics means that there is now greater reliance on non-culture diagnoses for surveillance.

Response to a case

- Public health action is indicated for confirmed or probable cases; it is not indicated for possible cases or infection in non-sterile sites (except for meningococcal conjunctivitis which is an indication for public health action because of the high immediate risk of invasive disease).
- There are four key actions for the public health practitioner

1 Ensure rapid admission to hospital and that preadmission benzyl penicillin has been given. Prompt action may reduce the case fatality rate by up to 50%

2 Ensure that appropriate laboratory investigations are undertaken (see Box 3.47.1).

3 Arrange for chemoprophylaxis for close contacts, and vaccine if the infection is due to a vaccine-preventable strain.

The aim of chemoprophylaxis is to eradicate the infecting strain from the network of close contacts, and thus prevent further cases among susceptible close contacts. Chemoprophylaxis should be given as soon as possible. Ciprofloxacin is now the antibiotic of choice for all ages, and in pregnancy (single dose)

Close contacts are defined as people who have had close prolonged contact with the case in the week before onset. This usually includes household members, girlfriends/boyfriends, regular childminders and sometimes students in a hall of residence. Classroom, nursery, and other social contacts do not need chemoprophylaxis. Chemoprophylaxis for health care workers exposed to a case is only recommended for those whose mouth or nose is directly exposed to large particle droplets/secretions from the respiratory tract of a probable or confirmed case of meningococcal disease during acute illness until the case has completed 24 hours of systemic antibiotics.

The aim of vaccination is to prevent late secondary cases. There is less urgency for vaccination, as chemoprophylaxis aims to prevent the early secondary cases. Conjugate vaccine should be offered to all close contacts of serogroup A, C, W135 or Y disease as defined above; the index case should also receive vaccine. Serogroup B vaccine (which is not a conjugate vaccine) is not recommended for the case or contacts, unless they are in a high-risk group, for example asplenia, splenic dysfunction or complement deficiency, or a second case occurs in the household. Contacts who have been previously vaccinated may need a booster dose (refer to local country recommendations).

4 Provide information about meningococcal disease to parents, GPs and educational establishments. The aim here is to improve the outcome of any secondary cases that may occur (through early presentation and treatment) and to prevent rumours and anxiety.

Investigation of a cluster

- Obtain serotyping or genotyping to see if cases are potentially linked
- Look for links to educational or other institutions

Response to an outbreak

- Seek expert advice and establish an outbreak control team.
- Information dissemination is essential.
- Where clusters occur in an educational establishment, the following action is recommended:

1 Two or more possible cases (see case definition): prophylaxis to household or institutional contacts is not recommended.

2 Two confirmed cases caused by different serogroups: only give prophylaxis to household contacts.

3 Two or more confirmed or probable cases which are, or could be, caused by the same strain within a four-week period: prophylaxis (antibiotics and vaccine if the strain is a vaccine preventable one) to household contacts and to a defined close contact group within

the establishment. This may include, for example, classroom contacts, children who share a common social activity or a group of close friends. For Men B clusters, vaccine should be given as well as chemoprophylaxis, unless molecular typing confirms that the cluster confirms that the cluster is not caused by a vaccine–preventable strain.

4 Two or more confirmed or probable cases which are, or could be, caused by the same strain separated by an interval of more than four weeks: consider wider prophylaxis, but seek expert advice.

- Where clusters occur in the wider community, age-specific attack rates should be calculated: the numerator is the number of confirmed cases and the denominator is the population within which all the cases reside. This may be difficult to define.
- Vaccination and chemoprophylaxis for the community may be indicated for clusters of serogroup A, C, W, Y or B disease where attack rates are high (e.g. above 40 per 100000).

Suggested case-definitions

Confirmed case: invasive disease (meningitis, septicaemia, or infection of other normally sterile tissue) confirmed as caused by *N. meningitidis*.

Probable case: clinical diagnosis of invasive meningococcal disease without laboratory confirmation, in which the public health physician, in consultation with the clinician managing the case, considers that meningococcal disease is the likeliest diagnosis. In the absence of an alternative diagnosis a feverish, ill patient with a petechial/purpuric rash should be regarded as a probable case of meningococcal septicaemia.

Possible case: as probable case, but the public health physician, in consultation with the clinician managing the case, considers that diagnoses other than meningococcal disease are at least as likely. This includes cases treated with antibiotics whose probable diagnosis is viral meningitis.

3.48 MRSA (Meticillin-Resistant *Staphylococcus aureus*)

Staphylococcus aureus (SA) is a gram-positive bacterium that commonly colonises the human skin and mucosa without causing infection. When infection occurs, usually because the bacterium enters the body via broken skin or medical procedures, it can produce a wide variety of disease including minor skin and wound infections, pneumonia, and life-threatening blood stream infections (septicaemia) and sepsis.

There are many clones of *S. aureus*, which may be distinguished via molecular genotyping methods. Most strains of SA are sensitive to commonly used antibiotics, and infections can be treated effectively. However, over 80% of *S. aureus* produce penicillinases and are resistant to benzylpenicillin. Laboratory identification of these resistant strains uses meticillin, an antibiotic no longer used therapeutically, and they are referred to as Meticillin-Resistant *Staphylococcus aureus* (MRSA). The mechanism of meticillin resistance is usually the production of a low-affinity penicillin-binding protein rather than the production of a beta-lactamase. Most MRSA are sensitive to vancomycin but isolates with intermediate-level resistance to vancomycin (VISA) have been reported. Staphylococcal food poisoning is intoxication rather than an infection (see Chapter 3.71).

Suggested on-call action

- The local health protection team should be prepared to assist the hospital infection control team to investigate and control nosocomial outbreaks of MRSA.
- The public health team may be asked to advise on the management of a cluster of cases of Meticillin-Sensitive *S. aureus* (MSSA) or MRSA infection in the community.

Epidemiology

In the UK, MRSA incidence in hospitals rose considerably in the late 1990s and early 2000s and became a major public health problem and source of public and political concern. This rise has been attributed to the appearance of new strains with epidemic potential, hospital patients who are increasingly vulnerable to infections like MRSA, failure to maintain good hospital hygiene including hand washing, more intensive bed usage, greater throughput of patients, more transfer of patients between wards and hospitals and reductions in staffing levels.

In England and Wales, MRSA bacteraemia as a proportion of total *S. aureus* bacteraemias increased from 2% in 1990 to 42% in the early 2000s but has since declined to 6.7% in 2016. The introduction of mandatory MRSA bacteraemia surveillance scheme for all acute hospitals in England in April 2001 alongside several control measures led to significant reductions in rates of hospital-onset MRSA bacteraemia over the past decade. In the first year of surveillance over 7000 cases were reported and since then, cases have declined to 6383 in 2006/2007, 1898 in 2009/2010, and 823 in 2016/2017. Currently only around 38% of reported bacteraemias occur three or more days after admission to hospital implying a shift towards more community associated cases although many of these community cases will have antecedent health care related risk factors.

Risk factors for MRSA bacteraemia include age (mean age 66 years), male gender (66% of patients), pre-existing medical conditions (renal failure, diabetes and immunosuppression) or invasive procedures (surgery, central or peripheral IV devices).

In 2016, data from 29 EU/EEA countries participating in the *European Antimicrobial Resistance Surveillance Network (EARS-Net)* showed that although the proportion of MRSA bacteraemia reports had continued to decrease since 2009, this has become less pronounced in recent years and some countries have observed an increase. The incidence of MRSA bacteraemia were generally lower in northern Europe (Netherlands, Norway, Sweden) and higher in the southern and south-eastern parts (Malta, Portugal, Romania). In 2016, MRSA percentages ranged from 1.2 (Netherlands) to 50.5% (Romania) with an EU/EEA population weighted mean of 13.7%. These large variations in MRSA levels in EU/EEA countries may be due to historical differences in their approaches to MRSA control.

In the community, meticillin sensitive *S. aureus* (MSSA) colonisation rates are around 30% while MRSA colonisation rates are 1–2%. Independent risk factors for MRSA colonisation in one study were age over 75 years, recent hospital admission and diabetes. The prevalence of MRSA among persons without risk factors is 0.24% or lower.

Clinical features

MRSA causes infection or colonisation in the same way as MSSA. However, because there are fewer antibiotic treatment options, MRSA infections are more difficult to treat and morbidity, length of hospital stay and treatment costs may all be increased.

Infections caused by strains of *S. aureus* that produce Panton-Valentine Leukocidin (PVL), a toxin that destroys white blood cells are now well recognised in Europe. PVL *Staphylococcus aureus* (PVL-SA) currently accounts for <2% of isolates of healthcare-associated *S. aureus* in the UK, irrespective of their meticillin susceptibility. PVL-SA usually causes mild Skin and Soft Tissues Infections (SSTI) and necrotising haemorrhagic pneumonia but rarely may cause other invasive infections such as necrotising fasciitis, osteomyelitis, and septic arthritis, affecting otherwise healthy young people in the community with high mortality. PVL-SA infections are usually sporadic but clusters and outbreaks can occur in community and healthcare settings.

In recent years, reports of Community-Associated MRSA (CA-MRSA) have increased in North America, Australia and parts of Europe. These are MRSA infections among young and healthy individuals without the

traditional healthcare risk factors. Isolates are usually characterised by their distinct genetic markers (almost all carry the PVL gene) and are relatively susceptible to antimicrobials. CA-MRSA has been linked to clusters of extensive SSTI and share similar risk factors with PVL-SA, including skin-to-skin contact and sharing contaminated items. Settings in which people are in close contact such as households, sports teams, military camps, prisons, and gymnasia are particularly likely to be affected. The epidemiology is evolving and there are now increasing reports of CA-MRSA causing nosocomial infections.

Laboratory confirmation

The laboratory diagnosis of *S. aureus* infection requires microbiological examination of appropriate clinical specimens. As a minimum, a Gram stain, culture and antibiotic sensitivities should be requested. New molecular laboratory techniques have allowed an improved and growing understanding of the molecular basis for virulence, antibiotic resistance and epidemiology. Molecular techniques, including Pulse-Field Gel Electrophoresis (PFGE) and Multilocus Sequence Typing (MLST), allow different genotypes or clones to be identified that have distinct epidemiological features and clinical presentations. Whole Genome Sequencing (WGS) is now increasingly being used in nosocomial outbreak investigations.

Transmission

The reservoir of *S. aureus* is colonised or infected humans and, rarely, animals. About one in three people are intermittently colonised with *S. aureus*, usually without any illness. The main sites of colonisation are the anterior nares and skin, whilst purulent discharges from wounds and other lesions are the main sources in infected persons. Infection is spread directly via hands and indirectly via skin scales, fomites, equipment and the environment. In about a third of cases infection is endogenous. Some carriers are more efficient at spreading infection than others. MRSA rarely invades intact skin, but can invade pressure sores, surgical wounds, and intravascular catheter sites and may then lead to severe infections.

Acquisition

The incubation period is 4–10 days and a person will remain infectious to others as long as the infection or carrier state persists. Risk factors for nosocomial acquisition of MRSA include prolonged hospital stay, intensive care, prolonged antimicrobial therapy and invasive and surgical procedures.

Prevention

- Guidelines are available for the control of MRSA and PVL-SA (see Appendix).
- In the UK, hospitals have adopted targeted MRSA screening for admissions (based on local risk assessments) to high risk specialties such as surgery, haemato-oncology, intensive care units, and transplant units and patients previously identified as colonised with or infected by MRSA.
- Patients recently hospitalised in countries with a high MRSA prevalence should also be screened on admission.
- In addition to standard infection control measures such as hand washing and use of contact precautions, interventions may include isolation, case finding by targeted microbiological screening of patients and staff and clearance of MRSA using topical or systemic antibiotics and antiseptic detergents.
- Movement of patients within and between hospitals should be minimised and appropriate antibiotic prophylaxis should be used during surgery.
- Attention to hospital hygiene, antimicrobial stewardship (Chapter 4.5), and support from senior management and a properly resourced infection control team are further important requirements.

Surveillance

- In England, MRSA is under mandatory surveillance and in the EU, surveillance is covered by the *EARS-Net* scheme.
- In the community, specimens for microbiological examination should be collected from cases of suspected staphylococcal infection.
- It is not usually necessary to report individual cases of MRSA in the community but clusters of cases should be reported to the local health protection team. In England, some cases of MRSA bacteraemia are subject to root-cause analyses (post-infection reviews) to identify and share lessons to inform prevention and control measures.
- Cases of PVL-SA infection should be reported to the local public health team so that risk factors can be considered with a view to identifying, screening, and de-colonising contacts of the case.
- Hospital alert organism surveillance: the infection control team should agree testing protocols. As a minimum all patients with clinical lesions should be sampled. In many hospitals nasal and skin swabs are collected on a targeted basis on patients who are admitted to high-risk areas of the hospital such as ITU.

Response to a case

- Treatment guidelines for cases and carriers in hospitals and the community should be used. Antibiotic treatment should be guided by the results of antibiotic sensitivity testing and local formularies.
- Discharging lesions should be covered with impermeable dressings if practicable.
- Contact with infants and other susceptible groups should be avoided and school-age children and cases in high-risk occupations should stay at home until no longer infectious.
- Colonisation with MRSA should not prevent a patient being discharged from hospital to their own home or to a nursing home if their general clinical condition allows it. There should be good communication between the hospital infection control team and the nursing home staff.

Investigation of a cluster and control of an outbreak

- Despite the implementation of infection control measures, outbreaks of MRSA are reported from hospitals, community nursing homes, military barracks, day-care settings and among groups of people participating in contact sports such as wrestling or rugby.
- An outbreak may be defined as an increase in cases of MRSA infection or colonisation or a clustering of new cases due to the transmission of a single strain in a particular setting.
- Outbreaks are investigated in a systematic fashion including search for infected cases and carriers; requesting appropriate laboratory tests; typing to confirm that cases are caused by the same strain; screening contacts and staff to detect carriers who may be the source of infection; environmental investigation and microbiological sampling; reviewing clinical practice such as wound closure and antibiotic use; and reviewing infection control practice, including hand washing, cleaning of equipment and care of catheter sites.
- In an MRSA outbreak additional control measures may be required including restricting or suspending admissions, restricting the movement of staff and patients, limiting the use of temporary staff and ward closure.

Suggested case-definitions for an outbreak

- A patient or staff member who has MRSA isolated for the first time from a clinical sample or screening swab.
  OR
- A patient or staff member who is positive for a second or subsequent time having been successfully treated and shown to be microbiologically clear of MRSA.

Cases are classified as infected if any of the signs and symptoms of infection are present otherwise they are classified as colonised.

3.49 Mumps

Mumps is a systemic viral infection characterised by parotitis. It is caused by a paramyxovirus. The public health significance of mumps is that complications are common and it is preventable by vaccination.

Suggested on-call action
None usually required.

Epidemiology

Before vaccination was introduced, mumps caused epidemics every three years, with the highest attack rates in children aged five to nine years. Following the introduction of mumps-containing vaccines, the incidence has declined throughout Europe, to a rate of 3.1 per 100 000 in 2015. In recent years, several countries have reported outbreaks in teenagers and young adults; many of whom were previously vaccinated. A number of factors have contributed to these outbreaks, including lack of catch up campaigns when mumps-containing vaccines were implemented, waning immunity after vaccination, and reduced effectiveness to some of the genotypes of wild virus that are currently circulating in Europe.

Deaths from mumps are rare, although meningitis is a relatively common complication: in the pre-vaccine era, mumps was the commonest viral cause of meningitis.

Clinical features

Tenderness and swelling of the parotid occur in about 70% of cases. It can be confused with swelling of the cervical lymph nodes. Other common features of mumps include meningitis (which is mild), orchitis (in adult males) and pancreatitis. Rare features are oophoritis, arthritis, mastitis and myocarditis.

Laboratory confirmation

The simplest method is by PCR detection of virus or IgM in oral fluid; virus can also be detected in throat swabs, nasopharyngeal aspirates, urine or CSF, up to nine days after the onset of parotitis. Serology (IgM or rising IgG) can also use be used.

Transmission

Humans are the only reservoir. Carriage does not occur. Mumps is moderately infectious, with transmission occurring through droplet spread and direct contact with saliva of a case.

Acquisition

The incubation period is 14–25 days (mean 18 days). Cases are infectious for up to a week (normally two days) before parotid swelling until several days after.

Prevention

Routine MMR vaccination; two doses required.

Surveillance

Notifiable disease in the majority of EU countries; enhanced surveillance (including laboratory confirmation) is co-ordinated by ECDC through the European Surveillance System (TESSy).

Response to a case

- Exclusion from school for five days from onset of parotid swelling.
- Check vaccination status.
- Arrange for laboratory confirmation.

Response to a cluster and control of an outbreak

As for a case, but also consider school, institution or community-wide vaccination if coverage is low or during outbreaks.

Suggested case-definition for an outbreak

Clinical: acute onset of parotid swelling, in the absence of other obvious cause.
Confirmed: positive by PCR, IgM, or fourfold rise in IgG. Does not need to meet clinical case-definition.

3.50 *Mycoplasma pneumoniae* infection

Mycoplasma pneumoniae causes acute respiratory infection and is a common cause of community-acquired pneumonia during its four-yearly epidemics.

Suggested on-call action

- None, unless outbreak suspected in institution containing frail individuals (if so, treat symptomatic contacts).

Epidemiology

Most *M. pneumoniae* infection is never diagnosed. Epidemics occur approximately every 3–5 years and last 12–18 months, peaking in winter(s). *M. pneumoniae* may be responsible for up to a third of community-acquired pneumonia during these epidemics. Outside epidemic periods, as little as 1% of pneumonias may be due to this organism. All ages are affected, with incidence highest in school-aged children. Outbreaks can occur in institutions, particularly amongst military recruits.

Clinical features

Mycoplasma classically presents with fever, malaise and headache with upper respiratory tract symptoms such as coryza, sore throat or unproductive cough. Up to 10% then progress to tracheobronchitis or 'atypical' pneumonia with a more severe cough, although mucopurulent sputum, obvious dyspnoea, and true pleuritic pain are rare. Onset is usually insidious, with presentation often delayed for 10–14 days. Asymptomatic infection may also occur, particularly in pre-school children. Neurological, dermatological, and other extrapulmonary symptoms can occur. Those with sickle-cell anaemia or Down's syndrome may be more severely affected.

Laboratory confirmation

Serology is increasingly being replaced by PCR of respiratory samples: lower respiratory samples, such as sputum, are preferred, but nose/throat swabs can be analysed. PCR can also be used to detect macrolide resistance. Serology requires demonstration of a fourfold rise in serum specific IgG antibodies: however it may take several weeks for such a rise to become apparent. Other alternatives may be available including culture on special media, detection of serum specific IgA or IgM (positive after 8–14 days of illness), and antigen detection. Other pathogens should be excluded, as asymptomatic carriage is also possible.

Transmission

Humans are the sole reservoir. Transmission requires relatively close contact: although school-age children appear to be the main vectors of transmission, they usually only infect family members and close playmates. Air-borne spread by inhalation of droplets produced by coughing is the main route of spread, but contact with items contaminated by nasal or throat discharges may also contribute. Asymptomatic and clinically recovered cases may also contribute to spreading infection. Outbreaks can occur in military, educational and healthcare institutions.

Acquisition

The incubation period is reported as ranging from 6 to 32 days. Two weeks is a reasonable

estimate of the median. The infectious period probably does not start until coryza or cough is evident. The serial interval is usually about three weeks. The length of infectiousness is unclear: three weeks from onset of illness can be used as a general guideline if coughing has ceased, although excretion may be prolonged despite antibiotics. Immunity is short-lived and re-infection can occur. Patients with functional asplenism may be more prone to overwhelming infection.

Prevention

- Avoid overcrowding in closed communities.
- Safe disposal of items likely to be contaminated by respiratory secretions.

Surveillance

- Report to local public health authorities if associated with an institution.
- Report laboratory confirmed cases to national surveillance systems.

Response to case

- Hygiene advice and care with respiratory secretions.
- Not to attend work or school whilst unwell.
- Avoid contact with those with sickle-cell anaemia, Down's syndrome or asplenism, where possible.

Investigation of a cluster

- Look for links to institutions: however, more likely to be links between families via school-age children.
- Although clustering of onset dates may indicate a common exposure, opportunities for active intervention are likely to be limited.

Control of an outbreak

- Re-inforce hygiene and infection control practices, especially in relation to respiratory secretions and handwashing.
- Avoid introduction of new susceptibles into affected institutions with frail individuals (e.g. nursing home).
- Warn local clinicians and remind them of appropriate antibiotics for cases with lower respiratory infection (macrolides, tetracyclines or quinolones, i.e. not the usual first choice for pneumonia).
- Consider feasibility of cohorting, for example separating coughing residents from asymptomatic ones.
- There is some evidence of the effectiveness of prophylactic antibiotics (check drug sensitivity of organism) to reduce the secondary attack rate for symptomatic infection in vulnerable populations.

Suggested case-definition for an outbreak

Confirmed: PCR or antigen positive respiratory secretions or serological confirmation of illness (IgM, IgA or fourfold rise in IgG).
Clinical: Pneumonia, bronchitis, or pharyngitis without other identified cause in member of affected institution.

3.51 Norovirus

Noroviruses (also known as NoV, small round structured viruses, SRSV, or Norwalk-like viruses) are the most common cause of gastroenteritis in Europe. Although generally causing mild illness, spread may be rapid, particularly in institutions. Other causes of viral gastroenteritis include other caliciviruses (e.g. sapovirus), rotavirus (Chapter 3.63), adenovirus, and astrovirus. The response to a case or outbreak of sapovirus is similar to that for norovirus.

Suggested on-call action

- If in group at risk for further transmission (Box 2.2.1), exclude from work or nursery.
- If you or the reporting clinician/microbiologist are aware of related cases, consult the local outbreak plan or SOP.

Epidemiology

Norovirus causes about 15–20% of all sporadic cases of acute gastroenteritis in Europe and an average of about 60% of all gastrointestinal outbreaks. All age-groups are affected and it is the most common cause of gastroenteritis in adults: a survey in England estimated an annual incidence of 12.5 cases per 1000 population, of which about one-sixth consulted medical services and only 1 in 300 were reported to national surveillance. Of those who presented to medical services, rates were highest in those under two years of age, followed by those aged two to four. Norovirus is usually more common from December to April hence its synonym of 'winter vomiting disease'. However, the extent of the winter peak can vary and infections and outbreaks can occur throughout the year. Epidemic strains, associated with a higher incidence of disease worldwide, are not uncommon.

Clinical features

Norovirus infection typically causes any or all of abdominal pain, nausea, vomiting and diarrhoea. Malaise and headache also occur in many cases and low-grade fever in a substantial minority. Vomiting may be sudden and forceful, but diarrhoea is usually mild and non-bloody. Symptoms last from one to five days, with infant, elderly, or previously infirm patients tending to take longest to recover. About 1% of cases require hospitalisation. Elderly or infirm patients are at increased risk of complications. Death rates in norovirus outbreaks are higher in hospitals and elderly care institutions. Asymptomatic infection is common.

Laboratory confirmation

Testing for norovirus may need to be specifically requested. Diagnosis may be by antigen testing (EIA), PCR or electron microscopy (EM) of faecal specimens, which should be collected within the first day or two of illness and preferably be unformed. Sensitivity of standard EIA tests can be low on single samples (33–44%), but collecting six to eight samples in an outbreak increases it to 80–90%. Sensitivities for PCR tests of 90% plus are reported, although some only detect genogroups I and II and some cannot differentiate between norovirus and sapovirus. Genotyping of isolates is possible: there are currently five different genogroups (with GI, GII and GIV the most common) and at least 32 distinct genotypes, with GII-4 strains the most common in recent years. Serology and EM of vomit samples are possible, but not routine.

If laboratory confirmation is lacking or awaited, epidemiological criteria can be used to assess the likelihood of an outbreak being due to norovirus (Box 3.51.1).

Transmission

- Humans are the only known reservoir of norovirus. Spread is from person to person, either by the faeco-oral or vomito-oral

Box 3.51.1 Epidemiological criteria for suspecting that an outbreak of gastroenteritis is due to norovirus

- Stool cultures negative for bacterial pathogens.*
  (NB, check that all relevant pathogens have actually been tested for).
- Incubation period, if known, of 15–50 hours.*
- Vomiting in over 50% of cases.*
- Diarrhoea generally mild without blood or mucus.
- Over half have nausea and abdominal cramps, and over a fifth have malaise, low-grade fever, myalgia and headache.
- Mean duration of illness is 12–60 hours.*
- High secondary attack rate. Even if originally food-borne, likely to be signs of ongoing person-to-person spread (see Box 2.2.3).
- Staff at institution are also affected.

**Kaplan criteria.*

routes, or indirectly by contamination of the environment, food or water.

- Norovirus is easily spread by these routes. Asymptomatic, pre-symptomatic, symptomatic, and post-symptomatic cases have all been shown to excrete norovirus. The risk is highest from onset of symptoms to about 48–72 hours after they cease (coinciding with the limit reported for detection by EM). Newer more sensitive tests can demonstrate virus in faeces for up to three weeks, but the relevance of this for infectivity in asymptomatic patients with good personal hygiene is not clear. Excretion may be prolonged in chronic illness or immunosuppressed individuals and in children under six months of age.
- Norovirus is identifiable in vomit and vomiting has been linked to many outbreaks. This can be directly from aerosols created by vomiting or contamination of food or the environment.
- Environmental contamination in outbreaks has been shown for bathroom surfaces, taps, door handles and light switches and on kitchen surfaces. Transmission of norovirus in faeces to such surfaces can occur via contaminated fingers and cloths. Norovirus may also remain viable on carpets or curtains.
- Norovirus is a commonly reported cause of food-borne outbreaks. This may be via infected foodhandlers or from the use of already contaminated foods such as oysters and other shellfish and imported soft fruit (norovirus is resistant to freezing). More than one norovirus genogroup can occur in the same outbreak, particularly those related to shellfish harvested from waters contaminated by human sewage.
- Drinking water that is inadequately treated or is contaminated post-treatment may transmit norovirus, as may swimming in contaminated water.
- Outbreaks are most commonly reported in hospitals, nursing homes and elderly care homes, but also occur in nurseries, schools, restaurants, hotels and cruise ships. The attack rates are usually highest in food-borne outbreaks (about 50%), lower in institutions (about 30%), and lowest in holiday venues (about 9%).

Acquisition

The average incubation period for norovirus is about 30 hours after exposure, with a range between 6 and 72 hours. The infective dose is extremely low (infection can occur from ingestion of less than 100 particles) and the high concentration of virus in faeces can lead to high attack rates. Immunity occurs post-infection, but may only last a few months (sufficient to remove recovered cases from the pool of susceptibles in an outbreak). This, plus the existence of several antigenic types, means later re-infection is possible.

Prevention

- Good standards of personal hygiene, including adequate handwashing with soap and running water. Alcohol-based hand-rubs are likely to be less effective.
- Good standards of infection control in hospitals and residential homes, including adequate environmental cleaning.
- Good food hygiene, including cooking raw shellfish and washing fruit before consumption.

Surveillance

- Laboratory confirmed cases should be reported to local and national surveillance systems.
- Cases with links to institutions such as hospitals, care homes, day care centres or restaurants should be reported to local public health authorities, as should any suspected outbreak.
- Feedback of surveillance of norovirus activity through laboratory reporting, outbreak reporting and syndromic surveillance of diarrhoea and/or vomiting in primary care may be useful to health and care services in winter.

Response to case

- Exclude cases in groups with risk of further transmission (Box 2.2.1) until 48 hours after resolution of diarrhoea and vomiting.
- Enteric precautions with particular attention to environmental contamination related to vomitus.
- Cases in institutions should be isolated where practicable.
- Treat symptomatic contacts in high-risk groups as cases.
- Hygiene advice to cases and contacts.

Investigation of a cluster

- Most recognised clusters are associated with an institution or a social function.
- If an institution, use Box 2.2.3 to help assess likelihood of person-to-person or food-borne source.
- If a social function, consider infected food handler, contaminated premises and contaminated food, especially shellfish.
- If a community outbreak, describe by person, place and time and obtain full food (especially seafood, fruit, salad, sandwiches), occupational, family and social histories including links to hospitals, residential institutions, hotels and restaurants) 6–72 hours before onset as a hypothesis-generating exercise. Organise further case-finding, for example requesting faecal samples from cases of gastroenteritis presenting to GPs.

Control of an outbreak

- Report to local public health authorities. Detailed local or national guidance documents should be available to support the local response.
- For outbreaks in institutions, form an outbreak team, which includes a senior manager who has authority to commit the institution to agreed action. There is evidence that earlier institution of enhanced infection control measures is associated with greater effect.
- Reinforce good infection control (especially handwashing) and food hygiene practices. Ensure toilet facilities are adequate.
- Increase cleaning, particularly of toilet areas and 'contact points' (e.g. taps and door-handles). Wear disposable gloves and aprons for cleaning potentially contaminated areas. Application of 1000 ppm hypochlorite disinfectant after use of detergent is the most effective method of decontamination.
- Immediate cleaning and decontamination of areas contaminated by vomiting.
- Isolate cases where practicable in residential institutions. Cohorting of cases otherwise.
- Exclude cases in non-residential institutions until symptom-free for 48 hours.
- Staff to wear gloves and aprons and to observe enteric precautions when dealing with infected patients.
- Exclude staff with gastrointestinal symptoms until 48 hours after resolution. Nausea and cramps may precede vomiting and diarrhoea; do not wait until they vomit on the premises!
- Do not admit more susceptible individuals into an outbreak area, preferably until 72 hours since last episode of diarrhoea or vomiting. Outbreaks in institutions will normally terminate in one to two weeks if new susceptibles are not introduced.
- Do not discharge potentially incubating patients into another institution.
- Restrict unnecessary patient and staff movements between wards: the main aim is to prevent transmission to other wards, whilst outbreak 'burns-out' in affected ward.
- Staff working in affected wards should not then work in unaffected wards until remaining asymptomatic for 48 hours from last exposure.
- Exclude non-essential personnel from the ward.
- Give advice on norovirus and hand hygiene to adult visitors and exclude those with symptoms. Restrict visiting by children if possible.
- Thoroughly clean before re-opening to admissions. Change curtains in hospital.

- Compliance with intervention can often be poor or relapse: the Infection Control Nurse or Environmental Health Practitioner will need to maintain constant supervision to ensure that the agreed actions are fully implemented and maintained.

Suggested case-definition for use in an outbreak

Vomiting, *or* diarrhoea, *or* both nausea and abdominal pain, in a member of an institution or party in which a norovirus outbreak has been microbiologically demonstrated.

3.52 Paratyphoid fever

Paratyphoid fever is a potentially severe infection. Although rare in developed countries, it is a potential hazard to travellers to developing countries and can be spread by infected foodhandlers. Paratyphoid and typhoid fevers (see Chapter 3.80) are both also known as enteric fever.

Suggested on call action

- Exclude cases and contacts who are foodhandlers.
- Exclude cases and symptomatic contacts in other risk groups (see later).

Epidemiology

There were 336 cases of paratyphoid fever reported in 27 EU/EEA countries in 2014, an incidence of 0.1 per 100000: of these cases, 248 were reported as Paratyphoid A, 65 as Paratyphoid B and 23 were unspecified. Data for Europe is usually reported as enteric fever (about one-third of enteric fever cases in Europe are paratyphoid), for which cases are more common in late summer, the incidence has fallen over the last decade and the large majority are imported. About 130 laboratory reports of paratyphoid are made annually in the UK: 92% of these are paratyphoid A, 7% paratyphoid B and 0.2% paratyphoid C. About 95% of UK cases had travelled abroad, most commonly to the Indian subcontinent.

Clinical features

Paratyphoid infection may cause gastroenteritis and/or enteric fever. The most commonly reported symptoms are fever, chills, diarrhoea, abdominal pain and headache. Other symptoms reported are nausea, vomiting, cough, constipation, anorexia and delirium. Examination may reveal splenomegaly, hepatomegaly, rose spots, bradycardia and possibly signs of bronchitis, tonsillitis or tympanitis. Paratyphoid A infection can be as severe as typhoid, although paratyphoid B is often less severe. Complications include hepatitis, perforation and relapse; death may result, but is rare in treated cases. Asymptomatic infection also occurs.

Enteric fever should be considered when patients returning from an endemic or epidemic area develop a febrile illness, even if diarrhoea is not reported.

Laboratory confirmation

Paratyphoid fever is caused by *Salmonella enterica* subspecies *enterica* serotype Paratyphi, more usually shortened to *S.* Paratyphi. There are three serotypes: A, B and C. Organisms initially reported as *S.* Paratyphi B may actually be *S.* Paratyphi B var. Java (*S.* Java), which has a similar antigenic profile (although it can be distinguished by biochemistry or genotyping), but causes a more typical salmonellosis rather than an enteric fever.

Culture for *S.* Paratyphi can be performed on samples of blood, stool, urine, rose spots, bone marrow and gastric or intestinal secretions. Blood, urine and faeces culture are usually the first line: faeces are usually positive

after the first week of illness and results should be available in 72 hours. The sensitivity of blood culture can be as high as 80%. PCR testing of faeces or stool may also be available in some laboratories: ideally PCR positives should be followed up with stool culture.

Antibiotics may suppress *Salmonella* below detection levels for several weeks after completion of the course. However, bone marrow culture has 90% sensitivity, even after five days of antibiotic therapy. The Widal test may be positive, although sensitivity may be lower than for typhoid. Phage typing may be available for unexplained clusters (the most common types in the UK are PT13, 1, 1a, 2, and 4). Genotyping may also be available from reference laboratories (e.g. WGS in England).

Transmission

Humans are the main reservoir, although environmental contamination may occur from human faeces. *S*. Paratyphi B occurs rarely in cattle. *S*. Java may be associated with poultry, tropical fish and cattle, and is common in poultry in the Netherlands and Germany.

Spread is faeco-oral, most commonly via a food-borne vehicle. Water-borne spread also occurs. Direct person-to-person spread is uncommon. *S*. Paratyphi B infection has been associated with milk and unpasteurised cheese. Laboratory acquired infection is also reported.

Acquisition

The incubation period has a range of 1–17 days, although up to 3 weeks is reported. Most cases occur within 10 days of exposure (median 3–7 days): 96% of enteric fever cases who have a travel history develop symptoms within 28 days of return from an endemic area.

A minority of cases will excrete the organism for some weeks and about 1–2% for more than a year. Cases and carriers are infectious whilst they are excreting the organism (carriers commonly excrete 10^7–10^{10} g^{-1} stool), but risk, other than through contamination of food or water, is low unless there are poor hygiene practices. About 95% of excretors are detected by three consecutive faecal samples; five consecutive negative faecal samples gives near certainty of microbiological clearance. Infection produces partial immunity.

Prevention

- Control depends on sanitation, clean water, handwashing and food hygiene.
- Advice on personal, food, and water hygiene to travellers to affected countries.
- There is no licensed vaccine against paratyphoid. Oral typhoid vaccine may have some cross-protection with paratyphoid B.

Surveillance

- Paratyphoid is a notifiable disease in most countries, including the UK. Some countries (e.g. England) have national enhanced surveillance systems for enteric fever.
- Report to local public health departments on clinical suspicion.
- Laboratory confirmed cases should be reported to local and national public health agencies.

Response to a case

- Usually requires antibiotic treatment, but check sensitivity of isolate.
- Advice on good personal and food hygiene to cases, carriers and contacts, especially handwashing.
- Enteric precautions for cases; consider isolation if hospitalised.
- National guidance documents for dealing with cases and contacts may be available (e.g. detailed evidence-based guidance is available via PHE website).
- Obtain food and travel history for the four weeks prior to onset of illness: a standard national enhanced surveillance may be available to assist this (e.g. via PHE website).

- Cases who have not visited an endemic country in the four weeks before onset should be investigated to determine the source of infection: this should include possible contact with those who have recently travelled to an endemic country.
- Cases, excretors and carriers who are higher risk for spreading infection (see Box 2.2.1) should be excluded from high risk activities, until no longer excreting the organism. This can be defined (as in UK guidance) as three consecutive negative samples taken at least 48 hours apart (faecal sampling should not start until one week after completion of antibiotic therapy). Cases not in high risk groups need only be excluded until clinically well with formed stools for 48 hours and hygiene advice has been given.
- Contacts, such as co-travellers, household and other close (including sexual) contacts, should be identified and questioned about whether they have suffered any symptoms compatible with paratyphoid and whether they are in a higher risk group for further transmission. All contacts should receive comprehensive hygiene advice. A faecal sample should be obtained from symptomatic contacts; co-travellers with similar exposure history who are in a higher risk group of onward transmission; and household and other close contacts of non-travel associated cases. The ongoing risk-assessment process may identify other cases suitable for screening. Symptomatic contacts in higher risk groups should be excluded whilst awaiting the result of the screening sample.
- Quinolones may reduce the period of carriage in those for whom exclusion is producing social difficulties.
- For *S.* Java, microbiological clearance is less likely to be advised and exclusion is 48 hours from last episode of diarrhoea or vomiting.

Investigation of a cluster

- Clusters should be investigated to ensure that secondary transmission has not occurred within Europe.
- Check each case (and their household contacts) for travel abroad.
- Interview cases to identify the source of infection. This could be contact with a chronic carrier, with faecal material, or with contaminated food, milk, water or shellfish. Obtain and compare food histories. Explore family and social links between cases.
- Obtain microbiological typing (e.g. WGS) from reference laboratory.

Control of an outbreak

- Exclude cases and contacts as above.
- Exclude and test food handlers in any associated institution or food premises. Ensure adequate personal and food hygiene.
- Organise testing and withdrawal of any implicated food. Ensure only pasteurised milk, treated water and cooked shellfish are used.

Suggested case-definition for an outbreak

Probable: a clinically compatible case epidemiologically linked to a confirmed case in an outbreak.

Confirmed: a clinically compatible case that is laboratory-confirmed (and with same phage/genotype if available).

3.53 Parvovirus B19 (fifth disease)

Parvovirus B19 is the cause of a common childhood infection, erythema infectiosum, also known as fifth disease or slapped cheek syndrome. It is important because of the risk of complications in pregnancy, in those with haemoglobinopathies and the immunocompromised.

Suggested on-call action

If the case is a healthcare worker in contact with high-risk patients, consider either exclusion from work or avoiding contact with high-risk patients.

Epidemiology

Infection occurs at all ages, although children aged 6–10 years are at greatest risk. Outbreaks in schools and nurseries are common, usually occurring in early spring. The disease tends to occur in three- to four-yearly cycles. By the age of 10, up to 50% of children will have been infected.

Clinical features

The main differential diagnosis is rubella; with the decline in rubella due to vaccination, parvovirus is now the more likely diagnosis in Europe. Fever is the first symptom, which lasts for two or three days until the rash appears. The rash is maculopapular and is found on the limbs, less commonly the trunk. The cheeks often have a bright red ('slapped cheek') appearance. The 'slapped cheek' rash lasts for one to four days. In a healthy person, the illness is usually mild and short-lived, although persistent joint pain, with or without swelling sometimes occurs, especially in young women, most commonly in knees, fingers, ankles, wrists and elbows.

Parvovirus infection in the first 20 weeks of pregnancy can cause intra-uterine death (9%) and hydrops fetalis (3%); it is however, not teratogenic. In patients with haemoglobinopathies it can cause transient aplastic crises, and in immunodeficient patients, red cell aplasia and chronic anaemia can occur.

Laboratory confirmation

This is important to distinguish from rubella, especially in pregnant women or their contacts. The diagnosis can be confirmed by testing serum for B19 IgM, which is positive from the day of onset of rash, or by rising IgG titres (first sample should be taken as soon as possible after exposure: in pregnant women an earlier booking sample may be available). The virus can also be detected by PCR from blood, saliva, respiratory secretions and CSF.

Transmission

Humans are the only reservoir; cat and dog parvoviruses do not infect humans. Transmission is from person to person by droplet infection from the respiratory tract; rarely by contaminated blood products. Long-term carriage does not occur.

Acquisition

Parvovirus is highly infectious. The incubation period ranges from 4 to 20 days, but is usually between 13 and 18 days. The infectious period is from seven days before the rash appears until the onset of the rash. In aplastic crises, infectivity lasts for up to a week after the rash appears, and immunosuppressed people with severe anaemia may be infectious for several months or even years. Immunity is lifelong.

Prevention

- Consider avoiding exposure of patients at risk of complications (see above) to potential cases in outbreak situations.
- Transmission is probably reduced by routine hygiene practices (e.g. handwashing).
- There is no vaccine available.

Surveillance

- Not notifiable in most European countries.
- May only come to the attention of the public health department as a result of investigation of a case of suspected rubella

or other rash illness, or when there is an outbreak of a rash illness in a school.

Response to a case

- Arrange for laboratory confirmation.
- Isolation or school exclusion of cases is of no value as any transmission occurs before the onset of symptoms (however see below for teachers).
- Consider exclusion of a non-immune healthcare worker (HCW) who has been exposed to a case and develops a fever, until either the rash appears or for 15 days from the last contact with the case. Alternatively advise the HCW to avoid contact with high-risk patients (women in the first 20 weeks of pregnancy, those with haemoglobinopathies and the immunocompromised), or to take respiratory precautions until a rash appears or for 15 days. Screening of HCWs may be justified for those who have frequent contact with high-risk patients, or for laboratory workers who work with infectious material known to contain B19 virus.
- If infection confirmed in a HCW, test high-risk contacts (as above) for immunity and monitor for evidence of infection, as they need specialist care if infected. Consider human normal immunoglobulin 400 mg kg^{-1} intravenously for 5–10 days for immunosuppressed contacts (efficacy uncertain).
- If infection is confirmed in a pregnant woman, consider regular screening for hydrops foetalis as intra-uterine transfusion improves outcome.

Investigation and control of an outbreak

- In addition to measures described earlier for a case, it may be worth excluding susceptible teachers who are in the first 20 weeks of pregnancy from a school in which an outbreak is occurring, until they are more than 20 weeks pregnant; consideration should also be given to excluding children with haemoglobinopathies and the immunocompromised.

Suggested case-definition

IgM or PCR positive in presence of clinically compatible illness.

3.54 Plague

Plague is a serious and potentially highly infectious disease caused by the Gram-negative bacterium *Yersinia pestis*.

Suggested on-call action

- Ensure that cases are isolated.
- Identify those at risk.
- Ensure staff monitoring is instituted.
- Ensure appropriate handling of clinical samples.
- Liaise with rodent and flea control experts if possibility of local acquisition.

Epidemiology

Yersinia pestis is enzootic in rodents (wild and peri-domestic rats, ground squirrels, gerbils, and so on) in many parts of the world. Plague is still endemic in Africa, Asia, the Americas and some parts of the former Soviet Union. In EU/EEA countries, autochthonous plague has not occurred for several decades and transmission risk is considered minimal. Natural reservoirs are rats and seasonal patterns have been observed but vary regionally.

Clinical features

Clinical presentation depends in part on the route of infection. Bubonic plague is the most common presentation and is acquired cutaneously. There is rapid onset of high fever,

malaise and delirium. Tender buboes (swollen regional lymph nodes) draining the site of infection develop. Petechial or purpuric haemorrhages are common. Septic shock develops with an untreated mortality of 60–90%.

Septicaemic plague presents with sudden onset of high fever without buboes. The clinical course is rapid with overwhelming sepsis, organ failure, and death within a few days.

Primary pneumonic plague, acquired by respiratory spread, is a severe illness with high fever, chest pains, tachypnoea, restlessness, and shortness of breath. Respiratory signs may be absent until frothy blood-tinged sputum is produced as a pre-terminal event; untreated mortality is 100%. Secondary pneumonic plague is more common and occurs through haematogenous spread of *Y. pestis* from a bubo or other source.

Laboratory confirmation

The organism can be isolated from the blood, sputum and bubo aspirates. Smears can be Gram-stained. Serology and antigen detection may also be available. The definitive tests for *Y. pestis* are:

- Culture from a clinical specimen with confirmation by phage lysis.
- A significant (≥4-fold) change in antibody titre to F1 antigen in paired serum samples.

Transmission

Bubonic plague is transmitted by the bite of infected rat fleas. Spread is from the bite site via lymphatics to lymph nodes. Transmission can also occur via direct contact with tissues or secretions of infected animals. Pneumonic plague is acquired directly by inhalation of respiratory droplets from another case of pneumonic plague.

Acquisition

The incubation period for bubonic plague is 2–6 days, and for pneumonic plague is 10–15 hours. Patients are infectious until at least 48 hours of appropriate chemotherapy is received and a favourable clinical response seen. Partial immunity results from infection.

Prevention

- Pest control (rodents and fleas) is essential.
- Laboratory staff handling the organism should do so only in Biosafety Level 3 facilities.
- A killed whole-cell vaccine (KWC) and a live whole-cell attenuated vaccine (LWC) exist but are only recommended in occupational groups that are likely to come into contact with the organism.

Surveillance

- Notifiable and cases should be reported to national authorities, ECDC and to the WHO.
- Suspected cases should be reported urgently to local public health departments.

Response to a case

- Streptomycin, gentamicin, tetracyclines, fluoroquinolones, or chloramphenicol are the drugs of choice. Treatment after 15 hours may not influence the course of pneumonic plague.
- Patients should be considered highly infectious and should be strictly isolated.
- All care should be taken with specimens.
- Staff should be monitored carefully for fever and treated promptly.
- Household contacts should be offered antibiotic chemoprophylaxis within seven days of exposure.
- Patients and possessions must be disinfected of fleas.
- If pneumonic plague in someone who has not been to an endemic area, consider deliberate release.

Investigation of a cluster and control of an outbreak

- Identify source as a matter of urgency and institute pest control.
- Contacts should be offered antibiotic prophylaxis.
- Consider deliberate release if two or more suspected autochthonous cases linked in time and place or if any confirmed case has not been to endemic area.

Response to a suspected deliberate release

- Report to local and national public health authorities.
- Define exposed zone and identify those exposed (include those who have left the scene).
- Cordon off exposure zone.
- Decontaminate those exposed: remove clothing and possessions, and then shower with soap and water.
- Mass antibiotic chemoprophylaxis (choice dependent on local guidelines) as soon as possible for those exposed.
- Record contact details for all those exposed.
- Some health and emergency workers may also need chemoprophylaxis.
- Collect appropriate environmental samples and monitor animal populations to assess the geographic extent of environmental contamination.

Suggested case-definition for an outbreak

Suspected case: The diagnosis should be considered if the following clinical presentations occur in previously healthy patients, especially if two or more cases arise that are linked in time and place:

- Sudden onset of severe, unexplained febrile respiratory illness.
- Unexplained death following a short febrile illness.
- Sepsis with Gram-negative coccobacilli identified from clinical specimens.

In the event of a known or suspected deliberate release, or among contacts of plague cases, the threshold for making a diagnosis of plague should be lower.

Confirmed case: A case that clinically fits the criteria for suspected plague and, in addition, positive results are obtained on one or more specimens by the Reference Laboratory.

3.55 Pneumococcal infection

Streptococcus pneumoniae ('pneumococcus') is the most common cause of community-acquired pneumonia and a common cause of bacteraemia and meningitis.

Suggested on-call action

- If case of meningitis, reassure contacts that no prophylaxis is needed.
- If an outbreak in an institution is suspected, consult the local outbreak control plan or SOP.

Epidemiology

Around 20 000 invasive pneumococcal infections are reported annually in the EU, but the true incidence is much higher; pneumococcal pneumonia is estimated to affect 0.1% of adults per annum. The overall European incidence in 2014 was 4.4%. All ages are affected, but the distribution is bimodal: with an incidence of 12.6 per 100 000 population in the over 64 years and 10.3 per 100 000 population in children below the age of 1 year, while in older children and young adults the incidence is below 2 per 100 000 population. Incidence rates between European countries vary 10-fold, probably reflecting differences in the surveillance systems. Pneumococcal

pneumonia and meningitis are both more common in the winter.

Pneumococcal infection is more common in smokers, heavy drinkers and those who live in overcrowded sleeping quarters. Incidence increases during influenza epidemics. An absent or non-functioning spleen increases the risk of invasive disease. Recurrent pneumococcal meningitis may occur in association with cranial defects, CSF leaks, cochlear implants or skull fractures. Although the incidence of pneumococcal meningitis is highest in young children, its relative importance is highest in middle-aged and elderly adults, in which it is the most common cause of bacterial meningitis.

Antibiotic resistance rates among European invasive isolates are highly variable between countries; 0–48% for macrolides and 1–28% for penicillin (I+R) in 2014. Resistance is particularly high in Southern and Eastern Europe, but generally lower in Western and Northern European countries.

Clinical features

The clinical spectrum of pneumococcal infections ranges from upper respiratory tract infections (acute otitis media and sinusitis) to pneumonia and invasive pneumococcal diseases (i.e. bacteraemia, meningitis and other focal septic infections). It is the most important bacterial cause of otitis media, which is particularly common in children under three years of age. The most common symptoms of pneumococcal pneumonia are cough, sputum and fever. Factors that may suggest pneumococcal rather than 'atypical' pneumonia in an outbreak include mucopurulent or blood-stained sputum, pleuritic chest pain and prominent physical signs. Respiratory symptoms may be less obvious in the elderly. Many cases have predisposing illnesses, such as chronic respiratory, cardiac, renal or liver disease, immunosuppression or diabetes. Bacteraemia may occasionally lead to meningitis. The case fatality rate for bacteraemia or meningitis is 20% and for pneumonia is about 10% (higher in the elderly).

Laboratory confirmation

Gram staining and culture of good quality sputum specimens remains the mainstay of diagnosis of pneumococcal pneumonia, allowing also for resistance testing. The low sensitivity (60%) and moderate specificity (90%) is a limitation. PCR from airway secretions has a high sensitivity and could be useful if antibiotic therapy has already started. However, a PCR test could also be positive due to asymptomatic carriage. Rapid tests for detection of pneumococcal antigen in urine are commercially available. Of cases of pneumonia, 25% will also have a positive blood culture, which can be useful confirmation that the pneumococcus is a pathogen rather than a co-incidental commensal. Gram-positive diplococci in CSF suggest pneumococcal meningitis. Serology may be available for retrospective clinical diagnosis.

Serotyping of strains is performed for epidemiological purposes in some laboratories. There are over 90 serotypes of varying pathogenicity. The 10 most common serotypes in young children (one to four years of age) with invasive pneumococcal disease in Europe are 24F, 19A, 14, 12F, 1, 23B, 3, 15B, 15A and 10A of which serotypes 24F, 12F, 23B, 15B, 15A and 10A are not included in any of the conjugated vaccines.

Transmission

Pneumococci find their ecological niche by colonising the human nasopharynx, especially in young children. Carriage is common, ranging from about 10% in adults to 50% in children in day-care centres, and is high in winter. Transmission requires extensive close contact with cases or carriers and is usually by droplet spread, but may also be via direct oral contact or article soiled by respiratory discharges. Elderly patients are mostly infected through contacts with children. In hospitals, spread is usually to patients in the next one or two beds. Staff may also become colonised. Cases of pneumococcal meningitis are viewed as sporadic.

Acquisition

After acquisition of a new serotype, clinical infection typically occurs within a few days. As nasopharyngeal carriage can be prolonged (mean carriage time seven weeks), endogenously acquired invasive disease in asymptomatic carriers may rarely occur at a late stage, giving an 'incubation period' of weeks.

The infectious period probably lasts as long as there are viable bacteria in nasal, oral, or respiratory discharges. Even though penicillin does not eradicate nasopharyngeal bacteria, treatment still renders patients with susceptible organisms non-infectious in 48 hours.

Type-specific immunity follows infection and is long-lasting. Colonisation may also lead to immunity: one study estimated that two-thirds of those who became colonised developed antibody within 30 days. Risk of infection is higher in those with splenic dysfunction (including sickle cell and coeliac disease) and immunodeficiency (e.g. due to chemotherapy, diabetes and HIV).

Prevention

Avoid overcrowding in institutions such as hospitals, day-care centres, military camps, prisons and homeless shelters.

Three pneumococcal conjugate vaccines, covering 7 (PCV7), 10 (PCV10) and 13 (PCV13) common serotypes, respectively are available. PCV7 protects against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F. PCV10 protects additionally against serotypes 1, 5 and 7F, and PCV13 protects also against serotypes 3, 6A and 19A. The conjugate vaccines reduce the risk of pneumococcal meningitis, bacteraemia, pneumonia and otitis media in vaccinated children (direct effect), but also provide an indirect 'herd effect' in elderly contacts to the children. Conjugate vaccines are now included in the national child immunisation programmes from the age of two to three months in almost all EU countries. In the age group one to four years, the overall incidence rate of invasive pneumococcal infection has decreased from 7.5 to 4.5 per 100 000 between 2010 and 2014. For the same age group, the incidence rate decreased from 1.87 in 2010 to 0.69 per 100 000 in 2014 for invasive infections due to serotypes included in PCV13 and increased from 1.07 to 1.80 per 100 000 for serotypes not included in PCV13, with large variations between the countries (serotype data not available from all countries). Detailed national data per country is available in the surveillance atlas for infectious diseases on the ECDC website.

PCV is also gradually replacing the old 23-valent polysaccharide vaccine for adults in whom pneumococcal infection is likely to be more common and/or dangerous. This includes all those aged over 65 years of age and those with chronic renal, heart, lung or liver disease, splenic dysfunction, immunosuppression, diabetes, cochlear implants or CSF shunts.

Surveillance

Isolates from blood, CSF or other normally sterile sites should be reported to the national surveillance systems. Isolates from sputum are not usually reported because of their uncertain clinical significance. Antibiotic susceptibility (especially penicillin and macrolides) should be given for all reported cases. Presently, invasive pneumococcal infections are reportable in 28 EU/EEA countries (data not available from Germany, Portugal and Liechtenstein)

Possible outbreaks of pneumococcal infection should be reported to local public health authorities.

Response to a case

Safe disposal of discharges from nose and throat.

Antibiotic therapy as appropriate to clinical condition and sensitivity will reduce infectivity.

There may be some value in separating patients from others with an increased risk of serious disease until 48 hours of appropriate antibiotics have been received.

Investigation of a cluster

Organise serotyping of strains.

Check for links via institutions. Otherwise no action is usually necessary.

Control of an outbreak

Immunise all contacts that are at higher risk of serious infection: polysaccharide vaccine usually protects more quickly than conjugate.

Check antibiotic susceptibility and serotype of isolates.

If outbreaks in institution/ward, vaccinate all residents (unless known to be strain not in vaccine). Institute case finding and early treatment of symptomatic cases for at least 7–10 days.

Ensure adequate environmental decontamination.

Suggested case-definition for use in an outbreak

Confirmed: Clinically compatible case with isolate of *S. pneumoniae* (of outbreak serotype if known) from a normally sterile site.

Probable: Clinically compatible case with *either*:

- isolate of *S. pneumoniae* (of outbreak serotype if known) from a normally non-sterile site (e.g. sputum); *or*
- detection of *S. pneumoniae* nucleic acid or antigen from a normally sterile site (e.g. urine).

3.56 Poliomyelitis

Poliomyelitis is an acute viral infection of the nervous system caused by poliovirus types 1, 2 and 3. Its public health importance lies in the ability of polioviruses to cause permanent paralysis and sometimes death. It is readily transmitted, causing both endemic and epidemic disease.

Suggested on-call action

- Arrange for urgent laboratory confirmation.
- Obtain vaccination and travel history.
- Notify national surveillance unit.

Epidemiology

Poliomyelitis has been eliminated from most countries by vaccination. The WHO European Region (which includes 53 countries) was certified as polio-free in 2002. Imported cases occur occasionally, from countries where endemic transmission still occurs). Vaccine-associated paralytic polio (VAPP), a complication of live oral polio vaccine (OPV), occurs at a rate of two cases per million doses. Vaccine derived polio is caused by a rare mutation of a vaccine polio virus (vaccine derived polio virus: VDPV) and can cause outbreaks in under-immunised populations.

Global eradication of polio has not yet been achieved, although numbers of cases continue to fall and there are now only three countries where endemic transmission of wild virus occurs: Pakistan, Nigeria and Afghanistan. Outbreaks of vaccine-derived polio have occurred recently in Syria and the DR Congo. Global eradication of polio remains a WHO target, and measures to restrict use of polioviruses in laboratories are being implemented throughout Europe as part of the polio end game.

Clinical features

Most cases of polio are asymptomatic or present with a sore throat or diarrhoea. A few cases develop meningitis that is indistinguishable from other causes of viral meningitis. Paralysis is relatively rare: the proportion of paralytic cases increases with age from about 1 in 1000 in infants to 1 in 10 in adults. After 15–40 years (one quarter of) patients can develop a post-polio syndrome (PPS), related to neural fatigue of affected limbs,

leading to disabling fatigue, with breathing and swallowing problems, and sleep apnoea. PPS is also seen in patients with a previous non-paralytic polio.

Poliomyelitis should be considered in any patient with acute flaccid paralysis, particularly if there is a history of recent travel to an endemic area. Vaccine-associated polio should be considered in an individual with acute flaccid paralysis recently vaccinated with OPV (particularly after the first dose) or in a close contact of a recently vaccinated individual. The main differential diagnosis is Guillain–Barré syndrome. The paralysis in polio is usually asymmetric and there is always residual paralysis in polio, whereas in Guillain–Barré syndrome the paralysis it is usually symmetrical and recovery is complete.

Laboratory confirmation

The most important diagnostic specimen is a stool sample, which should be sent for viral culture. Poliovirus can be recovered from faeces for up to six weeks and in nasopharyngeal secretions for up to one week from onset of paralysis. At least two stool samples, 24 hours apart, should be obtained within seven days of the onset of paralysis. Absence of virus does not however rule out the possibility of poliomyelitis; where available, molecular diagnosis by PCR is the technique of choice – this can be done on stool, throat swab, or CSF samples. All cases of acute flaccid paralysis should be investigated to exclude polio. The diagnosis can also be made serologically (two samples, 10–14 days apart, first sample from acute phase) or by CSF examination.

Transmission

Polio is spread by the faeco-oral route. Humans are the only reservoir and there is no carrier state (except rarely in immunodeficiency). The virus can survive in sewage, soil and infected water for a few weeks. Poor hygiene favours spread.

Acquisition

The usual incubation period is 7–14 days for wild cases and vaccine-associated (recipient) cases, although it may be as long as 35 days. For vaccine-associated (contact) cases the incubation period may be up to 60 days. Immunodeficiency is a risk factor for vaccine-associated paralysis, and immunodeficient patients with either vaccine-associated or wild polio may excrete virus for many months.

Prevention

- Two types of vaccine: oral polio vaccine (OPV) and inactivated poliovaccine (IPV) are available. All countries in Europe now use IPV. Three doses are given at 2, 3 and 4 months of age with further boosters at 3–5 years and 15–19 years.
- Boosters are required at 10-yearly intervals for travel to endemic areas and are routinely given to all adults in some countries.

Surveillance

- Notifiable in all countries in Europe. Report on clinical suspicion.
- Poliomyelitis is targeted for eradication. Highly sensitive surveillance for acute flaccid paralysis (AFP), including immediate case investigation, and specimen collection are critical for the detection of wild poliovirus circulation with the ultimate objective of polio eradication. All AFP cases under 15 years of age or with paralytic illness at an age where polio is suspected should be reported immediately and investigated within 48 hours, and two stool specimens should be collected 24–48 hours apart and within 14 days of the onset of paralysis.
- AFP surveillance is also critical for documenting the absence of poliovirus circulation for polio-free certification. Aggregated data on AFP cases should be included in routine monthly surveillance reports. Designated reporting sites at all levels should report at a specified frequency (e.g. weekly or monthly)

even if there are zero cases (often referred to as 'zero reporting').
- Regular weekly visits should be made to selected reporting sites that are most likely to admit acute flaccid paralysis patients (e.g. major hospitals, physiotherapy centres) to look for unreported AFP cases.

Response to a case or cluster

- Immediate notification, to the public health department. Request urgent stool virology.
- Treat a single case of indigenous wild polio as a national public health emergency; ECDC and WHO should be notified.
- If confirmed, mass vaccination with OPV would be required, possibly at the national or subnational level.
- For an imported case, notify national surveillance unit and WHO.
- For vaccine-associated cases, no specific action is required, although it may be an opportunity to review vaccine coverage locally.

Suggested case-definition

Possible: acute flaccid paralysis without other apparent cause.
Probable: acute onset of flaccid paralysis with decreased/absent tendon reflexes, without other identified cause, and without sensory or cognitive loss.
Confirmed: Serological evidence or positive virus culture or PCR, together with clinically compatible illness.

3.57 Psittacosis

Psittacosis (or ornithosis) is a potentially fatal systemic disease caused by *Chlamydia* (previously classified as *Chlamydophila*) *psittaci*. It is a zoonotic infection particularly associated with birds.

Suggested on-call action

- If linked cases suspected, institute the outbreak plan or SOP.
- If not, ensure case investigated promptly on next working day.

Epidemiology

Much of the reported epidemiology of psittacosis is based on a combination of respiratory symptoms and demonstration of *Chlamydiaceae* group antigen on serology: it therefore requires re-examination in the light of the discovery of the more common *Chlamydia pneumoniae* (see Chapter 3.9) which also causes disease fitting such a case-definition.

Psittacosis is reported to cause about 1–2% of community-acquired pneumonia. Around 50 cases of psittacosis are reported a year in Britain, about 40 in the Netherlands and about 15 in Germany, but all are likely to be considerable underestimates due to underdiagnosis. Cases occur worldwide and are more commonly reported in those exposed to birds occupationally (including poultry workers) or as pet owners. Cases occur mostly in adults and more often in males. There is no distinct seasonal pattern.

Clinical features

Onset may non-specific with fever and malaise, followed by an atypical pneumonia with unproductive cough, fever and headache, with 20% mortality if untreated. Other syndromes resemble infectious mononucleosis and typhoid. Asymptomatic infection also occurs. Most cases report fever and most (eventually) develop a cough. Headache, myalgia and chills are each reported in about half of cases. Relapses may occur.

Chlamydia abortus (also previously classified as *C. psittaci*) is a related organism that can cause serious infection in pregnant women, resulting in late abortion, neonatal

death and disseminated intravascular coagulation in the mother.

Laboratory confirmation

Culture is rarely used because of the risk of laboratory acquired illness and diagnosis is usually based on serology and/or PCR. As routine Complement Fixation Tests (CFTs) cross-react with *C. pneumoniae*, further testing may be necessary to confirm which species is responsible. Acute and convalescent samples of serum are usually collected two to three weeks apart. Microimmunofluorescence (MIF) tests are now available and have greater specificity for *C. psittaci*. PCR tests may be possible in some laboratories. Genotyping may also be available to assist public health investigation and may suggest the most likely source species (see the 'Investigation of a Cluster' section).

Transmission

Chlamydia psittaci is a zoonotic disease. Animal reservoirs include not only psittacine birds, such as cockatiels, parakeets, parrots, macaws and lovebirds, but also other birds, particularly poultry (ducks, turkeys, chickens) and pigeons (in that sense ornithosis is a more accurate name than psittacosis). *C. abortus* is primarily transmitted from mammals, especially small ruminants, such as sheep and goats.

Infection is transmitted to humans by inhalation of infected aerosols contaminated by droppings, nasal discharges or products of conception, in which it may survive for months at ambient temperatures. Person-to-person transmission is documented, but appears to be rare. Birds may excrete the pathogen intermittently and can be asymptomatic carriers of the organism. *C. psittaci* is destroyed by routine disinfectants such as bleach (1 : 100), quaternary ammonium (1 : 1000) and 70% isopropyl alcohol.

Groups at increased risk of disease include those in the pet trade, bird fanciers, poultry workers, abattoir workers, veterinarians and laboratory workers. Owners of pet birds and those exposed to wild bird droppings are also at risk: psittacosis in the UK and Sweden has been linked to importation of exotic birds for pets, and to people cleaning wild bird feeders.

Acquisition

The incubation period has been reported as anything from four days to four weeks. Most cases probably occur 5–15 days after exposure. Infection may result from only brief, passing exposure to infectious birds. The infectious period in birds may last for months. Human cases are not usually considered infectious for practical purposes. Protective immunity to re-infection is short lived. Those at risk of severe infection include pregnant women (especially to *C. abortus*) and the elderly.

Prevention

- Quarantine and other controls on imported birds.
- Masks, good ventilation and measures to avoid contamination in poultry plants and other areas where workers might be exposed.
- Advice to those in contact with birds (occupationally or recreationally) or to environments likely to have been contaminated by birds or their droppings (including wild bird feeders).
- Pregnant women to avoid exposure to sheep and goats, especially during lambing (*C. abortus*).

Surveillance

- Psittacosis should be reported promptly to local public health authorities: formally notifiable in many European countries, including Germany, Netherlands, Belgium and Sweden.

- Laboratories should report all clinically significant infections to national surveillance systems: English laboratories must notify *C. psittaci* to PHE.

Response to a case

- All cases should be reported promptly by the clinician or microbiologist for investigation by local public health officers.
- Look for exposure to psittacines, poultry, other birds and mammals. Trace source back to petshop, aviary, farm or similar. Involve veterinary and microbiological colleagues to test animals for infection. Infected birds should be treated or destroyed and the environment thoroughly cleaned and disinfected.
- Ensure other potential cases are tested.
- No need for isolation. Cough into paper towel for safe disposal.

Investigation of a cluster

- Discuss further investigation with microbiologist to confirm *C. psittaci* as cause, and to see if typing is possible. Different genotypes are associated with different animal sources, for example A with psittacines and other wild birds, B with pigeons and doves, C with ducks and geese and D with turkeys.
- Conduct a hypothesis-generating study to include pet birds (possibly illegal); pet mammals; hobbies (e.g. pigeon racing, cleaning bird feeders); visits to petshops, farms, bird centres, and so on; and occupational exposure to poultry (*C. psittaci*) or small ruminants (*C. abortus*). Document less defined exposures, for example walking through fields (potentially contaminated pasture?), roofing (exposure to pigeons?) and so on. Check if any institution or home visited had a pet bird.

Control of an outbreak

Work with veterinary colleagues:
- Look for infected birds or mammals.
- Treat or destroy infected birds.
- Thoroughly clean and disinfect environment.
- Case-finding to ensure those infected receive prompt treatment.
- Action to prevent recurrence.

Suggested case-definition for outbreak

Confirmed: Compatible clinical illness plus:
(a) PCR positive, *or*
(b) fourfold increase in specific IgG by MIF, *or*
(c) demonstration of specific IgM by MIF, *or*
(d) culture of *C. psittaci*, *or*
(e) epidemiological link to source animal/premises *and* fourfold increase by CFT antibody testing.

Suspected: Compatible clinical illness plus
(a) epidemiological link to confirmed case, *or*
(b) fourfold increase by CFT antibody testing, *or*
(c) single high IgG title by MIF

In an epidemiological investigation, you may wish to include asymptomatic individuals with clear microbiological evidence of recent infection (see criteria for confirmed cases) to help identity exposure.

3.58 Q fever

Coxiella burnetii – family *Legionellales,* order *Coxiellaceae* is a zoonosis. It causes Q fever, an acute febrile illness, which may occur in outbreaks. Long-term complications are chronic Q fever and Q fever fatigue syndrome.

Suggested on-call action

None required unless an outbreak is suspected (if so, consult the local outbreak plan or SOP).

Epidemiology

The true incidence of infection is unknown because of underdiagnosis and underreporting, partly due to the high proportion of asymptomatic and mild cases. The incidence of reported cases in Europe ranges from 0.01 to 0.38 per 100 000. England, France, Germany and Bulgaria have reported outbreaks in recent years, while The Netherlands experienced the largest number of simultaneous outbreaks from 2007 to 2011 related to dairy goat farming.

Most cases are reported in adults, with a peak in those aged 40–64 years. Reported cases in children are rare, probably because of an increased likelihood of asymptomatic infections or lack of diagnosis. Males are more than twice more likely to be reported than females. Cases are usually reported to peak in spring, although this is less obvious in some countries.

Occupationally acquired disease occurs in those who work with animals or animal products, including farmers, abattoir workers, veterinarians, taxidermists and laboratory staff.

Clinical features

Infection with *C. burnetii* may be asymptomatic (60%), or have symptoms varying from a mild febrile illness to severe disease (2–5%), with pneumonia, hepatitis, myocarditis or neurological symptoms. The most commonly reported symptoms in acute infection are fever, headache, myalgia and cough. Other symptoms include fatigue, chills/rigours/night sweats, anorexia/weight loss, arthralgia, nausea/vomiting and skin rash. Adverse pregnancy outcomes are also reported.

Up to 20% of symptomatic cases can develop Q fever fatigue syndrome that may last 10–15 years. Chronic Q fever can occur in about 1–2% of infections (clinical or subclinical). Diagnosis is often confirmed years after the initial infection. Important risk groups for chronic Q fever are those with pre-existing aneurysm, arterial graft, heart valve defect or prosthesis and the immunocompromised. Case fatality rates range from 5 to 50% depending on the progression, focus and treatment of the infection. The most common presentation differs by host and pathogen populations and can be a vascular infection (aneurism/vascular prosthesis), endocarditis, hepatitis or osteomyelitis. Serological follow-up of cases for chronic Q fever is advisable: a single test at 9–12 months for those without risk factors and repeat tests at 3, 6, 9 and 12 months for the higher-risk group.

Laboratory confirmation

The gold standard for diagnosis is IFA. The lag-time of seroconversion can be three weeks. PCR may be positive during this lag-time. Diagnosis is usually confirmed by a fourfold rise in serum antibodies. IgM phase II may be detected first: as IgM phase II usually persists for six months, a single high titre is non-diagnostic of an acute event. 'Phase II' antibody generally occurs in acute infection and 'Phase I', especially high IgG, in chronic infections (this can be accompanied by a positive PCR). The IFA serological cut-off for possible chronic Q fever differs per laboratory. Culture of this organism is potentially hazardous (BSL 3 laboratory required).

Transmission

The reservoir for *C. burnetii* is animals, particularly sheep, goats, cattle, cats, dogs, wild rodents, birds and ticks. Most infected animals are asymptomatic, although new infections during pregnancy may lead to abortion ('abortion storms' in small ruminant herds). In mammals, the infection localises to the endometrium and mammary glands and is reactivated during pregnancy, to be aerosolised during parturition. These aerosols may be inhaled or contaminate the environment for up to 40 months. *C. burnetii* spores are resistant to heat, drying and chemical disinfectants. Animal excreta or carcasses may also contaminate the environment. Human infection usually occurs via inhalation from

close exposure to animals (e.g. at parturition), wind-borne aerosols (usually within 5 km) or contaminated fomites on wool, straw and clothing. Transmission via raw milk, blood transfusion, intercourse, necropsy, laboratory work or human parturition is rare.

Acquisition

The incubation period for most cases is 7–32 days, with a median of 18–19 days, although shorter and longer incubations have been reported, depending on the infecting dose. The infective dose is one to five organisms, while 1 g of placenta from an infected sheep may contain 10^{10} bacteria. Immunity is probably lifelong. Females may be less susceptible than males. The immunocompromised and smokers are more susceptible.

Prevention

- Adequate hygiene practices in premises dealing with animals, particularly sheep, cattle and goats.
- Pasteurisation of milk.
- The effective vaccine has potential side-effects in those previously exposed to *Coxiella*. It is not commercially available for the general public in most countries, but may be given to individuals in high-risk occupations/or during an epidemic to those with a high risk for chronic Q-fever.
- Chemoprophylaxis with oxytetracycline late during the incubation period (preferably between 8 and 12 days after exposure) has been reported to be effective.
- Doxycycline is the treatment of choice for *C. burnetii* infections.

Surveillance

- Report laboratory-confirmed cases to local and national surveillance centres. Q fever reporting is compulsory in the majority of EU member states.
- Potential clusters or linked cases should be reported to the local public health authorities.

Response to a case

- Check for exposure to animals.
- Exclusion/isolation is not necessary, but avoid blood/tissue donation.
- Universal precautions in hospitals, including care with body fluids especially during parturition and at autopsy.

Investigations of a cluster

Undertake a hypothesis-generating study to cover six weeks before onset, including:

- Occupational history,
- Travel history,
- Exposure to:
  - sheep, cattle, goats and other farm animals or farm equipment, clothing, and so on.
  - pets, especially cats, or pet owners/household after parturition? Visit to pet shop.
  - potentially contaminated fomites including straw, hay, peat, manure and wool.
  - General outdoor exposure. Check local veterinary and meteorological data for clues (e.g. sheep abortions, wind conditions).

Consider possibility of bioterrorism incident (see Chapter 4.17).

Control of an outbreak

- Plot dates of onset as an epidemic curve: is there ongoing exposure?
- Remove any continuing source.
- Treat human cases.
- In large outbreaks, inform GPs, consider whether case finding to ensure acute cases are treated and/or surveillance of blood/tissue donors is warranted.

Suggested case-definition for an outbreak
Clinical presentation with fever, pneumonia or hepatitis, and fourfold IgG titre rise or positive IgM phase II or PCR of *C. burnetii*, in blood or respiratory material.

3.59 Rabies

Rabies is an infection of the central nervous system caused by a lyssavirus (a genus of rhabdovirus). The public health significance of rabies is that there are many animal hosts, the disease is always fatal and both human and animal vaccines are available.

Suggested on-call action

Possible exposure:
- Advise cleansing of wound if recent.
- Assess need for post-exposure prophylaxis. If in doubt, seek expert advice.

Possible case:
- Seek history of animal bite, travel and vaccination status.
- Contact virus reference laboratory to arrange lab confirmation.
- Arrange admission to specialist unit.
- Prepare list of close contacts and contacts with possible source.
- Inform national public health institute.
- Inform state veterinary service if not travel related.

Epidemiology

Rabies exists in animal populations in many countries of Europe, although human cases are rare, and almost always result from an animal bite outside Europe. The risk of rabies from an animal bite varies in different countries; most of Western Europe is rabies-free. Rabies was only detected in three countries in the EU in 2016, and a goal has been set to eliminate rabies from the EU by 2020. However, bats are a potential source of infection, even in those countries considered rabies-free such as Spain and the UK.

Clinical features

The early features of human rabies are often mistaken for hysteria, with altered personality and agitation. Pain or numbness at the site of an animal bite is a useful early clue. Painful spasms of the face induced by attempts to drink ('hydrophobia') are the classical feature. The case fatality is 100%.

Laboratory diagnosis

This is only possible after the onset of symptoms. The national virus reference laboratory must be involved. Serum antibodies appear after six days. Rabies virus can be isolated from saliva, brain, CSF and urine, or demonstrated by immunofluorescent antibody staining of impression smears of skin, cornea or other material. PCR is available for saliva specimens.

Transmission

Animal reservoirs in Europe include dogs, cats, foxes, wolves, racoons, and bats. Transmission is from the bite or scratch of an infected animal, or a lick on a mucosal surface such a conjunctiva. Air-borne spread has been demonstrated in bat caves, but is unusual. Rare cases have occurred in recipients of corneal grafts from patients who died of undiagnosed rabies, and from other organ transplants.

Acquisition

The incubation period is usually 3–12 weeks, but may be as short as 4 days or as long as 19 years, depending on the amount of virus introduced, the severity of the wound, and its proximity to the brain.

Prevention

- Control rabies in domestic animals by vaccination before travel to infected countries and implantation of a microchip device.
- Oral vaccination of foxes (using baits), the principal reservoir in Europe.

- Vaccinate high-risk travellers to endemic areas and those at occupational risk such as some laboratory workers and animal handlers (including bat handlers, although immunisation may not protect against some bat lyssaviruses). The primary course is three doses at days 0, 7 and 28, given in the deltoid (NB the response may be reduced if vaccine is given in the buttock) with a booster at 1 year.
- Give post-exposure prophylaxis with vaccine (and rabies-specific immunoglobulin for high-risk exposures) following a bite (or cat-scratch) in an endemic area. For appropriate schedule seek advice from national reference unit. Cleanse the wound thoroughly as soon after injury as possible: as a minimum with soap or detergent under running water for at least five minutes; antiseptics should also be used if available. Obtain as much information on the exposure as possible (place, species, bite/scratch, behaviour, owned/stray), including name and address of owner of the animal so it can be observed for the next 10 days for abnormal behaviour. All bat bites (some of which are not immediately obvious), including those in rabies-free countries such as the UK should be given post-exposure prophylaxis with vaccine. Expert advice should be sought as to whether immunoglobulin is also indicated.

Surveillance

Notifiable throughout Europe. Inform national public health institute immediately.

Response to a case

- Isolation in a specialist unit for the duration of the illness.
- Healthcare workers attending the case should wear masks, gloves and gowns.
- Vaccination and immunoglobulin for contacts that have open wound or mucous membrane exposure to the patient's saliva (according to the schedule above).
- Investigate source of infection.
- Disinfect articles soiled with the patient's saliva.
- Identify others that may have been exposed to source.

Investigation of a cluster and control of an outbreak

A cluster of human cases from an indigenous source is unlikely in Europe. Refer to the national plan for the control of animal rabies.

Suggested case-definitions

Clinical: acute encephalomyelitis in an exposed individual.
Confirmed: clinically compatible case confirmed by viral antigen, isolate or rabies neutralising antibody (in an unvaccinated individual).

3.60 Relapsing fever

Louse-borne relapsing fever (LBRF) is a systemic disease caused by the spirochete *Borrelia recurrentis*. Tick-borne relapsing fever (TBRF) may be caused by a variety of Borrelia species such as *Borrelia lonestari* and *Borrelia miyamotoi*.

Suggested on call action

- None required unless ongoing transmission suspected because of presence of lice, in which case institute delousing procedures.

Epidemiology

Louse-borne fever is found in Africa, especially highland areas of East Africa. Endemic tick-borne fever occurs on almost all

continents, and in Europe, there is a foci in the Iberian Peninsula. During periods of increased migration of refugees (displaced by wars and natural disasters) from endemic regions, there may be an increase in cases diagnosed in EU countries receiving these refugees.

Clinical features

The illness is characterised by relapsing episodes of high fever, in addition to nausea, headache, arthralgia and myalgia. The period of high fever last around three days (range: two to seven days) and is followed by an afebrile period that lasts around seven days (range: 4–14 days). The number of relapses is variable and if untreated, patients with TBRF can have up to 30 relapses of diminishing severity while patients with LBRF only have 1 relapse.

Laboratory confirmation

Definitive diagnosis is by visualising spirochetes in peripheral blood smear (thick and thin films stained with Wright, Giemsa or Acridine orange stains). Multiple smears may need to be examined and are best collected during the febrile period.

Transmission

LBRF and TBRF are vector-borne diseases; there is no person to person spread. Transmission from blood transfusions and transplacentally have been described but are rare. The disease is classically epidemic when spread by lice (*Pediculuis humanus)*, and endemic when spread by ticks (soft bodied ticks of the *Ornithodoros* genus).

Acquisition

The incubation period is 2–18 days with a median of 7 days.

Prevention

- Avoid tick infested areas.
- Avoid tick bites by using insect repellents containing DEET (N,N-diethyl-*m*-toluamide) and/or impregnation of clothes with repellents and permethrin in endemic areas.
- Maintain good personal hygiene.
- Post-exposure prophylaxis with doxycycline can be considered.

Surveillance

Relapsing fever is a notifiable disease in many countries, including the UK.

Response to a case

- TBRF and LBRF are more commonly reported in travellers from endemic countries. Consider during the assessment of febrile travellers. The case does not need isolation once deloused. The immediate environment should also be deloused.
- Treatment of choice is with tetracycline, doxycycline, erythromycin or chloramphenicol. A self-limiting systemic inflammatory reaction (Jarish–Herxheimer reaction) may occur in up to 50% of treated cases.

Investigation of a cluster/ control of an outbreak

LBRF outbreaks are dependent on high louse densities in human populations such as refugees in camps. Control can be achieved through measures aimed at louse vector control. TBRF may present as clusters among homeless persons.

3.61 Respiratory Syncytial Virus (RSV)

Respiratory Syncytial Virus (RSV) causes bronchiolitis in infants and upper and lower respiratory tract infection in all ages. It may cause

serious nosocomial outbreaks in children, the elderly and the immunocompromised.

Suggested on-call action

- Suggest case limits contact with infants, frail elderly and immunocompromised.
- If linked cases in an institution suspected, activate the outbreak control plan, or SOP.

Epidemiology

RSV epidemics occur every winter, peaking from November to January, with the peak in children usually before that in older adults. Almost all children who have lived through two epidemics in urban areas will have become infected, causing 20 000 hospital admissions a year in the UK. Most cases are not specifically diagnosed, but 80% of cases of bronchiolitis and 20% of pneumonia in young children are caused by RSV. Re-infections occur throughout life. About 5% of elderly people suffer RSV infection each year, and it is a significant cause of infection and outbreaks in nursing homes, day units and hospitals, particularly neonatal units. Male gender; age under six months; birth during first half of RSV season; crowding and/or siblings; day care exposure; tobacco exposure and lack of breast feeding are potential risk factors for RSV infection.

Clinical features

The most common presentation is upper respiratory tract infection with rhinitis, cough and possibly fever. Children may also get otitis media or pharyngitis. Bronchiolitis (wheeze, dyspnoea, poor feeding), pneumonia or croup may develop after a few days. Infants with congenital heart disease, chronic lung disease, or immunosuppression risk severe disease as do those under six weeks of age and premature infants. In adults, RSV infection is usually confined to the upper respiratory tract, but it may cause exacerbations of asthma or chronic bronchitis, or, particularly in the elderly, acute bronchitis or pneumonia. RSV infection in the frail elderly may be severe or even fatal. Few primary infections are asymptomatic.

Laboratory confirmation

PCR testing of respiratory secretions or nose/throat swabs is becoming more widely available and is more sensitive and specific than antigen detection, particularly in adults. Nasopharyngeal Aspirates (NPAs) taken early in the illness may be positive for RSV by antigen detection, which can provide immediate results, or viral culture, which takes three to seven days but is slightly more sensitive. NPAs may not be obtainable from elderly patients: nose or throat swabs are less sensitive and, as the elderly do not shed the organism for as long as infants and often present later in the illness, sensitivity is lower in this group. Serology is available for retrospective diagnosis. Strain typing by PCR is possible, but of limited epidemiological significance.

Transmission

Humans are the only known reservoir of RSV. Spread occurs from respiratory secretions either directly, through large droplet spread, or indirectly via contaminated hands, handkerchiefs, eating utensils or other objects or surfaces. RSV may survive for 24 hours on contaminated surfaces and 1 hour on hospital gowns, paper towels and skin. Infection results from contact of the virus with mucous membranes of the eye, mouth, or nose. Hospital staff and visitors are thought to be important vectors in hospital outbreaks and in the relatively common transmission of sporadic nosocomial infection.

Acquisition

The incubation period is 2–8 days with a median of 4.4 days. The infectious period lasts from shortly before to (usually) one

week after commencement of symptoms. Some infants and the immunosuppressed may shed RSV for many weeks. Immunity is incomplete and short-lived, although re-infections are usually milder. Those with defective cellular immunity are at increased risk of more severe disease.

Prevention

- Personal hygiene, particularly handwashing and sanitary disposal of nasal and oral discharges.
- Good infection control in hospitals (especially important in paediatric wards), nursing homes and day units. Avoid overcrowding.
- Avoid young infants, frail elderly and immunocompromised coming into contact with individuals with respiratory infection.
- Consider use of monoclonal antibody (palivizumab) prophylaxis for certain high risk groups during RSV season. Consult local guidance (e.g. JCVI Green Book for UK) for details, but groups to consider include:
  - Infants born up to 34 weeks gestation who have chronic lung or heart disease and are aged under 9 months at the onset of the RSV season; and
  - children aged less than two years who have severe combined immunodeficiency or are on long-term ventilation.

Surveillance

- RSV cases associated with institutions should be reported to local public health authorities.
- Laboratory confirmed cases should be reported to the national surveillance system.
- Hospitals should include RSV in nosocomial surveillance programmes.

Response to a case

- If contacts in target group for palivizumab prophylaxis, check whether this has been given.
- Contact isolation for hospital patients.
- Avoid contact with infants, frail elderly and immunocompromised until well.
- Exclude from nursery, work, school or non-residential institution until well.
- Sanitary disposal of nasal and oral discharges.

Investigation of a cluster

- Rarely investigated unless link to institution thought likely. Undertake case finding at any institution containing infants, elderly or immunosuppressed, if linked to a case.
- Antigenic and genomic fingerprinting may be used in investigating hospital clusters, but beware that more than one strain may be involved, that is, there may be more than one source.

Control of an outbreak

- Contact isolation and cohorting of suspected cases in hospitals. Closest feasible equivalent in nursing and residential homes.
- Reinforce hygiene and infection control measures, particularly handwashing, sanitary disposal of nasal and oral discharges and cleaning of potentially contaminated surfaces.
- Exclude staff and day attenders with respiratory infection from institutions until well. Restrict visiting.
- Active surveillance of new and existing patients in hospital for respiratory infection with rapid testing for RSV.
- Cancel non-urgent admissions until outbreak assessed as over (e.g. no new cases for two weeks may be deemed appropriate in some scenarios).
- Consider other measures to limit transfer of RSV by hospital staff (e.g. use of eye-nose goggles, gloves and perhaps gowns and masks).
- Maintaining adequate compliance with the above recommendations will require constant monitoring and reinforcement.
- Consider use of RSV specific prophylaxis in high risk individuals.

Suggested case-definition in an outbreak
Upper or lower respiratory tract infection and PCR, antigen or culture positive for RSV.

3.62 Ringworm

The dermatophytoses, tinea and ringworm are synonymous terms that refer to fungal infections of the skin and other keratinised tissues such as hair and nails. They are caused by various species of the genera *Trichophyton*, *Epidermophyton, Microsporum, Trichosporon* and *Piedraia*, and are classified according to the area of the body that is affected, namely corporis (body), faciei (face), cruris (groin), pedis (foot), manuum (hand), capitis (scalp), barbae (beard area) and unguium (nail). Black and white piedra are specific forms of capitis, and barbea/cruris.

Suggested on-call action
Advise on laboratory diagnosis and treatment.

Epidemiology

Superficial mycoses are common worldwide, affecting an estimated 20–25% of the world's population, with an increasing incidence in the last five decades. Infections are mainly found in pre-pubertal children, with the highest incidence in ages four to seven years. Tinea capitis is the most common dermatomycosis in school age. In developed countries the incidence is increasing. In Europe and the USA, the pattern of causative agents has changed over time as the anthropophilic agents *Microsporum audouiniii* and *Trichophyton schoenleinii* have practically been eradicated and have been replaced by a significant rise in cases due to *Trichophyton tonsurans* (Table 3.62.1). Tinea pedis incidence increased in Europe after the end of World War II, leading to a prevalence over 50% in Northern and Central, and 25% in Mediterranean Europe. Onchomycosis is less frequent and has large variations in prevalence (Denmark 4%, Canada 8%, Germany 12%). The epidemiology of causative agents (e.g. *M. audouinii* most prevalent all over Africa, *Trichophyton violaceum* in the horn of Africa and North and South, and *Trichophyton soudanense* in central Africa) is changing due to tourism and migration.

Clinical features

For clinical features, see Table 3.62.2.

Laboratory confirmation

Hairs infected with *Microsporum* species fluoresce green under filtered ultraviolet (Wood's) light. Hairs infected with most *Trichophyton* species do not fluoresce. Fungal spores and hyphae can be detected by microscopic examination of the hair after preparation in potassium hydroxide. Definitive diagnosis requires culture of the infecting fungus. Specimens for culture are collected by scraping the affected area with a scalpel or glass slide held at right-angles to the skin. Specimens for culture can also be obtained using a suitable brush: the brush should be passed through the hair firmly in an affected area several times and then pressed into the surface of an agar-coated Petri dish, which is then incubated for up to three weeks. A culture taken from an infected child will usually produce a fungal colony from each of the inoculation points, whereas one taken from a carrier will produce fewer colonies. Identification of the fungus helps determine the source of infection (either an animal or another child) and allows appropriate treatment and control measures. Pan fungal PCR is available in some laboratories. Specific PCRs are in development and sometimes already available (*Microsporum canis*)

Table 3.62.1 Epidemiological characteristics by body area

Tinea capitis	Most cases in Europe are caused by *M. canis*. Prevalence has increased due to anthropophilic *T. tonsurans* which is most prevalent in Mexico, Latin America and the USA, and is on the rise in Europe (related to outbreaks). Hair loss caused by *T. schoenleinii* is largely confined to eastern Europe and Asia.
Anthropophilic*: Trichophyton tonsurans, Trichophyton violaceum, Trichophyton soudanense, Microsporum audouinii, Trichophyton schoenleinii*	Spread occurs in families and at school and asymptomatic infection is common. Risk factors may include overcrowding within households or schools, exposure in hairdressing salons, use of shared combs, particular hair styles and ethnicity. *T. tonsurans* has also recently been reported in West and East Africa. In other countries *M. canis* is the commonest cause. Pet animals (rodents) have introduced new zoophilic agents (e.g. *Arthroderma benhamiae*).
Zoophilic*: Microsporum canis (cat, dog), Trichophyton verrucosum (cattle)*	
Piedraia hortae	Black piedra (*Piedraia hortae*) occurs in temperate and semi-tropical climates (Europe, Japan, southern USA).
Tinea corporis, Tinea cruris, Tinea barbae,	Since the 1950s, *T. rubrum* has replaced *M. audouinii* and *E. floccosum* in most developed countries as the most frequently isolated dermatophyte. In Southern Europe and the Middle East zoophilic dermatophytes, such as *M. canis* and *T. verrucosum*, are the most frequent.
M. canis, T. tonsurans, Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum	White piedra (*Trichosporon asahii*) is seen under hot and humid conditions, such as South America and South East Asia.
Tinea pedis	In Tinea pedis (Athlete's foot) the predominant dermatophyte is also *T. rubrum*, followed by *T. mentagrophytes* var. interdigitale and *E. floccosum*.
Tinea unguium (Onychomycosis)	*T. rubrum and T. mentagrophytes* account for 90% of onychomycoses. Increasing age, diabetes, acquired immunodeficiency syndrome and peripheral arterial disease are risk factors and there is a familial pattern. In Europe an increase is seen in children.
T. rubrum, T. mentagrophytes	

Table 3.62.2 Clinical features by body area

Tinea capitis	The clinical presentation comprises generalised diffuse scaling of the scalp, patchy hair loss (alopecia), broken-off hair stubs, scattered pustules, lymphadenopathy, boggy tumour (kerion), and favus.
	Infection with *Trichophyton tonsurans*, an endothrix dermatophyte whose growth and spore production are confined chiefly within the hair shaft, may cause lightly flaky areas of scalp, indistinguishable from dandruff or small patches of hair loss. Asymptomatic infection occurs with *T. tonsurans* and a carrier state may exist in which fungus is present in the absence of any hair or skin abnormalities. Black piedra is a specific tinea capitis showing firmly attached hard black nodules. In mild cases patients may only feel the nodules or report a metallic sound when brushing their hair.
Tinea corporis Tinea cruris	Lesions are found on the trunk or legs and have a prominent red margin with a central scaly area.
Tinea barbae, barber's itch	Infection of the beard area of the face and neck with both superficial lesions and deeper lesions involving the hair follicles. A specific tinea is white piedra that shows irregular, white, cream-coloured, or brown soft nodules or gelatinous sheaths along the hair shaft, in the hair of beard, moustache, genitals, and axilla.
Tinea pedis, athlete's foot	Affects the feet particularly the toes, toe webs, and soles.
Tinea unguium (Onychomycosis)	Infection of the nails, usually associated with infection of the adjacent skin. There is thickening and discolouration of the nail. The prevalence is higher in diabetics, and patients with keratinisation disorders (e.g. psoriasis).

Table 3.62.3 Zoophilic dermatophytes and their source of infection

Dermatophyte	Animal
Microsporum amazonicum	Rats
Microsporum bullosum	Horses, donkeys
Microsporum canis	Cats, rarely dogs (South America)
Microsporum gallinae	Chickens (seldom transmitted to humans)
Microsporum nanum	Pigs, cows
Microsporum persicolor	Moles, other rodents, e.g. mice
Microsporum praecox	Horses
Trichophyton equinum	Horses, morphology strongly resembles *Trichophyton tonsurans*
Trichophyton erinacei	Hedgehogs
Trichophyton interdigitale (zoophilic strains)	Rodents (e.g. guinea pigs, golden hamsters, rats, mice, chinchillas), rabbits, dwarf rabbits, ferrets
Trichophyton mentagrophytes	Mice and camels (in Middle East)
Trichophyton simii	Monkeys, chickens, guinea pigs, shrews
Trichophyton species of *Arthroderma benhamiae*	Guinea pigs, other small rodents
Trichophyton verrucosum	Calves, cows, other farm animals (e.g. horses, pigs, dogs, and cats)

Source: Westerdijk Fungal Biodiversity Institute (Utrecht, The Netherlands)

Transmission

The reservoir of some dermatophyte species such as *Trichophyton rubrum* and *T. tonsurans* is exclusively human (anthropophilic). Others species have animal reservoirs (zoophilic) including cats, dogs and cattle (see Table 3.62.3). Soil (geophilic) species are less common causes of human infection. Transmission of spores (arthroconidia) is by direct skin-to-skin contact through skin scales and hairs of an infected person or animal or (as spores can survive several months outside a host) by indirect contact with fomites (seat backs, combs and brushes) or environmental surfaces (showers, changing-rooms) contaminated with hair or skin scales. New infections particularly occur where there is broken skin.

The risk of spread is lower for zoophilic than for anthropophilic fungi. The secondary attack rate in families is 20%; in semi-closed communities (schools, day care), and groups with close contact (wrestling teams) clusters occur. Certain occupations, such as veterinary surgeons, are at risk of infections of animal origin.

Acquisition

The incubation period varies with the site of infection but is typically 10–20 days, but can be up to 6 weeks. The infectious period lasts for as long as infection is present which may be from months to years if untreated. Immunosuppressed patients, including those with HIV infection, are at increased risk of dermatophyte infection.

Prevention

- Early recognition of animal and human cases and carriers and prompt effective treatment.
- Maintain high levels of personal and environmental hygiene with attention to hand washing, care of pets, regular cleaning and maintenance of floors and surfaces at home, in schools and swimming pools and communal changing rooms.

Surveillance

- Cases of scalp and body ringworm in school-age children should be reported to the school nurse.

- Clusters of cases should be discussed with the local health protection team.
- Fungal culture results for tinea capitis should be collected from a number of sentinel diagnostic laboratories in order to monitor the spread of *T. tonsurans*.

Response to a case

- Anthrophilic dermatophytes can be spread between children at school, but exclusion of an infected pupil from school is unnecessary once appropriate treatment has started. However, activities involving physical contact or undressing, which may lead to exposure of others, should be restricted.
- Confirm diagnosis and identity of infecting fungus with skin, nail or hair samples for microscopy and culture.
- Start immediate effective treatment (treatment guidelines may be available). Most solitary lesions respond readily to topical agents used for two to four weeks but oral treatment (griseofulvin, terbinafine, itraconazole, fluconazole) is always required for nail (onchomycosis) and scalp infection (Tinea capitis). As topical antifungal agents do not penetrate the hair follicle, topical treatment in Tinea capitis can only be used as an adjuvant therapy. Topical treatment may reduce the risk of transmission to others before oral treatment is established. Selenium sulphide and ketoconazole shampoo (used five minutes twice weekly for two to four weeks), as well as fungicidal creams and lotions (once daily for a week) reduce the carriage of viable spores and may also reduce infectivity.
- If cultures show that the infecting fungus is of human rather than animal or soil origin, a search should be made for other cases. Signs of infection in others may be minimal and so samples should be requested for culture. Those with mycological evidence of carriage may be offered treatment.
- If the source is an animal, family pets should be screened by a veterinary surgeon.

Investigation of a cluster

- Clusters of cases of scalp or body ringworm may be reported from schools or nurseries, and wrestling teams (Tinea corporis gladiatorum).
- Nosocomial spread has also been documented from patients to nursing staff.

Control of an outbreak

- Confirmation of the diagnosis is important and all contacts should be examined to identify cases and carriers. Samples should be requested for culture.
- The local health protection team should be available to give advice and practical assistance.
- Prompt effective treatment should be offered to cases and carriers (see above).
- Exclusion from school is not normally necessary once treatment has started, but may be considered if control proves difficult.
- An environmental investigation should be carried out to ensure a high standard of hygiene, particularly in communal changing rooms. Additional cleaning may be recommended. Possible animal sources should be investigated.
- In hospitals and nursing homes, cases should be nursed with source isolation precautions, and gloves and aprons should be used.

Suggested case-definition for cluster investigation

Characteristic lesions reported amongst household or other close contacts, with or without laboratory confirmation by microscopy or culture.

3.63 Rotavirus

Rotaviruses are the commonest cause of childhood diarrhoea. The public health significance of rotavirus diarrhoea is the high level of morbidity and the availability of effective vaccines.

Suggested on-call action

- Exclude cases in risk groups (Box 2.2.1) until 48 hours after last episode of diarrhoea or vomiting.
- If linked to other cases in an institution, consult the outbreak control plan.

Epidemiology

Rotavirus is the main cause of gastroenteritis in children under two, in both developed and developing countries. Laboratory-confirmed cases represent only a small fraction of the total disease burden; it has been estimated that one-third of hospital admissions for childhood diarrhoea are due to rotavirus. The peak incidence is between four months and two years of age; clinical infection is unusual above five years, although subclinical infection is probably common. The illness may be more severe in the immunocompromised. In Europe, most cases occur in winter and spring, with a peak in March (Figure 2.2.1). Mortality is low in developed countries, although morbidity is substantial, with hospitalisation being common. In developing countries, mortality is also high (an estimated one million deaths each year). Many outbreaks are reported every year, mostly in residential institutions, nurseries or hospitals.

In countries that have implemented vaccination with high coverage, the incidence has fallen significantly, and there is less seasonal variation.

Clinical features

There is sudden onset of vomiting, followed by diarrhoea, often with a mild fever and dehydration. Vomiting, dehydration, fever and malaise are more common in rotavirus than in other causes of acute gastroenteritis. Occasionally there is blood in the stools. The illness usually lasts for a few days only; complications include dehydration and benign convulsions

Laboratory confirmation

This is needed to differentiate rotavirus infection from other viral infections of the gastrointestinal tract. Rotavirus particles can usually be demonstrated in diarrhoea stools by electron microscopy. PCR and antigen detection tests (e.g. ELISA) are available. There are three serogroups, of which group A is by far the commonest; rotavirus positive samples can also be characterised by genotyping. In Europe, six genotypes account for over 90% of infections.

Transmission

There are both animal and human rotaviruses, although animal-to-human transmission does not occur. Person-to-person transmission is mainly by the faeco–oral route, although there may also be spread from respiratory secretions and sometimes via contaminated water. Long-term carriage does not occur. Outbreaks may occur in nurseries, and nosocomial spread may occur in paediatric, and occasionally geriatric units, where the virus may contaminate the environment. Attack rates in close child contacts are usually high. It is resistant to many disinfectants, but is inactivated by chlorine.

Acquisition

The incubation period is one to four days. Cases are infectious during the acute stage of the illness and for a short time afterwards;

this is usually for less than 10 days in a healthy child, but may be as long as a month in an immunocompromised patient. Re-infection may occur after some months.

Prevention

- No specific preventive measures.
- General enteric precautions may help limit spread in households, nurseries and hospitals. In nurseries, children should have clothing to cover their nappies.
- Breast feeding has a protective effect.

Two live attenuated oral vaccines are available and have been introduced in many countries worldwide. The schedule is either two or three doses, starting at two months of age. Vaccine recommendations are now in place in several European countries; Belgium, Austria, Finland and the UK have all implemented mass immunisation with coverage above 90%.

Surveillance

- Usually based on laboratory reports. This significantly underestimates the true incidence, as only hospitalised cases are likely to be investigated. In the UK it is estimated that only 1 in 44 community cases were identified in national surveillance. Syndromic surveillance (e.g. GP consultations for cases of acute gastroenteritis) may also be valuable.
- European-wide surveillance, with strain genotyping, was established in 2007 (www.eurorota.net).
- Gastroenteritis is notifiable in some EU countries.

Response to a case

- Isolate cases with enteric precautions in hospital.
- Give hygiene advice to the family in the community.
- Exclude from nursery or school (or risk occupation – see Table 2.2.1) until 48 hours after last episode of diarrhoea or vomiting.

Investigation of a cluster

- Not often reported, unless linked to an institution.
- Consider also the possibility of a common source, for example contaminated water supply.

Control of an outbreak

- Remind the local population of the importance of good hygiene (although this will probably not play an important role in controlling the outbreak).
- In institutions with cases, ensure adequacy of hygiene and toilet facilities.

Suggested case-definition

Confirmed: diarrhoea or vomiting with laboratory confirmation.

Clinical: diarrhoea or vomiting in a person linked to a confirmed case.

3.64 Rubella

Rubella (German measles) is a systemic virus infection characterised by a rash and fever. Rubella virus is a member of the togaviridae. The public health importance of rubella is the consequences of infection in pregnancy and the availability of a vaccine.

Suggested on-call action

- Advise limiting contact with those known to be pregnant.

Epidemiology

Rubella is now uncommon in most of Europe, where immunisation programmes have been in place for many years. In the 12 months from December 2016 to November 2017, only 729 rubella cases were reported in Europe of which 93 were laboratory confirmed. The majority of cases (73%) were reported from Poland. Before immunisation, epidemics occurred at six-yearly intervals, affecting mainly children in primary school but also adolescents and some adults. During epidemics, up to 5% of susceptible pregnant women caught the disease, leading to congenital rubella syndrome and rubella-associated terminations of pregnancy.

Congenital rubella syndrome is now very rare in Europe; most cases are in women who were born outside Europe.

Clinical features

The main differential diagnosis is parvovirus, which is much more common than rubella. In rubella, there is sore throat, conjunctivitis, and mild fever for two or three days before the macular rash appears. The lymph nodes of the neck are often swollen. Recovery is usually rapid and complete, although, as in parvovirus infection, persistent joint infection sometimes occurs, especially in adults.

The features of congenital rubella syndrome range from mild sensorineural deafness to multiple defects of several organ systems.

Laboratory confirmation

This is particularly important in pregnancy or in those who have been in contact with pregnant women. Diagnosis is by detection of IgM or rising IgG titre in oral fluid. PCR testing of oral fluid, throat swabs, NPA, urine, CSF, amniotic fluid, placenta or foetal tissue is available and may be helpful, particularly in the diagnosis of congenital rubella syndrome.

Transmission

Humans are the only reservoir. Transmission is by direct person-to-person contact by respiratory droplets. There are no carriers.

Acquisition

Rubella is moderately infectious, although not as infectious as parvovirus or measles. The incubation period is 13–20 days. Infectivity is from one week before the onset of rash to about five days after onset.

The risk of congenital rubella syndrome in a susceptible pregnant woman infected in the first trimester is greater than 90%. This risk declines to about 50% in the second trimester and is zero near term.

Prevention

- Vaccinate all children with combined Measles, Mumps and Rubella (MMR) vaccine. Two doses are required to ensure seroconversion and maintain herd immunity. The only contraindications are immunosuppression and pregnancy, although women accidentally vaccinated in pregnancy can be reassured that the risk of foetal damage is minimal.
- Vaccinate healthcare workers, as they are likely to be in contact with pregnant women.

Surveillance

The disease is notifiable in all European countries, and surveillance is co-ordinated by ECDC. The clinical diagnosis is unreliable and surveillance should be based on obtaining laboratory confirmation.

Response to a case

- Seek laboratory confirmation, (e.g. oral fluid test) especially in pregnancy or if the case has been in contact with a pregnant woman.

- Check immunisation status of the case and arrange for vaccination if non-immune.
- Exclude children from school for five days from the onset of rash.
- Test pregnant women who have been in contact with a case, particularly during the first trimester, for susceptibility or evidence of early infection (see Chapter 2.4). For confirmed infections in pregnancy, termination may be an option available to the mother, depending on gestational age. Comprehensive guidelines for the investigation of suspected rubella and other rashes in pregnant women and their contacts are available on the Public Health England website (updated February 2016).

Investigation of a cluster and control of an outbreak

- Laboratory confirmation is essential. In addition to the measures described earlier for all cases, consider a community-wide immunisation programme if coverage is low.

Suggested case-definitions

Confirmed:
- presence of IgM in blood, urine or saliva; *or*
- fourfold or greater rise in haemagglutination inhibition antibody in serum; *or*
- positive PCR in relevant clinical specimen.

Suspected (for investigation):
- generalised maculopapular rash, fever and one of: cervical lymphadenopathy or arthralgia or conjunctivitis.

3.65 Salmonellosis

Salmonella infection is a common cause of gastroenteritis which can result in large outbreaks, particularly due to food-borne transmission, and severe infection in the elderly, immunosuppressed and pregnant women.

Most microbiologists use a system of nomenclature for *Salmonella* organisms, based on DNA relatedness, which suggests that all salmonellae probably belong to a single species, *enterica* which has seven subspecies. Most human pathogens belong to a subspecies also called *enterica,* which is further divided into serovars, e.g. *Salmonella enterica* subgroup *enterica* serovar Enteritidis or *S.* Enteritidis for short.

For *S. paratyphi* and *S. typhi:* see Chapters 3.52 and 3.80 respectively.

Suggested on-call action

Exclude cases in risk groups for onward transmission (Box 2.2.1) until passing formed stools for 48 hours.

If you or the reporting laboratory/clinician are aware of other potentially linked cases, consult the local outbreak plan.

Epidemiology

Salmonella infections occur worldwide and are one of the most commonly reported gastrointestinal infections in Europe: about 95 000 cases were reported in the EU annually in 2011–2015, an incidence rate of 20 per 100 000, with the highest reported rates in the Czech Republic, Slovakia and Hungary. The incidence has fallen from its peak in the early 1990s, particularly infections caused by *S.* Enteritidis PT4. All ages are affected, but reported cases are highest in young children. Cases peak in August and September (Figure 2.2.1). Travel abroad is a risk factor, and is a substantial contributor in lower-incidence countries: about 70% of reported cases in Scandinavia are travel-related. Reported rates underestimate true incidence: a UK study found that about only about one in five community cases were identified by surveillance: this proportion in likely to be substantially lower in some countries. The most common serovars in Europe are shown in Table 3.65.1.

Table 3.65.1 Frequency and some possible sources of common *Salmonella* serovars

Serovar	Number of human cases in the EU/EEA 2016[a]	Main animal reservoirs (DT/PT)	Some additional vehicles reported in outbreaks
S. Enteritidis	32 685	Chickens, other poultry, cattle (PT8)	Egg (from EU countries), dairy produce, Chinese meals
S. Typhimurium	14 678 (5 666 monophasic)	Cattle (104, U302, RDNC), Pigs (193, 104, U308a, U302, 170, Monophasic), Poultry (104, Monophasic), Sheep (104)	Halva (from Turkey), manure, salad
S. Infantis	1 596	Chickens, turkeys, calves, pigs, poultry	Chicken drumsticks
S. Newport	731	Turkeys, cattle	Peanuts (from China), lettuce, horsemeat, mango
S. Derby	570	Pigs, turkeys, sheep, cattle	Pork products
S. Kentucky	531	Pigs, Cattle	Dairy products
S. Stanley	520	Turkeys, occasionally chickens, rarely pigs or other animals	Peanuts, alfalfa sprouts, soft cheese, lime leaves. May be imported from east or south-east Asia.
S. Virchow	497	Chickens	Eggs
S. Saintpaul	441	Turkeys	Alfalfa sprouts, peppers, paprika, melon
S. Agona	418	Turkeys, chickens	Kosher snack

Rarer serovars associated with particular animals include *S.* Binza (gamebirds), *S.* Bovismorbificans (pigs, ruminants), *S.* Braenderup (poultry, cattle), *S.* Cerro (chicken), *S.* Dublin (cattle) *S.* Indiana (ducks), *S.* Hadar (Chickens, other poultry), *S.* Java (poultry, tropical fish, terrapins) *S.* Livingstone (chicken, ducks, pigs) *S.* Mbandaka (chicken) and *S.* Seftenberg (chicken).
[a] Source: European Food Safety Authority

Clinical Features

It is difficult to differentiate salmonellosis from other causes of gastroenteritis on clinical grounds for individual cases. The severity of the illness is variable but most cases have only moderate diarrhoea, without blood or mucus. Diarrhoea usually lasts three to seven days and may be accompanied by fever, abdominal pain, myalgia and headache. Other symptoms, particularly nausea, may precede diarrhoea, and malaise and weakness may continue after resolution of the gastroenteritis. A few cases develop more severe dysentery-like or cholera-like illness. Invasive complications include septicaemia, meningitis, osteomyelitis, septic arthritis, and abscess formation. Deaths do occur, particularly in the elderly and immunosuppressed. Factors that may suggest salmonellosis as the cause of a cluster of cases of gastroenteritis include fever in most cases, headache and myalgia in a significant minority, and severe disease in a few. With some serovars, for example *S.* Dublin, *S.* Choleraesuis and, to a lesser extent *S.* Virchow, septicaemia and extra-intestinal infection are more common.

Laboratory Confirmation

Diagnosis is usually confirmed by culture of a stool specimen, rectal swab or blood culture. Using a stool sample rather than a rectal

swab, collecting 5 g of faecal material and, especially when looking for asymptomatic excretors, collecting two or more specimens over several days all increase sensitivity. Excretion usually persists for several days to weeks beyond the acute phase of the illness. Refrigeration and/or a suitable transport medium may be necessary if there will be a delay in processing specimens, especially in warm weather. The laboratory may be able to issue a provisional report within 48 hours of receiving the specimen (further confirmatory tests will be necessary), although a further day is often required. Rapid diagnostic tests, such as PCR, may also be available in some laboratories.

Serotyping (e.g. 'Typhimurium') is available for all salmonellae and phagetyping ('Phage Type [PT]' or 'Definition Type [DT]') is available for *S.* Agona; *S.* Enteritidis; *S.* Hadar; *S.* Java; *S.* Pullorum; *S.* Thompson; *S.* Typhimurium and S. Virchow usually via reference laboratories. Genotyping may be available and has replaced sero/phagetyping in some reference laboratories: these tests have been shown to be useful in detecting and controlling outbreaks of salmonellae: WGS is now performed routinely in England and multiple-locus variable number tandem repeat analysis (MLVA) typing is being used to compare Enteritidis strains across Europe, including in multi-country outbreaks.

Transmission

Salmonella infection is acquired by ingestion of the organisms. In most cases this is through the consumption of contaminated food.

- *Salmonella* infection or carriage affects many animals (Table 3.65.1), leading to contamination of foodstuffs before their arrival in the kitchen. If such foods are eaten raw or undercooked, then illness can result. Such food sources include undercooked poultry or meat, raw or undercooked eggs and raw or inadequately pasteurised milk. Contaminated foodstuffs, particularly raw poultry or meat, may be the source of cross-contamination to other foods that may not be cooked before eating (e.g. salad). This cross-contamination may also occur via food surfaces or utensils. Contamination of food by an infected food handler may occur but is thought to be uncommon in the absence of diarrhoea. Salmonellae can multiply at temperatures ranging from 7 to 46 °C: thus inadequate temperature control will allow a small number of contaminating organisms to develop into an infective dose. Heating to at least 70 °C for at least two minutes is required to kill the organism.
- Imported foods (e.g. salad, halva, peanuts) may be contaminated before their arrival in Europe. *Salmonella* is also a risk to travellers abroad.
- Person-to-person spread via the faeco-oral route may occur without food as an intermediary. The risk is highest during the acute diarrhoeal phase of the illness. Person-to-person spread due to inadequate infection control practices may prolong food-borne outbreaks in institutions. Children and faecally incontinent adults pose a particular risk of person-to-person spread.
- Other, rarer, causes of salmonellosis include direct contact with animals, including pet reptiles; contamination of non-chlorinated water; nosocomially via endoscopes, breast milk, blood transfusion and soiled bedclothes; and contamination of bedding, toys and clothing by excreta.

Acquisition

The incubation period may range from 4 hours to 10 days and is affected by the number of organisms ingested. Most cases occur within 12–48 hours of ingestion. The infectious period varies enormously: most cases excrete the organism for a few days to a few months with a median duration of five weeks. Approximately 1% of adults and 5% of children under five years of age will excrete the organism for at least a year.

In most cases the infective dose for salmonellae is 10^3–10^5 organisms, but certain food vehicles are thought to protect the organism against gastric acid, reducing the infective

dose to only a few organisms. High fat foods such as chocolate and cheese may be examples. Immunity to *Salmonella* infections is partial, with re-infection possible, if milder. Those at increased risk include patients with low gastric acidity (including antacid therapy), immunosuppression, debilitation, those on broad spectrum antibiotics, and the young and the elderly.

Prevention

Prevention of food-borne salmonellosis is a classic case of the need for a 'farm to fork' strategy:

- At the farm, action is required to reduce infection and carriage in food animals, particularly poultry to reduce contaminated meat and eggs. Vaccination of poultry flocks is highly effective at reducing human cases and should be encouraged. Slaughter and processing practices for poultry require attention to reduce cross-contamination. The Scandinavian experience suggests that *Salmonella*-free poultry can be achieved.
- Commercial food processing should be subject to the HACCP (Hazard Analysis Critical Control Point) system to identify, control and monitor potential hazards to food safety. Specific measures for *Salmonella* include use of only pasteurised eggs and milk; adequate cooking of meat and poultry; practices to avoid cross-contamination; exclusion of food handlers with diarrhoea; and adequate temperature control. This is particularly important in establishments serving food to vulnerable groups (the very young, the very old and the immunocompromised).
- In the home, routine food and personal hygiene measures need to be supplemented by particular care with raw poultry and eggs. The public need to be made aware that all poultry should be viewed as contaminated and how to prevent cross-contamination from it. Consumption of raw or undercooked eggs should be avoided: date stamped eggs from vaccinated flocks are preferable.

Surveillance

- Report to public health authority: salmonellosis is mandatory notifiable in most EU countries.
- Laboratory isolates of *Salmonella* should be reported to local and the national surveillance systems. Isolates should be sent for further typing to aid epidemiological investigation.

Response to a case

- Hygiene advice, particularly on handwashing, should be given to all cases: ideally, the case should not attend work or school until he/she has normal stools (preferably for 24 hours).
- Occupational details should be sought: cases in risk groups A–D (Box 2.2.1) should be excluded until 48 hours after the first normal stool.
- Enquiry for symptoms in household contacts (or others exposed to the same putative source) should be made: those with symptoms, particularly diarrhoea, should be treated as cases.
- Enteric precautions for those admitted to hospital (especially for handling faeces or soiled bedding or clothing) should be followed.
- Asymptomatic excretors rarely require exclusion, provided adequate personal hygiene precautions are followed.
- If illness acquired in hospital, inform the hospital control of infection team.

Investigation of a cluster

- Arrange with local and reference laboratories for typing of strains.
- Some salmonellae are particularly associated with specific animal hosts (Table 3.65.1): the national reference laboratory can advise on this.
- Although some clues may be obtained by analysis of person/place/time variables, administration of a hypothesis-generating

questionnaire is usually necessary (see Chapter 4.2). A general semi-structured questionnaire for investigating clusters of food-borne illness should be routinely available: this can be modified in light of the epidemiology of the specific pathogen (e.g. known animal reservoirs or vehicles associated with previous outbreaks) and outbreak specific factors (e.g. most cases in children).

Control of an outbreak

- In food-borne outbreaks, microbiological examination of faeces from infected patients and food can reveal the organism responsible and a cohort or case–control study may reveal the vehicle of infection. However, in order to prevent recurrence the question 'how did the food consumed come to contain an infective dose of the organism?' needs to be answered. Particular factors to bear in mind in a food-borne outbreak of salmonellosis are:
  - were any potentially contaminated foods consumed raw or inadequately cooked? In the case of *S*. Enteritidis, was poultry inadequately cooked or were raw eggs used in any recipes? Can the raw food be checked for the organisms?
  - are food preparation procedures and hygiene practices adequate to prevent cross-contamination, particularly from raw meat or poultry?
  - did any food handlers have symptoms of gastrointestinal infection? All food handlers should provide faecal samples for analysis, but remember that they may also have eaten the vehicle of infection and so be victims of the outbreak rather than the cause.
  - what happened to the food after cooking? Was there scope for contamination? Was it refrigerated until just before eating? Was it adequately reheated?
- Many outbreaks require more than one problem to occur in food preparation. An example is a sandwich tea made for a sports match that used raw egg mayonnaise and then was stored in the boot of a car on a hot summer day until consumed.
- Secondary spread is common in outbreaks of *Salmonella* infection: outbreak cases should receive intervention as outlined earlier for sporadic cases. Plotting of an epidemic curve may help identify the contribution of person-to-person spread (see Box 2.2.3 for other clues).
- Outbreaks in hospitals or care homes require particular care because of the vulnerable nature of the residents.

Possible case-definition for analytical study of a *Salmonella* outbreak

Clinical: Diarrhoea or any two from abdominal pain/fever/nausea with onset between 4 hours and 10 days after exposure.
Confirmed: Clinical case with isolate of outbreak strain.

3.66 Scabies

Scabies is an inflammatory disease of the skin in humans and animals caused by the mite *Sarcoptes scabiei* var. *hominis*, var. *equi* (horse), var. *canis* (dog) and so on. Animal scabies in humans is self-limiting, and called mange or scrab.

Suggested on-call action

Advise on treatment and recommend immediate control measures.

Epidemiology

Scabies is reported to be common, with an estimated 130 million prevalent cases in the world. Although it can affect people of all

socio-economic classes, it is a major health concern in low-income countries where it is associated with overcrowding and poor living conditions. In 2009, the WHO declared it a neglected skin disease. Occurrence rates vary from 0.3 to 46%. In middle- and high-income countries, scabies is associated with clusters in hospitals, nursing homes and other similar institutions. It is more prevalent in children and young adults, in urban areas and in winter. Scabies shows a cyclical pattern with a periodicity of 15 (7–30) years. In temperate climates, scabies incidence is higher in winter (due to crowding and longer survival of the mite).

Clinical features

There may be no sign of infection for four to six weeks after exposure, when an allergy develops to mite excretions and an itchy symmetrical rash appears. The time period between exposure and onset of symptoms may be shorter in persons who have been sensitised by prior exposure. The rash comprises small, red papules and is seen anywhere on the body. If the person has had scabies before, the rash may appear within a few days of re-exposure. The itching is intense, particularly at night. Burrows are the only lesions caused directly by the mite and may be seen in the webs of the fingers and on wrists and elbows. In infants, young children, the elderly and the immunocompromised, mites can also infect the face, neck, scalp and ears. Scabies infestation will persist for life if untreated. In resource-poor tropical settings, the burden of infestation can be severe due to its indirect renal and cardiovascular complications.

Usually, only about 12 mites are present on an affected person at any one time but if there is impaired immunity or altered skin sensation hyper-infestation with millions of mites may be present and the skin is thickened and scaly. This condition is known as atypical, crusted, or Norwegian scabies. Repeated failure of treatment is seen in HIV+ crusted scabies patients.

Diagnosis

Diagnosis is based on history and physical examination, but may be difficult, as findings on examination can be subtle and history may be incomplete. The burrows can be seen as serpiginous white lines, classically occurring around the wrists, in the interdigital web spaces, in the areolae of female breasts, or male genitals and are indicative of infestation. Visualising burrows or the mite on dermoscopy can be helpful, with or without using ink to accentuate burrows. Skin scrapings can be examined under the microscope for mites, eggs, or faeces. In cases of diagnostic uncertainty, a skin biopsy may be performed.

Transmission and acquisition

The pregnant female, which is about 0.3 mm long, burrows in the epidermis and lays two to three eggs each day before dying after about three weeks. The eggs hatch after 2–4 days into larvae, which dig burrows and moult twice before developing into adults after 10–14 days. Mating takes place, the male mite dies and the female embeds in a new burrow within one hour.

Classic scabies is transmitted via direct skin-to-skin contact (10 minutes suffices), so that the risk of transmission is higher amongst family members. Patients with crusted scabies are frequently the source for large outbreaks as transmission occurs via skin scales on bedding, clothes, and upholstery. Scabies patients remain infectious until 12 hours after the start of treatment. Animal scabies can be passed to humans but is self-limiting as mites are species specific and cannot multiply in other species and soon die out.

Prevention

Prevention of scabies depends on early recognition of cases and prompt effective treatment. This in turn depends on public and professional education and a high level of awareness and diagnostic suspicion. The burden of

disease in resource-poor tropical settings, has led to efforts to control scabies using mass drug administration strategies (International Alliance for the Control of Scabies [IACS]).

Surveillance

Scabies is not notifiable in most countries of the EU; however, clusters of cases of scabies in residential and daycare settings should be reported to the local public health team.

Response to a case

The response should be directed at both patient and contacts (all people with whom skin-to-skin contact has been made for a prolonged period within the previous two months, that is household, close and sexual contacts, including asymptomatics) and consist of simultaneous treatment and washing or airing of clothing and bedding; reduction of itching and application of soft skin care to avoid dehydration and irritations.

Treatment

Topical permethrin 5% should be applied to the whole body, including the scalp, neck, face, ears, between the fingers and toes and under the nails (using a soft toothbrush). Prior to application nails should be clipped. A hot bath prior to application should be discouraged as it increases systemic absorption. Ideally, the scabicide is applied in the evening before going to bed and should be left on for 24 hours and should be re-applied if the hands are washed during that time. The patient should then have a bath or shower, dress in clean clothes and change bed sheets. A second application after 7–14 days will kill any larvae that hatch from eggs that survived the first application. Malathion can be used if permethrin is not appropriate.

- Oral ivermectin (as a single oral dose of 200 $\mu g\,kg^{-1}$ or two doses one week apart) is an alternative in those situations that whole body application is practically impossible (e.g. psychogeriatric wards) and should preferably be administered two hours after evening dinner (no food intake two hours before and after tablet intake).
- Itching may continue for two to three weeks after successful treatment and may require treatment with antipruritics. Some patients consider the continued itching as unsuccessful treatment and reapply scabicides, leading to prolonged skin irritation and psychological stress.
- Cases can return to school or work after the first application of scabicide.

Environment

- Clothing and bedding should be laundered on a hot washing machine cycle. Smaller items that cannot be washed in this way can be placed in a sealed bag for three days. Bigger items should be set aside and not used for seven days. Under these conditions mites will become dehydrated and die. Normal hygiene and vacuum cleaning of chairs, beds and soft furnishings will minimise environmental contamination with skin scales.

Crusted Scabies

- In crusted scabies, more intensive treatment is necessary, which may be continued for some time. Combined topical and oral treatment may be required. A wide definition of contacts (in person and time) and subsequent tracing is essential in stopping an outbreak that started with a crusted scabies case.

Control of an outbreak

Clusters of cases of scabies may be reported from hospitals, nursing homes or other residential health or social care settings.

- Confirmation of the diagnosis is important in these settings.
- Form a multidisciplinary institutional scabies outbreak team. Coordination is

Table 3.66.1 Responsibilities in control of scabies

Local Public Health Service	Receive reports of scabies in community settings
Local Health Protection Team (CCDC and CICN in England)	Advise on management
	Involve district nurses, health visitors, school health nurses, GPs, managers and owners of residential and nursing homes
	Make information available on scabies for the public and professionals
GPs	Maintain a high level of diagnostic suspicion
	Diagnose, treat and follow up cases of scabies amongst their patients and contacts
	Make referrals and request second opinions as appropriate
	Discuss with local HPT whenever an outbreak of scabies is suspected in a residential or nursing home
	Co-operate with the local HPT in dealing with such an outbreak
Residential and nursing home managers, owners and staff	Remain vigilant to the possible diagnosis of scabies
	Involve the GP in diagnosing, treating, referral and follow-up
	Recognise outbreaks and alert the local PT
	Co-operate with the local HPT in dealing with such an outbreak
Families of those with scabies	Ensure treatment is carried out correctly
	Inform all close contacts, particularly those in a daycare or nursing setting if scabies is suspected
	Follow advice from their GP or the local HPT, particularly relating to treatment and exclusion from work or school

CCDC, Consultant in Communicable Disease Control; CICN, Community Infection Control Nurse; HPT, Health Protection Team.

crucial for contact tracing, simultaneous treatment, and communication with patients and contacts.

- All patients and residents may need to be examined in an attempt to identify the index case who is often someone with an unrecognised case of crusted scabies. The GP of the patient, client, or service user should be asked to advise. He/she may ask for a second opinion from a consultant dermatologist. A high level of diagnostic suspicion should be maintained.
- Atypical scabies can spread from patients to nurses and others who provide close care. Use of standard precautions including gloves and aprons will minimise this.
- The cases, whether members of staff or residents, should be promptly treated (see earlier).
- Staff can return to work once treatment has been completed.
- If practicable, while affected residents are undergoing treatment they should be separated from other residents.
- If the case is a member of staff, treatment is recommended for his/her close household contacts.
- If the case is a resident it may not be practicable to treat everyone else in the residential setting, but if there are several cases and the situation appears to be out of control then it may be necessary to treat all residents, staff and their families simultaneously on an agreed treatment date.
- A skin monitoring record form should be used for each person following treatment so that apparent treatment failures and recurrences can be assessed.
- If itching persists for two to three weeks after treatment and close monitoring of skin condition shows no improvement, then misdiagnosis, treatment failure (incorrect application, possible drug resistance) or re-infection should be suspected. The patient should be re-examined to confirm the diagnosis, further co-ordinated applications of scabicide correctly applied may be advised and a search should be made for

an unrecognised source case of crusted scabies. As long as there is no animal model or laboratory condition to grow *S. scabiei*, drug testing is not performed in practical routine situations. Trial and error may be the only option.
- Outbreaks of scabies in a community setting should be referred to the local public health team (Table 3.66.1).

Suggested case-definition for an outbreak
A rash of typical appearance and itching, particularly at night. Often with other similar cases reported amongst household and other close contacts.

3.67 Schistosomiasis

Schistosomiasis (bilharzia) in humans is a parasitic infection in the (sub)tropics caused by trematodes of the genus *Schistosoma*. Intestinal symptoms are caused by *Schistosoma mansoni*, *Schistosoma intercalatum*, *Schistosoma mekongi* and *japonicum*; *Schistosoma haematobium* causes bladder involvement (urinary schistosomiasis). In Europe local transmission of a *S. haematobium* and *Schistosoma bovis* hybrid has been identified in Corsica (France). *Bulinus* snails are the intermediate host. In warm European summers bird schistosomes can cause 'swimmer's itch' in humans all over Europe (cercarial dermatitis).

Suggested on-call action
Not generally applicable.

Epidemiology

An estimated 200 million people in 74 countries are infected, of whom 120 million have symptoms, and 20 million suffer serious disease. Mortality in Sub-Sahara Africa (85% of infected people) reaches 130000–150000 annually. The five types are geographically localised: *S. mekongi* in Laos, Cambodia; *S. japonicum* in China, Philippines, Thailand, Sulawesi; *S. mansoni* in Sub-Saharan Africa, Middle East, Caribbean and South America (Brazil); *S. haematobium* in Sub-Sahara Africa, Eastern Mediterranean Basin (Egypt); *S. intercalatum* in Central Africa. In Europe the intermediate host (*Bulinus* snails) are found in Portugal, Spain, Italy (Sardinia), France (southern and Corsica). Local transmission of *S. haematobium* was seen in Corsica in 2013 and possibly also in 2001 and 2014. In Europe, schistosomiasis is otherwise seen among migrants and travellers returning from endemic areas. In a 2010, in a study from travel clinics (EuroTravNet), 40% of 152 reported cases occurred in missionaries, volunteers and aid workers, followed by tourists (19%), visiting friends and families (16%), and immigrants (13%).

Clinical features

Symptoms are associated with the infection phase: *invasion phase* rarely causes transient itching papulae (allergic reaction to penetration of the larvae or cercariae, hence 'cercarial dermatitis'); *migration* and *maturation phase* (acute schistosomiasis and Katayama syndrome) can cause non-specific symptoms as fever, muscle ache, night sweats, coughing, diarrhoea, joint pain, hepato- and splenomegaly, urticarial exanthema, and eosinophilia in the blood smear. In the *established infection* intestinal schistosomiasis can cause diarrhoea, stomach ache, blood and mucous in faeces, dysentery; while urinary schistosomiasis typically causes haematuria and dysuria at end of micturition. Serious *chronic infection* is seen only after continuous multiple exposures: intestinal (all four types) can lead to portal hypertension, portal fibrosis, oesophageal varicose veins, and urinary *chronic infection* to hydroureter, hydronephrosis, bladder polyps, bladder cancer. Atypical localisations of eggs

can cause unusual symptoms (myelitis transversa, epilepsy, salpingitis/pelvic inflammatory disease, hematospermia, genital ulcers).

Laboratory confirmation

Diagnosis can usually be confirmed by serology (ELISA or IFAT) five to eight weeks after first infection, but seroconversion may occasionally take up to three months. The sensitivity of serology could be low, especially for *S. japonicum,* and given the potentially severe consequences of a missed diagnosis, treatment should be considered based on clinical and epidemiological grounds. In the chronic phase, eggs can be demonstrated in faeces or urine. Egg production differs over time and can be low, therefore concentration methods are used and negative tests should be repeated over time. In long-established infections of *S. haematobium* and *S. intercalatum* the typical eggs can be demonstrated microscopically in a rectal snip (superficial mucosa).

Transmission

Adult male and female schistosomes live in pairs in the smaller arteries of humans (especially of the liver), where they produce eggs with larvae (miracidiae). These migrate to the lumen of intestine or bladder and are excreted with faeces or urine. In warm fresh water (20–30 °C) the eggs hatch and the free-swimming miracidium survives 8–12 hours to find and penetrate the soft body of *Bulinus* snails. Three to seven weeks later, thousands of free-swimming cercariae are released in the water, which can then penetrate the skin of the new host.

Acquisition

The route of infection for humans is skin exposure to infested fresh water during routine occupational, recreational or domestic activities. This includes drinking untreated water. The incubation period after skin penetration by larvae (cercariae) differs per phase: *invasion* hours to days; *migration and maturation* two to six weeks; *established infection* months; *serious chronic infection* months to years.

Prevention

In areas where schistosomiasis is a public health problem, elimination of snails can reduce disease burden (increase water flow, reduce vegetation, reduce pollution with organic matter, use of chemical molluscicides). Programmatic prevention can be successful if sanitation projects are combined with heath education to prevent urine and faeces contaminating fresh water. Mass treatment (school-age children) reduces excretion. Elimination of runoff from pastures where infected buffalo graze (*S. japonicum*) can prevent introduction. Individuals can prevent schistosomiasis by avoiding fresh water contact (swimming, wading, drinking). Immediate vigorous towel drying after swimming (edges of swimming suit) might reduce the number of cercariae that succeed in penetrating the skin.

Surveillance

Reporting of cases is not generally required. In view of the changing geographical epidemiology a travel history is advised to find possible newly infested areas.

Response to a case

If someone is infected, the other members of the party frequently are also infected. Screening and treatment is advised to prevent disease.

3.68 Shigellosis

Shigellae cause intestinal infection including ‘bacillary dysentery’. *Shigellae sonnei* is the most common species in Europe and causes

relatively mild illness. Most disease caused by *Shigellae flexneri* and all *Shigellae boydii* and *Shigellae dysenteriae* may be more severe and the latter two are usually imported. *S. dysenteriae* type 1 may cause very severe illness due to production of an exotoxin.

Suggested on-call action

- If case in risk group for further transmission, advise exclusion as suggested in the 'Response to Case' section.
- If you or the reporting clinician/microbiologist are aware of other linked cases, activate the local outbreak plan or SOP.
- If infection with *S. dysenteriae*, obtain details of household and ensure symptomatic contacts excluded as suggested later.
- If *S. dysenteriae* serotype 1, ensure symptomatic contacts receive medical assessment.

Epidemiology

The annual incidence of *Shigella* infection is reported to be about 30 cases per 100 000 population, although only about 1.5 per 100 000 cases are reported to public health authorities in Europe, with the highest rates in Bulgaria and Slovakia. Infection occurs most frequently in late summer and has been reported as peaking 40 days after a peak in ambient temperature. *S. sonnei* is the most commonly reported species in Europe, followed by *S. flexneri*. Risk groups for infection include day-care attenders, travellers abroad and men who have sex with men. Shigellosis is endemic in many developing countries: in some European countries (e.g. Scandinavian countries) the large majority of cases are travel-related, but in others (e.g. Hungary, Greece, Slovakia, Belgium) almost all are domestically acquired. Outbreaks occur mostly in day-care centres and schools, but are also reported from residential institutions, restaurants, camps, religious communities, microbiology laboratories and hospitals. In recent years, outbreaks of *S. sonnei* and *S. flexneri* among men who have sex with men have occurred, particularly in the UK and the Netherlands.

Clinical diagnosis

The most common symptoms of *S. sonnei* infection are diarrhoea, abdominal pain/cramps and fever. Between 10 and 50% also develop bloody diarrhoea. Nausea and/or vomiting, anorexia, headache or malaise may also occur. Illness lasts from one day to two weeks (average four to five days). Approximately 3% require hospitalisation. Asymptomatic excretion can occur with all *Shigella* species.

S. flexneri also causes diarrhoea, abdominal pain/cramps and fever, but it is often more severe than *S. sonnei* infection. Dysentery is common, illness can be prolonged and hospitalisation rates may be much higher. Abdominal cramps and fever may precede the onset of diarrhoea. Reactive arthritis and Reiter's syndrome may be a late complication of shigellosis.

S. boydii causes diarrhoeal diseases of varying severity, broadly in line with that produced by *S. flexneri*.

S. dysenteriae serotype 1 infection is more severe than that from other shigellae, due to the production of Shiga-toxin. Dysentery occurs in most cases and there is an appreciable death rate. Complications of infection include toxic megacolon, Haemolytic Uraemic Syndrome (HUS), Disseminated Intravascular Coagulation (DIC) and sepsis. Complications may be more common in children, the elderly and the immunosuppressed. *S. dysenteriae* serotypes 2–15 do not produce this toxin.

Laboratory confirmation

Diagnostic testing from faecal specimens is routine in most laboratories. Provisional results are usually available within 48 hours. Speciation should always be carried out as control measures can vary between species.

Serotyping based on 'O' antigens is also available if epidemiologically indicated, for example any case of *S. dysenteriae* (15 serotypes), possible clusters of *S. boydii* (20 serotypes) or *S. flexneri* (six serotypes, and two variants e.g. 'type 2a'). *S. sonnei* is antigenically homogeneous, but genomic (e.g. whole genome sequencing in England) or phage typing may be available from reference laboratories. PCR testing for the *ipaH* gene that is shared by all shigellae (also shared with Enteroinvasive *Escherichia coli* or EIEC) is also available in some laboratories (the rare but severe *S. dysenteriae* serogroup 1 will also Shiga-toxin (*stx*) positive: however a dual infection with STEC and another *Shigella* could also produce a combined *ipaH* and *stx* positive result, so culture is also necessary). PCR positives should be followed up by confirmatory culture; PCR is more sensitive than culture, so PCR negative cases would not normally need further tests.

Transmission

Humans are the only significant reservoir of infection. Transmission to other humans is via the faeco-oral route either directly, by contamination of food, water or the environment, or via sexual contact (particularly in men who have sex with men).

Direct person-to-person spread is extremely common in households and institutions, particularly those with young children: 30–50% of household or nursery contacts became infected. Cases with diarrhoea are a much greater risk than asymptomatic excretors, with inadequate handwashing after defaecation the main cause. Such individuals may also contaminate food. Young children may act as a transmission link between households.

Shigellae, particularly *S. sonnei* may survive for up to 20 days in favourable environmental conditions (cool, damp, and dark). This may lead to transmission via lavatory seats, towels, and any other vehicle that could become contaminated by faeces, either directly or via unclean hands. Flies may also transfer the organism from faeces to food.

Food- and water-borne outbreaks are relatively uncommon, but do occur. Food-borne outbreaks are often caused by an infected food-handler, but outbreaks in Europe have also been linked to imported vegetables or herbs. Water-borne infection can be via drinking water or recreational water.

Acquisition

The incubation period is between 12 hours and 4 days (usually 1–3 days; median 2 days), but may be up to 1 week for *S. dysenteriae* type 1. The infectious period is primarily during the diarrhoeal illness: however, cases maintain a low level of infectivity for as long as the organism is excreted in the stool, which usually ranges from 7 to 26 days, although prolonged excretion is documented, including in immunosuppressed people. The infective dose is very low: the mean infectious dose is about 1000 organisms, but infection may follow ingestion of as few as 10 organisms of *S. dysenteriae* type 1. Immunity post infection does occur and lasts for several years, at least for the same serotype. Longer-term immunity does not appear to be important.

Prevention

- Adequate personal hygiene, particularly handwashing after defaecation.
- Adequate toilet facilities in nurseries and schools. Supervised handwashing in nursery and infant schools. Regular and frequent cleaning of nurseries and schools, particularly for toilet areas.
- Safe disposal of faeces and treatment of drinking and swimming water.
- Care with food and water for travellers to developing countries.
- Safe sex messages to men who have sex with men, including information on how to reduce the risk of transmission of gastrointestinal pathogens.
- Routine cooking kills shigellae.

Surveillance

All clinical cases of dysentery should be reported to public health authorities and *Shigella* infection is statutorily notifiable in most EU countries. Standard surveillance questionnaires may be available and should include travel, food, attendance at educational/care/work facilities, exposure to other IID cases and, for adult males, sexual history.

Response to a case

- Follow national guidelines or the local SOP if available.
- Hygiene advice to case and contacts.
- Enteric precautions for case and symptomatic contacts. In institutions, isolate if possible.
- Exclude cases and symptomatic contacts from work or school until well.
- For higher risk groups (Box 2.2.1) with *S. sonnei*, exclude until 48 hours after first normal stool and hygiene advice given.
- For higher risk groups (Box 2.2.1) with non-*sonnei* shigellae, exclude from high risk activities until a negative faecal culture specimen obtained (two samples taken at least 24 hours apart for *S. dysenteriae* 1). This policy may also be adopted for children over five with *S. dysenteriae*. If species not yet available, manage as non-*sonnei Shigella*.
- Symptomatic contacts of cases in risk groups should be excluded as for cases and if contacts of a case with a non-*sonnei Shigella* should also be screened microbiologically.
- Obtain details of any nursery or infant school attended. Check to see if other cases and reinforce hygiene measures. Check that adequate toilet facilities and supervision available.
- For species other than *S. sonnei*, check that case has been abroad in the four days before onset (seven days for *S. dysenteriae* type 1) or has been in contact with another case that was ill abroad or on return. If no link abroad, obtain details of contacts (including sexual contacts in adult males) and full food history for four days before onset (seven days for *S. dysenteriae*).
- Mild cases will recover without antibiotics. Where needed, antibiotics have been shown to be effective and can reduce carriage, but antibiotic resistance is increasing. Drugs that reduce intestinal motility are usually avoided.

Investigation of a cluster

- Liaise with the microbiologist to organise typing of isolates (may be more than one type in an outbreak).
- Does epidemic curve suggest point source (plus secondary cases) or continuing exposure?
- Does age/sex/ethnic/geographic analysis of cases suggest common factor (e.g. mostly adult males)?
- Look for links via institutions such as nurseries, schools, social clubs and care facilities and links between affected families via child networks. Administer a hypothesis-generating food questionnaire for four days before onset. Ask about water consumption, hobbies, swimming, social functions, occupation and, if mostly adult males, sexual contact. For non-*sonnei* species, look for social networks that include travellers to developing countries.

Control of an outbreak

- For outbreaks in institutions, public health staff should satisfy themselves of the adequacy of hygiene and toilet facility arrangements. Handwashing by children should be supervised in nurseries and primary schools. Intensive and frequent cleaning and adequate disinfection, especially of 'touch points' is required.
- Exclusion of cases as above, with hygiene advice to families to limit spread within the household, is recommended.
- Further measures in outbreaks need to be appropriate to the situation. Exclusion of

all cases of shigellosis until microbiologically negative is one option. Antibiotic treatment of cases can be undertaken, either as an adjunct or an alternative. Cohorting of convalescent cases can be considered instead of exclusion in prolonged outbreaks, if facilities and staffing are adequate to implement this effectively, although the effectiveness of this policy is not proven. Closure of the institution may even be necessary.

Suggested case-definition for an outbreak

Confirmed: Diarrhoea, *or* a combination of abdominal pain with fever; and *Shigella* species of outbreak strain identified in faeces.

Probable: Diarrhoea, *or* abdominal pain with fever; and faecal sample positive by PCR or by non-speciated culture.

Clinical: Diarrhoea, *or* abdominal pain with fever, in a contact of a case or affected institution, without alternative explanation.

3.69 Shiga toxin-producing *Escherichia coli* (STEC) and other diarrhoeagenic *E. coli*

Many different strains of *Escherichia coli* can cause gastrointestinal illness, which can be classified into seven main syndromes. The most serious illness is that caused by Shiga toxin-producing *E. coli* (STEC) strains, also known as Verocytotoxin Producing *E. coli* (VTEC) strains. STEC strains that also show the attaching-effacing effect of Enteropathogenic (EPEC) strains are known as Enterohaemorrhagic *E. coli* (EHEC). STECs, particularly EHEC strains, have the potential to cause serious disease, including Haemolytic Uraemic Syndrome (HUS, the commonest cause of acute renal failure in children) and death; some STEC strains may be classified by their presumed ability to cause HUS, as 'HUSEC' strains. The syndromes caused by other types of *E. coli* are summarised in Table 3.69.1

The most common STEC strain in most European countries is *E. coli* O157, but others include O8, O26 (the most common in Ireland), O45, O55, O80, O91, O103, O104, O111, O113, O116, O117, O119, O121, O128, O130, O145, O146 and O174. STECs can cause large outbreaks with the potential for secondary spread.

Suggested on-call action

1 If *E. coli* O157 or other STEC:
- Undertake rapid risk assessment (e.g. by telephone).
- Exclude if in high risk group (Box 2.2.1).
- If other cases known to you or reporting clinician or laboratory, consider whether part of an outbreak and whether to implement the outbreak plan.
- If no other cases known, ensure risk factor details collected within 24 hours.

2 If other *E. coli* gastroenteritis:
- Exclude if in high risk group (Box 2.2.1).

Epidemiology

The reported incidence of STEC infection in Europe in 2015 was 1.5 per 100 000 population per year, although many additional cases are likely to not be identified by surveillance systems and much higher rates are recorded in Ireland, the Netherlands and Sweden. The highest reported incidence is seen in children under five and there is a higher rate in females. STEC infections tend to increase in the summer, with a peak in August to September (Figure 2.2.2). Incidence may be higher in rural areas.

Table 3.69.1 *E. coli* causing diarrhoea (other than STEC)

Designation	Epidemiology	Illness	PCR findings[a]	Incubation period	Sources	Main 'O' serogroups
Enteropathogenic (EPEC)	Sporadic cases and outbreaks in children, usually aged less than 2 years, especially in developing countries. Outbreaks reported in schools, neonatal units, food premises, hotels.	Watery diarrhoea, abdominal pain, nausea, vomiting and fever. Fatigue, myalgia, or headache may occur. Duration 6 hours to 4 days (but diarrhoea may be prolonged)	*eae* positive (also positive in with EHEC, but EPEC is *stx* negative) *bfp* positive (typical EPEC)	2–73 hours (median 8–18)	Faeco-oral, e.g. via fomites and hands in nurseries and hospitals. Cases excrete for up to 2 weeks, but infectious dose fairly high. Contaminated infant foods in developing countries.	18, 25, 26, 44, 55, 86, 111, 114, 119, 125, 126, 127, 128ab, 142, 158, 608.
Enterotoxigenic (ETEC)	Major cause of travellers' diarrhoea. Dehydrating diarrhoea in children in developing countries. Outbreaks associated with restaurants/caterers.	Watery diarrhoea and abdominal pain. Headache, fatigue, nausea, anorexia, vomiting or fever may occur. Average duration 6 days.	Enterotoxin (*lt*, *sth* or *stp*) positive	1–166 hours (median 10–50)	Food and water contaminated by humans. Nosocomial outbreaks reported. Cases excrete for up to 7 days, but infectious dose high.	6, 8, 11, 15, 20, 25, 27, 63, 78, 80, 85, 114, 115, 128ac, 148, 149, 153, 159, 167, 173.
Enteroinvasive (EIEC)	Occasional cause of travellers' diarrhoea or outbreaks in developed countries. Serious infection common in children in developing world.	Watery diarrhoea, Abdominal pain, fever, malaise, weakness, nausea. Lasts up to 2 weeks.	*ipaH* positive *virF* positive (both also positive in *Shigella* sp)	1–168 hours (median of 21).	Contaminated food. Contaminated water. Probable human reservoir. Infectious dose probably high.	28ac, 29, 52, 112ac, 115, 124, 136, 143, 144, 145, 147, 152, 159, 164, 167.

(*Continued*)

Table 3.69.1 (*Continued*)

Designation	Epidemiology	Illness	PCR findings[a]	Incubation period	Sources	Main 'O' serogroups
Enteroaggregative (EAEC, EAggEC)	Common in developing countries (inc. Indian subcontinent) and a risk for travellers. Children more commonly affected. Outbreaks reported in Europe (schools, neonatal units, restaurants, hotels).	Diarrhoea, usually watery and/ or mucoid, may be prolonged low grade fever, nausea, tenesmus, borborygmi. Often chronic in children or AIDS.	May vary by strain. *aggR* positive *astA* positive (may also be expressed by DAEC strains) *pic* positive aatA positive aaiC positive	8–52 hours	Contaminated food and possibly water. Infectious dose probably high. Likely human reservoir.	3, 4, 15, 19, 42, 44, 62, 73, 77, 86, 92, 98, 111, 113, 126, 127, 134, untypable
Diffuse-adherence (DAEC)	Preschool children in developing countries.	Diarrhoea, often watery; may be persistent	Varies by strain, often: *afaB* positive *daaE* positive	Unclear	Probably food. Infectious dose may be lower. Adults may be asymptomatic carriers.	–
Adherent invasive (AIEC)	Association with Crohn's disease.	Diarrhoea, abdominal pain, fever, blood and or mucus.	Unclear	Unclear	Unclear	–
	Control: Enteric precautions for cases, personal hygiene. Exclude risk groups until 48 hours after first normal stool. Advice to travellers abroad. Good food hygiene and safe water. Handwashing and environmental cleaning in nurseries.					

[a] *targets vary by test; sensitivity and specificity also vary.*

Table 3.69.2 Causes of Haemolytic Uraemic Syndrome

Typical ('post-diarrhoeal', 'epidemic', 'D+'):
- *E. coli* O157, particularly O157:H7
- Other STEC (e.g. O26, O45, O55, O80, O91, O103, O104, O111, O113, O121, O145)
- *Shigella* dysentery
- *Campylobacter*

Atypical ('sporadic', 'D'):
- Other infections, e.g. *Streptococcus pneumoniae*, coxsackie virus, influenza, HIV, *Mycoplasma*, *Histoplasma*
- Familial disorders, e.g. complement fixation pathway defects
- Systemic disease, e.g. SLE
- Malignancy, e.g. acute lymphoblastic leukaemia
- Drugs, e.g. mitomycin C, cyclosporin, quinine, crack cocaine, oral contraceptives
- Pregnancy
- Idiopathic

Most cases are sporadic or limited to close contacts. Outbreaks may affect communities (often via food vehicles), nurseries/day-care centres, schools, restaurants, nursing homes, hospitals, open farms, campsites and swimming pools/lakes. In some countries, a significant proportion is associated with foreign travel.

HUS has an incidence of about 7 per 100 000 children under 5, of which 90% are 'typical' (diarrhoea associated, Table 3.69.2).

Clinical features

Infection with *E. coli* O157 may cause no symptoms; a diarrhoeal illness, often accompanied by abdominal cramps; haemorrhagic colitis with bloody diarrhoea and severe abdominal pain, often without fever; haemolytic uraemic syndrome (HUS) with renal failure, haemolytic anaemia and thrombocytopaenia, particularly in children; and thrombocytopenic purpura, particularly in adults, which may add neurological complications to the features of HUS. About a third of diagnosed cases are admitted to hospital.

HUS may occur 2–14 days after the onset of diarrhoea (usually 5–10 days). It affects 2–11% of all reported cases, with the risk highest in young children. Other risk factors are bloody diarrhoea, vomiting, female sex, hospitalised patients over-60, receiving beta-lactam antibiotics, phage-type (PT21/28 and PT2) and toxin type (*stx* 2, particularly 2a, 2c and 2d). STEC, especially *E. coli* O157:H7 is the most common cause of HUS and causes the more common glomerular ('typical') form of the disease (Table 3.69.2). The case fatality rate of severe infection (HUS or TTP) is reported as 3–17%. Mortality may be particularly high in outbreaks affecting elderly care patients.

Laboratory confirmation

Diagnosis is traditionally based on stool culture and is more likely to be successful if specimens are obtained within four days of onset of symptoms. Most *E. coli* O157 differ from other *E. coli* in not fermenting sorbitol and this is the most common screen performed in diagnostic laboratories (with subsequent confirmation by biochemistry or latex as O157), although STEC infection due to sorbitol fermenting strains of O157 have been reported and non-O157 STEC strains (including EHEC/HUSEC strains) commonly ferment sorbitol.

STEC strains produce one or both of two Shiga toxins (*stx*1 and *stx*2, which can be further divided into subtypes): tests for these toxins are available at reference laboratories and can help identify non-O157 STEC strains. Recently a number of local laboratories have introduced PCR testing for the *stx* gene, which is more sensitive than culture, particularly for sorbitol-fermenting strains, although the specificity is not yet clear. PCR positives should also undergo local culture and culture-negative PCR positive samples should be referred to reference laboratories for further evaluation. Results for other virulence factors, particularly the attaching-effacing intimin (eae) gene may be available and is particularly useful for assessing the pathogenicity of non-O157 strains. Phage typing

and/or genotyping may be available from reference laboratories to aid epidemiological investigations. Serology can be used for retrospective diagnosis, and salivary testing is also possible.

Methods exist for examining food, water, environmental and animal samples for STEC.

Transmission

The natural reservoir of STEC is the gastrointestinal tract of animals, particularly cattle, but also sheep, goats, deer, horses, pigs, rabbits, dogs, birds and flies. Humans are infected via:

- Contaminated foods: the most commonly reported food vehicle is beef, particularly ground beef dishes such as beefburgers, followed by raw salad, fruit, or vegetable products, such as lettuce, sprouted seeds, spinach, melon, and apple juice. Dairy products and other foods have also been reported as vehicles of infection. Infection may result from inadequate cooking of already contaminated food, for example beefburgers, or from cross-contamination of food that will be eaten raw, such as cold cooked meats. The organism is relatively resistant to acid, fermentation and drying.
- Direct contact with animals, for example at farm visitor centres. Excreting animals are usually asymptomatic. Soil and water contaminated by animal faeces has led to outbreaks in campers and is also linked to sporadic infection.
- Secondary faeco-oral spread from infected cases is common, particularly in families and institutions with children under five years old, with attack rates of 20–38% reported in nursery outbreaks. Asymptomatic excretion is common in family contacts of cases. Outbreaks attributed to food handlers have been reported.
- Drinking and bathing in contaminated waters (from animals or humans) have both been linked with incidents of infection.
- Nursing and laboratory staff have acquired infection through occupational exposure.

Acquisition

The incubation period ranges from 6 hours to 10 days, although 2–4 days is most common. The incubation period may depend on the number of organisms ingested.

Patients can excrete the organism in the faeces for between 2 and 62 days, with reported median excretion periods ranging from 5 to 40 days. Excretion may be intermittent or prolonged (particularly in children) and excreters commonly have at least 10^6 viable organisms per gram of stool. The infectious dose is low (possibly less than 100 organisms), so patients are presumed to be potentially infectious as long as the organism can be detected in the faeces. Microbiological clearance is usually viewed as two consecutive negative faecal samples, taken at least 24 hours apart.

Immunity is thought to develop following exposure to *E. coli* O157.

Prevention

- Minimise contamination of carcasses at slaughter.
- Adopt the Hazard Analysis Critical Control Point (HACCP) approach in both food-processing and food-service industries to prevent survival of, or contamination by, STEC.
- Good kitchen practices including separation of raw and cooked foods to avoid cross-contamination, washing of fruit and vegetables and storage of foods below 10 °C.
- Cook beef, lamb and other meat products so that any contaminating organisms are subjected to minimum of 70 °C for two minutes. Cook beefburgers until juices run clear and no pink bits remain inside.
- Pasteurisation of milk and dairy products.
- Handwashing is effective at reducing the risk of gastroenteritis from many organisms and has been shown to be effective for *E. coli* O157. Antibacterial soap may increase the effectiveness of handwashing.
- Adequate hygiene and toilet facilities in nurseries, schools and healthcare premises.

Routine disinfectants are effective against *E. coli* O157. Supervised handwashing in nurseries and infant schools.
- Precautions during farm visits by children, including:
  - Handwashing after touching animals.
  - Avoid eating and drinking whilst visiting animals.
  - Keep face away from animals.
  - Do not put hand to mouth.
  - Do not touch animal droppings.
  - Clean shoes after visit.
- Keep animals off fields for three weeks before using the fields for recreation.
- Protection and treatment of drinking water supplies.
- Good hygiene practices at public swimming pools.

Surveillance

- All cases of infectious bloody diarrhoea or HUS should be reported to the local public health authority as a matter of urgency.
- All presumptive isolates of STEC (including PCR positives) should be reported to local public health authorities.
- Cases should be reported to national surveillance systems: statutorily notifiable in most EU countries. Enhanced surveillance schemes are operational in some countries, including the UK.
- Laboratories should test all samples from cases of diarrhoea or bloody stools for STEC and should send culture or PCR positives to a reference laboratory for confirmation and typing.

Response to a case

The severity of disease, particularly in children and the elderly, the small infectious dose and the ability to spread person to person and via contaminated food means that even single cases require prompt investigation and control.
- Enteric precautions during diarrhoeal phase.
- Adequate fluid and electrolyte replacement and monitoring for the development of HUS. Antimotility agents are usually not recommended. Referral to hospital if complications such as bloody diarrhoea occur. The use of antibiotics in the treatment of *E. coli* O157 is not usually recommended and may be associated with an increased risk of developing HUS. If antibiotics are being considered, an appropriate specialist should be consulted.
- Report to public health authorities: compulsorily notifiable in most European countries.
- National guidelines may be available and should be consulted (updated UK guidelines due to be published in 2018).
- Collect standard dataset (e.g. using national enhanced surveillance form) and undertake a risk assessment.
- Hygiene advice should be given to cases and contacts, particularly on handwashing. Suggest remaining off work/school until normal stools for 48 hours for those in non-high-risk groups.
- If case in high-risk group for further transmission (Box 2.2.1) exclude from work or nursery until asymptomatic and two consecutive negative faecal specimens taken at least 24 hours apart (in some cases, a single PCR *stx* negative result may be taken as evidence of clearance). In risk groups A, C and D, a risk assessment may allow restriction of activities or re-deployment for asymptomatic cases awaiting formal clearance. Children in risk group B are usually excluded until clearance, but those who suffer prolonged shedding and exclusion may be risk assessed to see if an acceptable way can be found to manage the risk, although this may not be possible.
- Household contacts in high-risk groups to be screened. Exclude those in all high-risk groups (Box 2.2.1) until two negative faecal specimens obtained from the contact after the index case becomes asymptomatic. Exclude other symptomatic contacts until they are 48 hours symptom free.
- Assess detailed history from all cases for all 10 days before onset covering food, water, animal contact, farms, swimming, nursery/school, other institutions and travel.

Compare to previous cases. Potential sources of infection should receive follow up appropriate to the risk.

Investigation of a cluster

- Organise phage-typing, toxin-typing, and genotyping with reference laboratory.
- Undertake a hypothesis-generating study to cover all food and water consumed in 10 days before onset of illness, and all social, school and work activities and visits undertaken. Include exposure to farm animals, pets and cases of gastroenteritis. Ask specifically about minced beef or lamb products, cooked meats, milk, salad and other raw vegetable/fruit consumption. Look for links to institutions and restaurants.
- Investigation of social networks may reveal potential for person-to-person spread via common (possibly asymptomatic) contacts.

Control of outbreaks

An outbreak of STEC is a public health emergency and requires a prompt and thorough response. Detailed national guidance may be available; particular actions include:

- Hygiene advice to all cases and contacts.
- Exclude cases as detailed earlier.
- Enhanced cleaning in all institutional outbreaks.
- Supervised handwashing for children in affected nurseries and infant schools.
- Exclude all cases of diarrhoea from affected (non-residential) institutions, until normal stools and two consecutive negative samples taken at least 24 hours apart received.
- In day-care establishments for children under six (high risk of HUS and poor hygiene) screen all attenders. Exclude all positives until microbiological clearance achieved. Adopt similar approach for confused or faecally incontinent elderly attending day-care facilities.
- In residential accommodation for children under six or the elderly, screen all residents. Maintain enteric precautions for all positives until microbiological clearance achieved. Preferably nurse in private room with own washbasin and exclusive use of one toilet whilst diarrhoea continues.
- In outbreaks linked to open farms, restriction of access to animals and to areas potentially contaminated by them should be considered, whilst inspection, sampling and risk reduction measures implemented.
- Institute *urgent* withdrawal of any implicated food. If local supplier involved, ensure personally that this is done. If national or regionally distributed food, contact relevant government department: for example the Food Standards Agency in the UK.
- Issue 'boil water notice' for contaminated drinking water.
- Monitor cases at increased risk of HUS or TTP to ensure prompt referral.
- Antibiotic prophylaxis not generally recommended.

Suggested case-definition for outbreak

Confirmed	Diarrhoea with demonstration of STEC of outbreak strain in stools
Presumptive	**1** HUS occurring after diarrhoea with no other cause identified. *or* **2** Diarrhoea with laboratory diagnosis of STEC awaiting typing. *or* **3** Acute bloody diarrhoea in a person with an epidemiological link to outbreak, for example via confirmed case, affected institution or with onset within 10 days of implicated meal.
Clinical	Diarrhoea in person epidemiologically linked to outbreak with further investigations awaited.

3.70 Smallpox

Smallpox is an acute contagious disease caused by the variola virus, a DNA virus member of the orthopox genus. Naturally occurring infection has been eradicated worldwide, so its public health importance now lies in the potential of a deliberate release in a bioterrorist attack and the consequent need to re-consider vaccination and other control strategies.

Suggested on-call action
If diagnosis is likely, isolate at the point of contact and notify national surveillance unit urgently. Refer to the 'Response to a Case' section.

Epidemiology

The WHO confirmed the global eradication of smallpox in 1980. There are concerns that the virus may exist outside the two official WHO designated laboratories.

Clinical features

There are two clinical forms of the disease – variola major (severe) and variola minor (mild). In variola major there is typically a rapid onset of flu-like symptoms – fever, headache, malaise and aching head and back. The distinctive vesicular rash then appears over the next one to two days, eventually covering the whole body. Vesicles are most concentrated peripherally – on the face, arms and leg, also the mouth and throat (unlike chickenpox, which is commonest on the trunk). The vesicles develop into pustules over the next week; these crust and fall off over the next three to four weeks, leaving permanent pitted scars. The case fatality rate in a non-immune person is 30%. There is no specific effective treatment, although vaccination early in the incubation period can modify the course of the disease and reduce mortality. In malignant smallpox, the most severe form, the rash is haemorrhagic, and the case fatality rate is over 90%. Variola minor has a much less severe course and most patients recover. In vaccinated individuals a modified clinical presentation is seen ('varioloid'), with rapidly changing smaller lesions; variola sine eruptione is also reported in vaccinated individuals (fever without pocks).

Smallpox may be confused with chickenpox: diagnostic clues are given in Table 3.70.1. Other differential diagnoses include disseminated herpes simplex infection, and (rarely) cowpox and monkeypox.

Laboratory confirmation

This is by Electron Microscopy (EM) identification of orthopox virus from vesicular fluid, scrapings from the base of lesions, scabs or vesicle crusts. This must be confirmed by Polymerase Chain Reaction (PCR) and viral isolation from culture. Confirmation can only be done in a specialised containment level 4 laboratory.

Varicella and herpes simplex viruses are easily distinguished from parvovirus on EM. Parapox particles (e.g. from orf) should also be distinguishable from orthopox viruses (such as smallpox). If an orthopox virus is found on routine EM, a clinical history will be required.

Transmission

There is no known animal reservoir or vector. The virus spreads from person to person by droplet nuclei or aerosols expelled from the orophayrynx of an infectious case. Close contact (e.g. household, hospital ward) is normally required; however air-borne transmission via draughts and air conditioning can occur, also from contaminated clothing and bedding. Varioloid is regarded as infectious, but transmission has not been reported. Under normal conditions, the virus is unlikely

Table 3.70.1 Distinguishing smallpox from chickenpox in a well, non-immune person

	Smallpox	Chickenpox
Overall illness	Almost always severe	Usually mild
Initial signs	Headache, back pain	Mild malaise
First spots	Forehead, face, scalp, neck, hands and wrist	Trunk
"Cropping"	Pocks in one area, e.g. face appear all at once	Generalised
Limb distribution of spots	More on hands and wrists than upper arms; similarly, more on feet and ankles than the thighs	More on upper arms than hands and wrists, more on thighs than feet and ankles
Evolution of spots	Various stages can be seen at the same time	One stage at a time
Hands and feet	Circular flattened grey vesicles are characteristic	Such vesicles never seen in chickenpox
Itchiness	Not in first few days of rash	Common in the first few days of the rash and then continuing

to survive more than 48 hours in the environment, although prolonged survival is possible in dry scabs.

Acquisition

The incubation period is usually 10–14 days (range 7–19 days). Patients are infectious from the onset of fever until the last scabs fall off. Immunity following natural infection is lifelong. Past vaccination offers some degree of protection.

Prevention

- Smallpox vaccine is a live vaccine produced from vaccinia virus. It is delivered by multiple skin puncture with a bifurcated needle; a 'take' is successful when a pustule develops, which progressively crusts. Serious vaccine complications occasionally occur (encephalitis, eczema vaccinatum) and can be treated with cidofovir and Vaccinia Immunoglobulin (VIG). Revaccination is recommended after 3 years for those at continuing risk; after revaccination protection lasts for about 10 years.
- Contraindications: HIV+, immune suppression, malignancies, (family members of persons with) chronic eczema, chronic dermatitis. Consider using VIG in persons with an urgent vaccine indication and contraindication.
- Vaccination should be considered for laboratory workers working with closely related viruses and for frontline workers who might have to care for cases in the event of a deliberate release.
- New vaccinia strains in development, growing in cell culture (not calf skin), are not registered.

Surveillance

- Any suspected case must be reported immediately to the national surveillance unit.
- Notifiable throughout the EU.
- All suspected cases must be reported to WHO; a number are investigated every year, and usually turn out to be another poxvirus infection, usually monkey pox (which occurs mainly in Central Africa).

Response to a case

- Isolate any probable or confirmed case at point of diagnosis, pending transfer to a high security unit with negative-pressure isolation. Patients should be isolated until all crusts have fallen off.

- Confirm the diagnosis (with appropriate precautions).
- Decontaminate all waste before disposal by autoclaving.
- Vaccination of contacts in the first four days of the incubation period reduces mortality by 50%. Antiviral drugs may also be considered.
- Any confirmed case should be assumed to be a deliberate release.

Investigation and management of a cluster

Assume deliberate release and implement control plan (see next section). Many health and emergency planning agencies would be involved with central Government co-ordination.

Response to an overt deliberate release

- Define exposed zone and identify exposed people.
- Decontaminate exposed people: remove clothing, shower and wash hair.
- Vaccinate all exposed.
- Trace those who have left the scene for decontamination and vaccination.
- Isolate exposed zone to allow natural decontamination: formal decontamination unnecessary.
- Full biological protective equipment for those who enter exposed zone.
- Vaccination of frontline workers.

Suggested case definition

Clinical – acute onset of fever >38 °C, which is persistent, followed by a vesicular or pustular rash with lesions all at the same stage of development without obvious cause and with a centrifugal distribution

Confirmed – identification of orthopox particles by EM and PCR; in an outbreak EM alone is adequate for cases with epidemiological links with others.

3.71 Staphylococcal food poisoning

Staphylococcal Food Poisoning (SFP) is an uncommon food-borne disease caused by heat-stable enterotoxins produced when certain strains of *Staphylococcus aureus* multiply in food.

Suggested on-call action

If you or the reporting clinician/microbiologist know of any associated cases, consult the outbreak control plan or SOP.

Epidemiology

SFP occurs throughout the world and is responsible for about 5% of reported food poisoning outbreaks in Europe. However, many cases of SFP will never be diagnosed and therefore not recorded in surveillance data.

Clinical features

There is sudden onset of nausea, vomiting, cramps and diarrhoea. Hypotension and prostration may occur. The illness lasts one to two days; serious sequelae are uncommon, but admission to hospital may occur because of the intensity of symptoms.

Laboratory confirmation

Staphylococcus aureus may be cultured from unheated food vehicles at levels of at least 10^5 organisms per gram or from the vomit or faeces of cases. Enterotoxin may be detected in food samples and can survive in food that has been heated; culture of heated food vehicles may be negative, but the (heat killed) organism may be seen on Gram staining. The same

strain of *S. aureus* may be found in the implicated food vehicle and on the skin or lesions of food handlers.

Transmission

Food handlers colonised with *S. aureus* or with infected skin lesions can contaminate foods such as cooked meats, sandwiches and pastries. These are stored with inadequate refrigeration, allowing the organism to multiply and produce toxin before being eaten. Two hours at room temperature may be long enough to produce a significant amount of toxin. Even with further cooking or heating the toxin may not be destroyed. Outbreaks have followed contamination of dairy products as a result of staphylococcal mastitis in cattle.

Acquisition

The incubation period of SFP is 0.5–8 hours (usually 2–4 hours). It is not communicable from person to person.

Prevention

SFP can be prevented by:
- Strict food hygiene including kitchen cleaning and hand washing.
- Minimising food-handling.
- Safe food storage, in particular temperature control above 60 °C or below 10 °C.
- Excluding food handlers with purulent lesions. Nasal carriers do not need to be excluded.

Surveillance

- Cases and outbreaks should be reported to local public health departments.
- Outbreaks should be reported to national surveillance centres; reporting of food poisoning outbreaks in mandatory for EU member states.

Response to a case

- Enquire about food consumed in the 24 hours before the onset of symptoms.
- Exclude risk groups (Box 2.2.1) with diarrhoea or vomiting.

Investigation of a cluster

- Discuss further microbiological investigation (e.g. genotyping) with microbiologist.
- Undertake a hypothesis-generating study covering food histories, particularly restaurants, social functions and other mass-catering arrangements.
- Investigate the origin and preparation methods of any food items implicated in the outbreak. Submit any leftover food for laboratory analysis.
- Search for food handlers with purulent lesions.

Control of an outbreak

- Identify and rectify faults with temperature control in food preparation processes.
- Exclude any implicated food handler.

Suggested case definition for an outbreak
Vomiting occurring 0.5–8 hours after exposure to potential source, with appropriate laboratory confirmation.

3.72 Streptococcal infections

Streptococci are part of the normal flora and colonise the respiratory, gastrointestinal and genitourinary tracts. Several species cause disease, including:
- Group A streptococci (beta-haemolytic streptococci, BHS, *Streptococcus pyogenes*)

cause sore throat and skin infection (impetigo, cellulitis, pyoderma), scarlet fever, necrotizing fasciitis, wound infections, pneumonia and puerperal sepsis. Invasive group A streptococcal infections (iGAS) occur when the organism enters the bloodstream, and can lead to streptococcal toxic shock syndrome. This is most likely following necrotizing fasciitis.
- Group A organisms may also cause post-infectious syndromes, such as rheumatic fever, glomerulonephritis and Sydenham's chorea.
- Group B streptococci (*Streptococcus agalactiae*) cause neonatal meningitis and septicaemia.
- Group C and G streptococci can cause upper respiratory infections such as tonsillitis.
- For *Streptococcus pneumoniae* (pneumococcus) see Chapter 3.55.
- Viridans streptococci are a common cause of bacterial endocarditis.

Suggested on-call action
Not usually necessary unless outbreak suspected.

Epidemiology

Streptococcal sore throat and scarlet fever are found worldwide, though less commonly in the tropics. Up to 20% of individuals may have asymptomatic pharyngeal colonisation with group A streptococci. Particular 'M types' are associated with various sequelae (for examples 1, 3, 4, 12 with glomerulonephritis). The incidence of sequelae depends upon the circulating M types. The *emm* gene codes for the M-protein. There are 120 *emm* types in GAS. In the 1980s there was an increase in iGAS in Western world, unexplained but possibly related to circulating more virulent *emm*-types. Acute rheumatic fever has become rare in most developed countries, though occasional cases and outbreaks are seen. It is associated with poor living conditions and is most common in the 3–15 age group.

Impetigo is most commonly seen in younger children. The M types associated with nephritis following skin infection are different from those associated with nephritis following upper respiratory infection.

Asymptomatic carriage of Group B Streptococci (GBS) is common in pregnant women.

Clinical features

- *Sore throat*: it can be difficult to differentiate streptococcal from viral sore throat; various scoring systems have been proposed but they lack predictive power.
- *Skin infection*: streptococcal skin infection commonly presents as acute cellulitis or impetigo (especially seen after chickenpox), erysipelas, pyoderma.
- *Scarlet fever*: may accompany pharyngeal or skin infection and is characterised by a skin rash, classically a fine punctate erythema, sparing the face, but with facial flushing and circumoral pallor. During convalescence, desquamation of the finger and toe tips may occur. Rare under three years of age.
- *Puerperal infection*: puerperal fever occurs in the postpartum or post abortion patient and is usually accompanied by signs of septicaemia.
- *Necrotising fasciitis*: involves the superficial and/or deep fascia; group A streptococci are implicated in about 60% of cases.

Laboratory confirmation

Streptococci are classified by a number of systems including haemolytic type, Lancefield group and species name.

Group A streptococcal antigen can be identified in pharyngeal secretions using rapid antigen detection; negative tests require confirmation. Detection of antibody to streptococcal extracellular toxins may be useful in the diagnosis of necrotizing fasciitis.

Confirmation is by culture on blood agar, the production of a zone of haemolysis and showing inhibition with bacitracin.

A rise in antistreptolysin O, anti-DNase or antihyaluronidase antibodies between acute and convalescent sera may be helpful in retrospective diagnosis.

In case of a possible cluster serotyping can be performed (T-types), DNA sequencing can identify *emm*–types (that have replaced the serological M-typing). Other typing systems are PFGE, MLST and Random Amplified Polymorphic DNA typing (RAPD).

Transmission

Human mucosa (nose, pharynx, vagina, perianal) and skin is the reservoir. Streptococcal infection is commonly acquired by contact with patients or carriers, through respiratory secretions (particularly nasal carriers) or skin contact. Healthcare workers failing to wash hands in between patient contact can transmit the bacterium. Transmission via contaminated foodstuffs, particularly unpasteurised milk and milk products is recognised. Group A streptococci can also be transmitted through environmental contact, for example contaminated towels and bedding.

Group B disease is acquired by the newborn while passing through the genital tract of the mother.

Acquisition

Group a streptococcal pharyngitis

The incubation period is 2–4 days (sore throat), 2–7 days (scarlet fever), 1–10 days (puerperal sepsis post-partum). The mean time for appearance of immunological sequelae is: 10 days for acute glomerulonephritis; 19 days (1–5 weeks) for acute rheumatic fever; and several months for Sydenham's chorea. The infectious period is commonly 2–3 weeks for untreated sore throat. Purulent discharges are infectious. Penicillin treatment usually terminates transmissibility within 48 hours.

Group B Infection in Infants

Early-onset infection occurs at a mean age of 20 hours. Late-onset infection occurs in infants with a mean age of three to four weeks, range one week to three months.

Immunity develops to specific M types and appears to be long-lasting. Repeated episodes due to other M types occur.

Prevention

Primary

- Personal hygiene, especially important for healthcare workers.
- Avoid unpasteurised milk.
- Reduce need for illegal abortions.

Secondary

- Prevention of immune-mediated sequelae.
- Prompt recognition, confirmation and treatment of streptococcal infection.
- Those with a history of rheumatic fever should be offered antibiotic prophylaxis to prevent cumulative heart valve damage. Prophylaxis should be for at least 10 years; for patients with established heart disease at should be at least until 40 years of age.

Prevention of group B streptococcal infection

- Intrapartum antibiotic treatment of women colonised with group B streptococcus appears to reduce neonatal infection and should be considered particularly if risk factors are present (prematurity, prolonged rupture of membranes, previous baby with neonatal GBS disease). The drug of choice is IV Penicillin G; IV clindamycin is an alternative for those allergic to penicillin.
- Routine screening to detect maternal colonisation is recommended in some countries (USA, Australia), but not in Europe at the present time.
- No vaccine is available, although several candidates are in development.

Surveillance

- Scarlet fever and/or puerperal fever are notifiable in some EU countries.
- STSS and necrotising fasciitis is also notifiable countries in some countries, and clusters in most.

Response to a case

- Report acute cases of scarlet fever, puerperal fever and post-streptococcal syndromes to local health authorities.
- Careful handling of secretions and drainage fluids until after 24 hours penicillin treatment.
- Personal hygiene advice to case and contacts. In hospital contact hygiene precautions for patients with necrotising fasciitis.
- Consider school/nursery exclusion until: 48 hours after start of antibiotic treatment.
- Hospital-acquired invasive group A streptococcal infections should be investigated for a possible source and isolates saved for six months.
- Antibiotic chemoprophylaxis is not routinely indicated for close contacts of a case of group A disease. Only administer antibiotics to mother and baby if either develops invasive disease in the neonatal period or to close contacts if they develop symptoms of localised group A disease. Oral penicillin V is the first line drug; azithromycin is a suitable alternative for those allergic to penicillin.

Investigation of a cluster

- Does epidemic curve suggest point source, ongoing transmission (or both) or continuing source?
- Type streptococcal isolates of patients in the cluster.
- Determine mode of transmission, exclude food-borne source, and particularly milk, urgently.
- Search for and treat carriers if considered a potential source of infection.

Control of an outbreak

- Activate the outbreak plan.
- Identify and treat carriers.
- For hospital outbreaks of invasive group A streptococcal infections, cleaning and decontamination of communal facilities, for example baths, bidets, showers, especially in high risk areas such as maternity units.
- Antibiotic chemoprophylaxis for household contacts of invasive group A disease is indicated when there are two or more cases within 30 days, or as a control measure in a community cluster or outbreak.
- Identify and remove contaminated food sources.

3.73 Tetanus

Tetanus is an acute illness caused by the toxin of the anaerobic tetanus bacillus, *Clostridium tetani*. The bacterium is able to form spores that are widely present in the environment and under specific circumstances are able to grow into a vegetative form and start producing toxin. Its public health significance is the severity of the disease and its preventability by vaccination.

Suggested on-call action
None required for public health team.

Epidemiology

Tetanus is rare in Europe, although there is probably significant under ascertainment of mild cases. In 2014 there were 48 confirmed cases (0.02 per 100 000) of which 35 were reported in Italy. There has been a steady decline in cases in recent years. Most cases are in unvaccinated people over 65 years of age, although outbreaks have occurred among

young-adult injecting drug users. The case fatality is about 10%. Neonatal tetanus, due to infection of the umbilical stump, is common in parts of Asia and Africa. In 2015 there were an estimated 34 000 deaths from neonatal tetanus. This is a 96% reduction since 1988, and represents substantial progress towards the WHO goal of elimination of maternal and neonatal tetanus.

Clinical features

In classical tetanus there are painful muscular contractions, especially of the neck and jaw muscles (hence the name 'lockjaw'), muscular rigidity and painful spasms, leading to high case-fatality. The symptoms can be mild in a vaccinated person. There is usually a history of a tetanus-prone wound (which may be a minor prick) or a burn, although not always.

Laboratory confirmation

This is infrequently obtained and unnecessary in typical cases. It is sometimes possible to culture the organism from the site of the original wound.

Transmission

The reservoir is the intestine of horses and other animals, including humans. Tetanus spores are found in soil contaminated with animal faeces. Transmission occurs when spores are introduced into the body through a dirty wound, through injecting drug use, and occasionally during abdominal surgery. Person-to-person spread does not occur.

Acquisition

The incubation period is 3–21 days, depending on the site of the wound and the extent of contamination; occasionally it may be up to several months. Under specific circumstances (low oxygen) the spores germinate and the bacterium starts producing a toxin that causes the symptoms. The toxin does not cross the blood–brain barrier; transport to the CNS is through neurones. Natural immunity does not follow an attack of tetanus.

Prevention

- Vaccination with tetanus toxoid. Three doses in infancy with two additional boosters are required. Further boosters may be required at the time of injury. In a fully vaccinated individual, routine boosters are not justified, other than at the time of injury.
- Give tetanus vaccine (and tetanus immunoglobulin for tetanus-prone wounds) at the time of injury where more than 10 years have elapsed since the last dose of vaccine. This may also be an opportunity to boost immunity against diphtheria, pertussis and polio.
- Give tetanus vaccine and tetanus immunoglobulin (TIG) as soon as possible after injury in unvaccinated and immune incompetent patients. The dose of tetanus immunoglobulin is 250 IU by i.m. injection; 500 IU if more than 24 hours have elapsed since the time of injury; unlikely to be of value if given more than 3 weeks after injury.
- Promote safe techniques in injecting drug users (see Chapter 4.9)

Surveillance

- Notifiable in most European countries.

Response to case

- Seek injury history, ascertain vaccination status and arrange for primary course or booster, depending on history.

Response to a cluster or outbreak

- Outbreaks of tetanus are rare. Look for a common source, for example surgery, injecting drug misuse.

- Injecting drug misuser outbreak – liaise with drug services to promote safer drug use and with clinicians to promote early diagnosis and treatment.

Suggested case-definition
Physician diagnosis of tetanus.

3.74 Threadworms

Suggested on-call action
None

Epidemiology

Threadworm (pinworm) infection is an intestinal infection with *Enterobius vermicularis,* a nematode of the family *Oxiuridae*. It is widespread in temperate regions, particularly among school-aged children. Clusters of cases may occur in household and residential care settings. It is estimated that between 5 and 24% of children are positive for *E. vermicularis* in western societies, although the prevalence has been decreasing over time. Studies of Swedish children between 4 and 10 years old showed a high prevalence (24–28%), with a peak prevalence of 33% in 6–7 year-old children. The highest prevalence has been reported among children aged five to eight years, and it is unusual to find *E. vermicularis* in children less than two years old.

Clinical features

Infection is commonly asymptomatic. In symptomatic infections there is perianal itching and sleep disturbance. Appendicitis, vulvitis and chronic salpingitis are rare complications of worm migration. Adult worms live in the caecum and may be seen in faeces or on perianal skin.

Transmission and acquisition

Humans are the only known host. Mature female worms are 8–12 mm in length and migrate through the anus and lay thousands of eggs on the perianal skin. These infectious eggs develop within five to six hours and, as a result of perianal scratching, are transferred directly to the mouth or to others on fingers. They are also spread indirectly on fomites such as bedding, clothing, and in environmental dust. Eggs can survive in moist conditions for up to three weeks. Larvae emerge from the eggs in the small intestine and develop into sexually mature worms. Adult worms do not live for longer than six weeks. Re-infection is common and retro-infection can also occur as a result of hatched larvae migrating back through the anus from the perianal region.

Diagnosis

The diagnosis can be confirmed by the presence of eggs on a strip of transparent adhesive tape that has been pressed on to the anal region early in the morning and then examined under a microscope. Diagnostic yield improves with repeated sampling.

Prevention

Control is by prompt recognition and treatment of cases and their household contacts, health education and attention to personal and environmental hygiene, particularly hand washing. The perianal area may be washed each morning to remove eggs and bedding and nightclothes should be changed regularly. Exclusion from school is unnecessary.

Response to a case/cluster/outbreak

- Anti-helminthics such as albendazole or mebendazole are effective against adult worms, but must be combined with strict

personal hygiene measures to break the cycle of auto-infection.
- All household members should be treated at the same time (may include institutional residents, classmates, and so on).
- An initial course of treatment should be followed by a second course two weeks later to kill worms which have matured in the intervening time period.

3.75 Tick-borne Encephalitis

Tick-Borne Encephalitis (TBE) is a flavivirus infection of the Central Nervous System (CNS), characterised by a biphasic meningo-encephalitis.

Suggested on-call action
No specific public health action usually required.

Epidemiology

TBE has a focal distribution throughout forested areas of countries in central and eastern Europe and parts of Scandinavia. Based on serological criteria three subtypes of the virus (TBEV) are identified with specific geographical spread: European (TBEV-Eu), Siberian (TBEV-Sib), and Far-East (TBEV-FE). TBE became notifiable at the EU level in 2012; in 2015 there were 1949 notified cases, an incidence of 0.4 per 100 000. The incidence is highest in the Baltic states. In the last decades several new endemic foci have been identified in Europe. Disease reports have increased (except in Austria) due to better detection, behavioural change (recreation), housing (in endemic areas) and climate change. Related infections occur in Russia (but more severe), and North America. The disease is most common in early summer and autumn.

Clinical features

It is not certain whether asymptomatic infections can occur. Classical symptoms are fever, headache, fatigue and general body pain, varying from mild to severe, partly depending on TBEV subtype. Disease due to TBEV-Eu (Früh-Sommer-Meningo-Encephalitis FSME) is biphasic (a viremic and a neurological phase), less severe, has neurological symptoms, Case-fatality of <2% and chronic sequelae. Russian epidemic encephalitis (TBEV-FE) is monophasic, runs a more serious course, has frequent encephalitis symptoms, high mortality (5–35%), but no chronicity or sequelae. TBE due to TBEV-Sib is also monophasic, less severe, has a case-fatality of 1–3%, but has no chronicity.

Diagnosis

The diagnosis should be considered in a patient with neurological symptoms with a history of a tick bite in an endemic area. Laboratory confirmation is by serology (IgG and IgM) or virus isolation from blood or CSF (preferably in a specialist laboratory, as cross reaction from other flaviviruses may occur, requiring virus neutralisation assays). Other tick-borne flaviviruses including louping ill (which occurs occasionally in Scotland and Ireland), langat virus and Powassan virus produce a similar encephalitis.

Transmission and acquisition

Ixodes ricinus, the woodland tick, is the principal reservoir in central and northern Europe for TBEV-Eu; for TBEV-Sib and TBE-FE in Eastern Europe and Russia, *Ixodes persculatus* is the principal reservoir. In a small geographical area in and surrounding St Petersburg (Karelia, eastern part of Estonia and Latvia), all three subtypes are found. The virus is transmitted immediately after the bite in tick saliva. Early tick removal does not prevent infection (unlike Lyme disease, where it does prevent transmission). Infection by

unpasteurised milk occurs. Rarely transmission is reported through breast milk, blood transfusion, while slaughtering, in the laboratory. Sheep and deer are also hosts for louping ill.

The incubation period is 7–14 days (range 2–28 days, average 8 days); after ingestion of contaminated milk, 3–4 days. Person-to-person transmission does not occur.

Prevention

- Wear protective clothing against tick bites in endemic areas.
- Use insect repellent, for example those containing DEET.
- Inspect skin frequently and remove any attached ticks (may prevent Lyme disease).
- Killed vaccines are available and are recommended for at risk travellers and residents, particularly those in occupations such as forestry and farming. A national vaccination campaign in Austria reduced incidence from 600 per annum in 1980s to 60 in 2000.

Response to a case

- No specific public health action usually required.
- Post-exposure prophylaxis with a specific immunoglobulin is no longer available in Europe, as disease was more serious in immunised individuals.

3.76 Toxocariasis

Toxocariasis is a zoonotic infection caused by a parasitic roundworm of dogs (*Toxocara canis*) or cats (*Toxocara cati*) which occasionally infects man.

Suggested on-call action
None required

Epidemiology

Infection is found worldwide and is more common in young children and owners of cats and dogs. Reported seroprevalence of *Toxocara* spp. infections in humans varies between 3 and 19% in European countries, varying by diagnostic methods, age profile (highest in young people) and cultural habits.

Clinical features

Infection is commonly asymptomatic. There are two main clinical categories of toxocariasis:

Visceral larvae migrans is a self-limiting illness that is more common in children under the age of six years and is characterised by cough, fever, wheezing, an urticarial rash and eosinophilia.

Ocular larvae migrans usually occurs in children aged 5–10 years and is characterised by unilateral impairment of visual acuity.

Covert toxocariasis is a less common form with a subtle presentation that may include such symptoms as abdominal pain, cough and headache.

Laboratory confirmation

Diagnosis is based on detecting antibodies to *T. canis* larvae using an ELISA test.

Transmission

Toxocariasis is not spread by person-to-person contact. Humans are infected by ingesting viable eggs and the highest risk is in children with pica (eating dirt).

The larvae can remain dormant in dogs for long periods; migrate transplacentally and from the mother's milk to infect the pups. Most pups are infected at the time of whelping; the adult worms produce eggs until the majority are expelled, usually when the pups are six months old. The eggs, which are the source of human infection, survive in the

environment for many years, particularly in settings such as play sandpits and recreational parks.

Acquisition

Incubation period is variable and lasts between one week and two years.

Prevention

- Regular deworming of dogs.
- Hygienic disposal of dog faeces and regular cleaning of pet areas.
- Maintain good levels of hand hygiene.
- Cover play sandpits when not in use.

Response to a case

- No public health response is usually needed in response to cases.
- Most patients recover without specific treatment, but anthelminthic drugs can be considered.

3.77 Toxoplasmosis

Toxoplasma gondii is a protozoan parasite that causes a spectrum of disease from asymptomatic lymphadenopathy to congenital toxoplasmosis, ocular toxoplasmosis, and encephalitis in the immunocompromised.

Suggested on-call action
None required unless food-borne outbreak is suspected

Epidemiology

Human exposure to toxoplasmosis is worldwide and common. It is estimated that around two billion people worldwide are infected with *T. gondii*, although seroprevalence studies show considerable geographical variation. Seropositivity rates vary from <10 to >80%; in the UK seroprevalence is between 20 and 40% in adults while seroprevalence is higher in Central Europe, South and Central America, and in West Africa (30–80%) and similar or lower in South East Asia, China and Korea (4–39%) and Scandinavia (11–28%).

Clinical features

There are a number of clinical presentations. Infection is usually asymptomatic in around 80–90% of immunocompetent cases, but may produce an influenza or mononucleosis-like illness. Infection can be fatal in immunocompromised persons. Congenital infection, which may follow acute infection during pregnancy, is characterised by CNS involvement, retinochoroiditis and can cause intrauterine death. Immunocompromise may result in cerebral reactivation of toxoplasmosis with may present as encephalitis.

Laboratory confirmation

Acute toxoplasmosis may be diagnosed serologically. Specific IgM antibodies appear during the first two weeks, peak within four weeks, and then typically become undetectable within several months. IgG antibodies rise more slowly, peak in two to three months, and usually persist for life.

Serology is less useful for diagnosis of toxoplasmosis in patients with AIDS. Cerebral toxoplasmosis is usually diagnosed on the basis of clinical features, a positive agglutination test and CT/MRI scan appearance. PCR on fluid or tissue, or culture may be helpful in cerebral, ocular and congenital disease.

Transmission

The cat is the definitive host and oocysts are shed in cat faeces. Hand-to-mouth transmission occurs through contact with oocysts

from pets, soil, or sandpits; oocysts can survive in the environment for over a year.

Infection may also occur through contact with, or ingestion of, tissue cysts in raw or undercooked infected meat; water containing oocysts; or very rarely through transplanted solid-organs.

Acquisition

- Incubation period: 10–25 days.
- Transmissibility: No person-to-person spread.

Prevention

- Advice to maintain adequate levels of hygiene (particularly food and hand hygiene).
- Pregnant women in particular should avoid raw or undercooked meat. Contact with soil or food possibly contaminated with cat faeces should be avoided.
- Chemoprophylaxis has been recommended for AIDS patients with positive IgG serology once CD4 cells are low.
- Protect sandpits and play areas from cats.

Surveillance

Report to local public health authorities. Some countries have surveillance of congenital toxoplasmosis.

Response to a case, investigation of a cluster and control of an outbreak

Investigate likely exposure to cat faeces, and raw or undercooked meat.

Suggested case definition for an outbreak

Confirmed: Isolate or IgM antibody confirmed.

Probable: Acute fever and lymphadenopathy in person linked epidemiologically to confirmed case.

3.78 Tuberculosis (and non-tuberculous mycobacteria)

Tuberculosis (TB) is an infection of the lungs and/or other organs, usually by *Mycobacterium tuberculosis*, but occasionally by other species such as *Mycobacterium bovis* or *Mycobacterium africanum*. TB may have a long incubation period, produces chronic infection with risk of reactivation and, without treatment, would often be fatal.

Suggested on-call action

If the case is a healthcare worker, teacher or other person in contact with particularly susceptible individuals, consult the outbreak control plan or SOP. However action can usually wait until the next working day.

Epidemiology

Over 60 000 cases of TB were reported in 30 EU/EEA countries in 2015, an incidence rate of 11.7 per 100 000; this rate has fallen consistently in the last decade reported (2006–2015). TB incidence rates vary 17-fold across the EU (Table 3.78.1) and rates have not declined in Cyprus, Germany and Malta. About 30% of EU/EEA cases are in people who originate from outside the reporting country (definition varies by country): rates are substantially higher in south Asia and are extremely high in much of Sub-Saharan Africa, where many immigrants originated. Where data were available, incidence rates in the prison population was an average of 10 times that in the general population. About 4.1% of EU/EEA cases who were tested had multi-drug resistant TB (MDR TB), with the highest rates in the three Baltic countries: about 20% of MDR cases tested were classified as extremely resistant (XDR TB). Much higher rates of drug resistant TB are

Table 3.78.1 TB rate in European countries, 2015

Country	Rate per 100 000
Iceland	2.1
Greece	4.4
Czech Republic	4.9
Finland	5.0
Netherlands	5.1
Luxembourg	5.3
Slovakia	5.8
Italy	6.2
Denmark	6.3
Slovenia	6.3
Norway	6.3
Ireland	6.7
Austria	6.8
Germany	7.2
France	7.2
Cyprus	7.4
Malta	7.5
Sweden	8.4
Belgium	8.8
Spain	9.0
Hungary	9.2
UK	9.6
Croatia	11.5
Estonia	16.5
Poland	16.9
Portugal	20.5
Bulgaria	23.0
Latvia	36.3
Lithuania	51.6
Romania	76.5

(Source: Reports to ECDC).

reported from (non-EU) countries of the former Soviet Union (up to 50%), including those that border the EU, with rates particularly high in previously treated cases. An estimated 4.6% of cases in EU/EEA countries are also infected with HIV, with the highest proportion in Latvia (26%). Over 4500 deaths from TB are estimated to have occurred in the EU/EEA in 2015, a mortality rate of 0.9 per 100 000 population.

2016 data for England shows that 5664 cases were identified by enhanced surveillance, a rate of 10.2 per 100 000; this is the lowest rate since 2000, although the rate of decline has slowed. Marked ethnic differences are apparent: about 75% of cases are now in non-white groups, with rates highest in Black Africans and South Asians. Rates are about 15 times higher in those born abroad, with a median time from entry (to the UK) to development of disease of 9 years (interquartile range 3–16 years): the most commonly reported countries of birth are India, Pakistan, Somalia, Bangladesh and Romania. Rates, at least in whites, are higher in deprived communities and rates are generally higher in inner city areas. Other risk factors for TB include HIV infection, other causes of immunosuppression, previous diagnosis of TB, chronic alcohol misuse and socially marginalised groups such as the homeless, refugees, drug users and prisoners. Exposure to infectious TB cases in institutions such as hospitals, schools and prisons are regular public health incidents.

Clinical Features

TB is a biphasic disease. Only about 5% of those who have primary infection develop clinically apparent primary disease, either from local progression in the lungs, or haematogenous or lymphatic spread to other sites. Such spread may lead to serious forms of the disease such as meningitis or miliary TB occurring within a few months of the initial infection.

In the remaining 95%, the primary TB lesion heals without intervention, although in at least half of patients, bacilli survive in a latent form that may reactivate in later life. Of those originally infected, 5% will develop post-primary disease. The risk of reactivation increases with advanced age, chronic disease and immunosuppression (e.g. AIDS). Reactivated TB is often pulmonary and, without treatment, carries a high mortality. The risk of reactivation is lifelong, but half of cases occur within five years of the original infection and most primary infections will never re-activate.

Two-thirds of TB in the UK is pulmonary disease, which is initially asymptomatic, although it may be detected on chest X-ray. Early symptoms may be constitutional, such

Table 3.78.2 Typical action in response to tuberculin test results (UK example)

Test Result		Interpretation and action	
Heaf Grade	*Mantoux (100 units ml^{-1})*	*Scar from previous BCG*	*No BCG scar*
0/1	0–5 mm	Negative No action[a]	Negative Give BCG[a]
2	6–14 mm	Positive Compatible with previous BCG: usually no action[b]	Positive Risk assessment[c]
3/4	15 mm plus	Strongly positive Investigate	Strongly positive Investigate

[a] *Unless contact of case (may need repeat test).*
[b] *But does not rule out active TB.*
[c] *Action will vary with reason for test, size of reaction and patient circumstances.*

as fatigue, fever, night sweats and weight loss, and often insidious in onset. Chest symptoms often occur in later disease, including cough (usually productive), haemoptysis and chest pain. Hoarseness and difficulty swallowing may occur in laryngeal TB. Symptomatic screening for cases is highly sensitive (most cases have symptoms on enquiry), but not very specific (many other diseases also cause similar symptoms). Chest X-ray has high sensitivity and medium specificity. Specificity is high for sputum smear and very high for sputum culture, but smears detect only about 60% of culture-positive cases.

Non-pulmonary TB is more common in children, ethnic minorities and those with impaired immunity. The most commonly affected sites are lymph nodes, pleura, genitourinary system and bones and joints. Constitutional or local systems may be reported. Diagnosis may be supported by a tuberculin test (Table 3.78.2), CT/MRI/ultrasound imaging, and biopsy results: Over 90% of non-AIDS cases are tuberculin test positive. Interferon-gamma release assays (IGRA), which use whole blood to measure T-cell interferon-gamma release in response to TB antigens, have become available and can help identify active and latent infection: IGRAs may offer advantages over tuberculin testing, in vaccinated populations or in areas with high exposure to environmental mycobacteria or in immunocompromised patients/contacts or in hard-to-reach groups.

Laboratory Confirmation

Rapid presumptive diagnosis of infectious cases can be achieved by microscopy of sputum samples (preferably early morning and deep cough samples): *M. tuberculosis, M. bovis* and *M. africanum* all stain poorly with Gram-stain, but staining with Ziehl–Neelson (ZN) stain reveals acid-fast (and alcohol-fast) bacilli (AFB). In most laboratories, mycobacteria are detected by auramine fluorescent staining and the results are available within one working day. As a general rule, sufficient bacilli in the sputum to be detectable by standard methods equates to sufficient to be infectious and three consecutive negative sputum smears is usually assumed to represent non-infectiousness. Although this test is usually sufficient to begin treatment and contact tracing, follow up culture (preferably liquid culture) is essential as AFBs may occasionally be other species of mycobacteria (see Box 3.78.1), culture also increases the sensitivity of diagnosis for cases of lower infectivity, and it allows antibiotic sensitivities to be checked.

Box 3.78.1 Non tuberculous mycobacteria (NTM)

- Also known as atypical, environmental, anonymous, tuberculoid or opportunistic mycobacteria or mycobacteria other than TB (MOTT).
- Includes *Mycobacterium avium, Mycobacterium intracellulare, Mycobacterium chaemera* and *Mycobacterium scrofulaceum* (collectively known as *M. avium* complex). Also includes *Mycobacterium kansasii, Mycobacterium malmoense, Mycobacterium marinum, Mycobacterium xenopi, Mycobacterium fortuitum, Mycobacterium chelonae, Mycobacterium absessus, Mycobacterium haemophilium, Mycobacterium marinarum, Mycobacterium paratuberculose, Mycobacterium simiae, Mycobacterium ulcerans* and others.
- Common environmental contaminants. Occasionally found in water supplies, swimming pools or milk. Some cause nosocomial infections, for example through contamination of medical equipment. Person-to-person spread rare.
- Varying pathogenicity. *M. avium* complex and some others may be a rare cause of pulmonary disease in immunocompetent individuals, disseminated disease in immunosuppressed people and cervical lymphadenitis.

Specimens should be cultured using rapid automated liquid culture and by conventional solid culture. *M. tuberculosis* is usually detected and identified within 7–21 days, depending upon biomass. Laboratories may also offer direct molecular testing of samples which is more sensitive than a smear, but less sensitive than culture: these tests will identify some smear negative, culture-positive cases much more rapidly than culture, which will allow earlier treatment, although the infectivity of such cases is unclear: these tests can also confirm that AFBs seen on a smear are from the *M. tuberculosis* complex, which may be helpful in immunocompromised patients or when large contact-tracing exercises are being considered. Molecular tests can also be used on non-respiratory samples. Positive samples or isolates should be submitted to a reference laboratory, where identification normally includes DNA analysis. Drug sensitivity testing should be performed and results are usually available in 14 days.

Genotyping is useful in identifying and investigating clusters of cases, with WGS being more discriminatory than MIRU-VNTR, and may be available from reference laboratories: genotyping is routine in England.

Transmission

Almost all TB in Europe is contracted by inhalation of *M. tuberculosis* bacilli in droplet nuclei. These nuclei derive from humans with pulmonary or laryngeal TB predominantly by coughing, although sneezing, singing or prolonged talking may contribute. Such nuclei may remain suspended in air for long periods. The risk of transmission depends upon the amount of bacilli in the sputum, the nature of the cough, the closeness and duration of the interaction and the susceptibility of the contact (Box 3.78.2). Without treatment, an average case of pulmonary TB would infect 10–15 people per year.

Bovine TB may be contracted by ingestion of raw milk from infected cows and occasionally via the air-borne route. Although *M. bovis* has increased in cattle in the UK and some other European countries in recent years, human cases may also represent reactivation of infection acquired before routine treatment of milk supplies and testing of cattle.

Direct transmission, either through cuts in the skin or traumatic inoculation (e.g. prosector's wart) is now rare. Droplet aerosols may be generated in healthcare settings from

Box 3.78.2 How to assess the likelihood of transmission of TB

1 How infectious is the source case?
- Sputum smear positive: infectious to any close contact.
- Smear negative, culture positive: possibly infectious to highly susceptible contacts.
- Sputum negative, bronchial washing positive: possibly infectious to highly susceptible contacts.
- Three consecutive sputum negatives: not infectious.
- Two weeks appropriate treatment: not infectious.
- Non-pulmonary/laryngeal disease: not infectious.
- Children, even if smear positive, are usually less infectious than adults.

2 How significant is the exposure?
- Exposure to coughing is the most important risk, but sneezing, singing and long (more than five minutes) conversation can also produce many infectious droplets.
- Prolonged or multiple indoor exposure usually needed to infect most contacts. Eight hours is often taken as a proxy (e.g. for exposure on aircraft).
- Aerosols may persist after case leaves room.
- Dishes, laundry, and similar items not infectious.
- Estimates of risk from specific exposures to infectious case in one review (although there may be reporting bias inflating some of these figures):
  - Household: 1 in 3
  - Dormitory: 1 in 5
  - Bar or social club: up to 1 in 10
  - Nursing home: 1 in 20
  - School or workplace: 1 in 50 to 1 in 3
  - Casual social contact: 1 in 100 000
  - Background rate: 1 in 100 000

3 How susceptible is the contact to infection and/or disease?
- Susceptibility by age: Neonates, very high; Age under five years, high.
- Bacille Calmette–Guérin (BCG) vaccine reduces risk by 50–80% in developed countries.
- Immunosuppressed at very high risk: includes AIDS, lymphoma, leukaemia, cancer chemotherapy, solid organ transplant and oral corticosteroids (equivalent to 15 mg prednisolone per day)
- Severe malnutrition leads to increased risk. Post-gastrectomy or jejunal-ileal bypass patients at risk if underweight.
- Other risk factors for progression to active disease include excessive alcohol intake, injecting drug use, diabetes, chronic kidney disease, treatment with anti-tumour necrosis factor-alpha or other biologic agents and silicosis.

surgical dressing of skin lesions, autopsy, bronchoscopy and intubation.

Acquisition

The incubation period, as defined by reaction to a tuberculin test, is usually 3–8 weeks (occasionally up to 12 weeks). The latent period may be many decades, with the risk lifelong.

The infectious period is for as long as there are viable organisms in the sputum: cases are usually considered infectious if organisms demonstrable on sputum smear. Appropriate chemotherapy renders most patients non-infectious in two weeks.

Acquisition of an infective dose usually requires prolonged exposure and/or multiple aerosol inoculae, although some strains appear to be more infectious.

Immunity usually occurs after primary infection and involves several responses, including delayed-type hypersensitivity, the basis of the tuberculin test. Conditions such as AIDS, which affect cellular immunity, increase the risk of disease. Reactivation of latent disease may also be triggered by treatment of autoimmune disorders with anti-TNF drugs. Other risks are given in Box 3.78.2.

Prevention

Control of TB in developed countries has a number of components:

- Limitation of infectiousness by early diagnosis and treatment. This includes encouraging earlier presentation in the general population, earlier diagnosis by clinicians and targeted case-finding in higher-risk groups.
- Limitation of antimicrobial resistance by appropriate multidrug therapy (consult national guidelines) and measures to maximise compliance, such as directly observed therapy (DOTS) and patient-centred case-management, particularly in socially marginalised groups and those already identified as having a drug-resistant infection. Tuberculosis outcome surveillance is important to assess the effectiveness of control services.
- Identification and treatment of further cases by contact tracing in response to notifications of TB (see Chapter 4.10). Up to 10% of clinical cases in the UK are found by this method. In addition, potentially latently infected individuals can be identified and non-immune contacts offered BCG immunisation.
- Those contacts aged up to 35 years with evidence of infection without active disease (latent infection) can be protected by chemoprophylaxis to prevent later disease developing (either 3 months isoniazid, pyridoxine + rifampicin, or 6 months isoniazid + pyridoxine): it can also be considered for adults aged 35–65 years if hepatotoxicity is not a concern. Prophylaxis may also be recommended for young children or those with HIV who are contacts of an infectious case of TB, even if tuberculin negative.
- BCG vaccine of infants reduces the risk of TB disease and death. Immunisation of previously-unvaccinated school children has an efficacy against TB of about 77%, lasting at least 15 years. A similar effect would be expected against drug resistant strains. Vaccination is recommended in the UK (provided the individual has no previous BCG, is tuberculin test negative and has no other contraindications) for:
  - All infants living in areas where the annual incidence is 40 per 100 000 or greater.
  - Children under 16 with a parent or grandparent born in a country where the annual incidence is 40 per 100 000 or greater (tuberculin test first for those aged six years or over).
  - Children under 16 who are contacts of cases of respiratory TB.
  - Children under 16 who were born in or have lived for a prolonged period in or are going to live with local people for more than three months in a country where the annual incidence is 40 per 100 000 or greater.
  - New arrivals aged 16–35 from sub-Saharan Africa or a country with a TB incidence of 500 per 100 000 or more.
  - Healthcare staff of any age who have contact with patients or clinical specimens.
  - People in occupations with increased risk of coming into contact with TB, (if under 35 years old) for example certain roles in veterinary, prison, care home and hostel settings.
- BCG is not recommended in many European countries: check national policy.
- Screening of immigrants and refugees from high prevalence countries for active disease, latent infection and lack of immunity may be offered as part of a total health package in their new district of residence. Such individuals can be identified from a combination of Port Health forms, GP registers, school registers, refugee hostels and community groups.
- Improving services for people who have social risk factors, including homeless people, those in contact with the criminal

justice system, and those with drug, alcohol or mental health problems. This includes active case finding (e.g. mobile X-ray for homeless/drug user settings, new prisoner screening) and improving treatment completion rates.
- Infection control and occupational health services in healthcare settings to reduce exposure of patients to infected healthcare workers or potentially infectious patients, with particular care in units dealing with immunocompromised patients and units likely to admit patients with TB, including pre-employment screening.
- More detailed guidance from a 2016 systematic review of preventing, identifying and managing TB can be found at: www.nice.org.uk/guidance/ng33.

Surveillance

- All forms of clinical TB are notifiable in almost every European country, including the UK.
- The two main sources of surveillance data are notifications of clinical cases from clinicians (such as respiratory physicians) and positive reports from microbiology laboratories. Other potential sources are pathologists (histology and autopsy), surgeons and pharmacists. Reliance on only one source will lead to incomplete ascertainment.
- District TB registers are useful and may include data on
  - Age, sex, ethnicity, country of birth, place of residence, social risk factors.
  - Type of disease, sputum status, antibiotic sensitivities.
  - Treatment outcome.
- Enhanced surveillance of TB has been introduced into a number of EU countries, including the UK, where district co-ordinators collect a standardised dataset on all new cases, which is forwarded to regional and national databases, to be linked to laboratory data.
- Genotyping data, if available, can be used to detect possible clusters for further investigation.
- The joint ECDC/WHO surveillance programme collects data on TB from national centres throughout Europe. However, reporting systems differ substantially between contributing countries, making comparisons difficult.

Response to a case

- All TB cases should be notified to local public health departments.
- Investigate whether infectious by three early morning deep cough sputum samples for microscopy and culture.
- Ensure isolate tested for drug resistance.
- Early treatment with standard multidrug therapy: see national guidelines (e.g. www.nice.org.uk/guidance/cg117 in UK). Modify if tests reveal drug resistance.
- Consider appropriate measures to maximise compliance with treatment, for example directly observed therapy in higher risk cases.
- Most cases can be treated at home and this is encouraged for those who do not require hospital-level care. There is no need to segregate cases from other household members, unless they are neonates or immunocompromised, but congregate settings should be avoided until the first two weeks of appropriate treatment has been successfully completed.
- Those treated in hospital who are smear positive (or pulmonary or laryngeal disease with results pending) should be segregated in a single room, preferably with measures to reduce airflow to other patient areas. Particular care is needed in units containing immunocompromised patients or if the case is suspected to have drug-resistant TB: those with multi-drug resistant TB should ideally be placed in a negative pressure room.
- Adults with smear-negative disease, non-pulmonary disease and most of those who have been on appropriate treatment for two weeks do not require isolation. Persons visiting children with TB in hospital (one of whom may be the source case) should

be segregated from other hospital patients until they have been screened.
- Screen household contacts of cases of TB. For smear-positive cases, also assess other close contacts with household level exposure, for example boyfriend/girlfriend and frequent visitors.
- Inform and advise other contacts.
- Casual contacts (such as social and workplace contacts) do not require routine screening. This can be re-considered if the case is smear positive and either:
  - the contact is unusually susceptible to TB (e.g. young child or immunocompromised adult), or
  - the case appears to be highly infectious (e.g. more than 10% of contacts infected).
- Check that the index case and any secondary cases are not healthcare workers, teachers or others who work with susceptible people (Box 3.78.3).

Investigation of a cluster

- Aim is to discover whether there is an unrecognised infectious source.
- Check diagnosis of cases. Are they confirmed microbiologically? Beware the occasional 'pseudo-outbreak' (e.g. if all cases confirmed by same laboratory).
- Liaise with reference laboratory for genotyping of all isolates to look for potentially linked cases.
- Any clinical or epidemiological clues as to whether cases have recent or old infection?
  - age and previous residence abroad.
  - clinical and radiological signs.
  - risk factors for new infection (e.g. contact with case or travel to, or visitor from, high prevalence country)?
  - risk factors for reactivation (e.g. diabetes, renal failure)?
- Obtain microbiological samples on all non-confirmed cases.

Box 3.78.3 How to manage specific TB scenarios

(NB – Check if national guidelines available, e.g. *NICE in UK)*

1 *If the case is a healthcare worker with patient contact* (or a patient found to have TB after admission onto an open ward):
- Decide how infectious the case is:
  (a) respiratory or laryngeal TB?
  (b) cough, or cavities on chest X-ray?
  (c) sputum smear and/or culture positive?
  (d) results of screening of close contacts?
  (e) duration of treatment + antibiotic sensitivity (e.g. multidrug resistant)?
  (f) infection control procedures in place before isolation?
- Decide how long the case has been infectious, in particular duration of cough.
- If case is thought to be infectious, convene Incident Management Team including the following:
  (a) hospital control of infection staff;
  (b) senior hospital manager;
  (c) local health protection consultant (CCDC);
  (d) physician with expertise in TB;
  (e) contact tracing services (TB health visitor);
  (f) medical records manager;
  (g) manager of affected ward/unit;
  (h) occupational health;
  (i) press officer,

- Draw up list of contacts. Consider:
  (a) inpatients, outpatients, referrals from other consultants;
  (b) other members of staff;
  (c) classifying contacts by level of exposure (e.g. patients for which case was 'named nurse' could be classified higher exposure and other patients on ward as lower exposure. For patient index, higher exposure could be defined as eight hours in same bay as infectious case with cough).
- Decide whether any of these contacts are particularly susceptible to TB (Box 3.78.2):
  (a) ask medical and nursing staff who treated them; and
  (b) review case notes.
- Organise screening of highly susceptible contacts (remember incubation period of up to three months since last contact with case).
- Inform and advise other contacts and their clinical team and write to their GPs so that exposure is noted.
- Consider need for helpline and press release for worried patients.
- Reconsider actions when results of screening and culture results are known.

2 *If the case is a teacher or pupil at a school*

- If the teacher is potentially infectious, assess all children in relevant teaching groups during the last three months.
- Although children rarely infectious, if child case is sputum smear-positive, risk assess need to test other children who share classes with the case.
- Consider other pupils and staff based on infectivity of index case, susceptibility of contact and proximity and duration of contact.
- Explain plan to staff and parents and prepare for press interest.
- Treat secondary cases of smear-positive TB as index cases for further contact tracing.
- Reassess in light of initial screening results.
- If potential source not found for child case in screening of household or in school and child not in a higher incidence group, consider contact tracing and screening of other staff.

3 *If the case has recently been a passenger on an aircraft*

- Check if patient sputum smear (and preferably culture) positive.
- Was flight within last three months and over eight hours in duration?
- Did the passenger have a frequent cough at time of flight or does patient have multi-drug-resistant TB?
- If the criteria above are satisfied, ask the airline to identify passengers in the same part of the aircraft and contact them by letter.
- 'Inform and advise' letter to recommend passengers to contact their own doctor and give a central telephone number for advice.
- Inform health authorities for areas with affected passengers.
- An interactive flowchart, based on the recommendations of a systematic review of the evidence for investigation and management of contacts is available from NICE at: https://pathways.nice.org.uk/pathways/tuberculosis#path=view%3A/pathways/tuberculosis/tuberculosis-contact-tracing-and-testing.xml:S_P_I_A_M_Pcontent=view-index. Other flowcharts (e.g. managing latent TB) are also available from this site.

- Undertake a hypothesis-generating study. Include family links, social networks, social venues, leisure and hobbies, links to institutions, especially those containing highly susceptible individuals and/or overcrowding (hospitals, nursing homes, schools, jail, homeless hostels) and for travel to (or visitor from) a high prevalence country.
- Social network analysis can be useful in complex community outbreaks to identify potential key individuals and places involved in transmission, to demonstrate potential transmission chains and to ensure that all potential cases and contacts are identified and followed up.
- Check drug sensitivities and compliance with treatment for known respiratory cases associated with cluster.

Control of an outbreak

- Undertake contact tracing for known cases to identify and treat undiscovered infectious cases (and others with infection or disease who would benefit from treatment).
- In outbreaks linked to hospitals:
  1 Look for an unsuspected infectious source, for example:
  - patient with MDR TB remaining infectious despite prolonged therapy (check sensitivity results).
  - smear negative cases infecting highly susceptible contacts (check culture and PCR results).
  - delayed diagnosis in AIDS cases (do not rely on classic clinical picture or Mantoux).
  - health care worker, patient or visitor with undiagnosed TB (chronic cough unresponsive to antibiotics?).

  2 Consider breakdown in infection control procedures, for example:
  - procedures such as bronchoscopy, sputum induction, and pentamidine inhalation may generate aerosols.
  - inadequate isolation of sputum positive patients.
  - inadequate decontamination of multi-use equipment.

Suggested case-definition for use in an outbreak

Confirmed: Clinically compatible illness with demonstration of infection with outbreak genotype.

Probable: Culture or PCR positive or demonstration of acid-fast bacilli with clinically compatible illness and epidemiological link, but no genotype available.

Clinical: Clinical diagnosis leading to initiation of antituberculous therapy in individual with epidemiological link to outbreak.

Under investigation: Contact of case with (1) positive Tuberculin test or IGRA or (2) chronic cough awaiting testing.

3.79 Tularaemia

Tularaemia (Rabbit fever; Deer-fly fever; Ohara disease; Francis disease) is a zoonotic infection caused by the bacteria *Francisella tularensis*, normally transmitted to humans from animal hosts, most frequently hares (*Lepus europaeus*). It is also a potential bioterrorism agent.

Suggested on-call action

None usually required

Epidemiology

Tularaemia is endemic throughout the Northern Hemisphere (30–70° latitude). In Europe outbreaks have been reported from Finland, Sweden, the Balkans and, most recently, the Czech Republic and Hungary. In 2014, 526 confirmed cases were reported in the EU. Most of them were seen in Sweden (150), Norway (46), Hungary (140), the Czech Republic (48), and Spain (62). The overall

notification rate among males is twice that of females. Most cases occur between July and September.

Clinical features

The clinical manifestations (ulceroglandular, oropharyngeal, oculoglandular, pneumonic, septicaemic and typhoidal) depend on the portal of entry. Symptoms include high fever, body aches, swollen lymph glands, and difficulty swallowing. Fatalities occur mainly from typhoidal or pulmonary disease but are rare in Europe. With appropriate antibiotic treatment, the case-fatality rate is negligible.

Laboratory confirmation

Diagnosis is usually clinical and confirmed by a rise in specific serum antibodies, which are usually detectable after two weeks of the illness. Cross-reactions with *Brucella* species occur. Two of the four subspecies of *F. tularensis* (F. t.) can cause human disease: *F. t. tularensis* (type A) is more virulent than *F. t. holarctica* (type B) (case-fatality rate 5–15% versus <1%). *F. t. holarctica* is present in Europe and North America, *F. t. tularensis* restricted to North America.

Transmission

Tularaemia is a zoonosis. There are three main routes of transmission: direct from the animal reservoir (especially hares), vector bites, and environmental (water, earth, aerosolisation of infected hay). Reservoirs include wild rabbits, hares and muskrats as well as some domestic animals and ticks. It is suggested that there is a terrestrial and an aquatic cycle for *F. t. holarctica* in Europe. In the terrestrial cycle (central Europe: France, Germany, Austria, Slovakia and the Czech Republic), the tick *Dermacentor reticulatus* transmits the bacterium between rodents and other small animals. Humans are only sporadically infected by a tick bite, or by handling infected hares (*L. europaeus*). In the aquatic cycle (Turkey, Bulgaria, Kosovo, Sweden and Finland) voles (*Microtus* spp) and water rats (*Arvicola amphibius*) excrete the bacterium in urine. Humans are frequently infected through infected surface water and insect bites, and outbreaks occur more frequently. Tularaemia in Sweden and Finland is generally regarded as a mosquito-borne disease.Japan, Russia and the USA are reported to have developed *F. t. tularensis* as weapon, by enabling aerosolisation of large quantities of bacteria.

Acquisition

The incubation period is usually three to five days, but may be as long as two weeks. It depends upon strain virulence, type, inoculum size, and portal of entry; the ID_{50} is below 10 type A organisms by the inhalational route. Person-to-person transmission has not been reported.

Prevention

Health education to:

- avoid tick bites,
- avoid untreated potentially contaminated water,
- ensure meat from rodents is cooked thoroughly,
- ensure hunters handle animals with care, and
- promote prevention of occupational infections in laboratories.

Surveillance

- Tularaemia is notifiable in most EU countries.
- Cases should be reported to the Public Health Authorities so that assessments of risk can be made.
- Severe unexplained cases of sepsis or respiratory disease in otherwise healthy individuals should be reported to local public health authorities.

Response to a case

No public health action usually necessary.

Investigation of a cluster

- Search for a common source of infection related to arthropods, animal hosts, water or food (especially hares).
- Consider deliberate release if two or more suspected cases linked in time and place or single confirmed case if either not explained by occupational risk or travel to endemic area.

Control of an outbreak

- Investigate and control identified source.
- Emphasise prevention.

Response to a deliberate release

- Report to local and national public health authorities.
- Define exposed zone and identify individuals exposed within it (some may have left scene).
- Cordon off exposed zone.
- Decontaminate those exposed: remove clothing and possessions, and then shower with soap and water.
- Chemoprophylaxis (currently ciprofloxacin) as soon as possible for those exposed.
- Record contact details for all those exposed.
- Some health and emergency workers may also need prophylaxis.
- Police may take environmental samples.
- More general information in Chapter 4.17 and specific advice on PHE website.

Suggested case-definition
Compatible clinical illness with laboratory confirmation of tularaemia

3.80 Typhoid fever

Typhoid fever is a potentially severe infection that is rare in developed countries, but is a risk for travellers abroad and can be spread by food handlers. Typhoid and paratyphoid (Chapter 3.52) are both also known as enteric fever.

Suggested on-call action
Exclude cases and symptomatic contacts in risk groups (see below).

Epidemiology

The highest incidence is in south-central and south-east Asia (>100 per 100 000 cases pa); medium incidence areas are the rest of Asia, Africa, Latin America and the Caribbean and Oceania (except Australasia) (10–100 per 100 000); Europe, North America and the rest of the developed world are low incidence (<10 per 100 000). About 600 cases of typhoid fever were reported to ECDC in 2014 by 24 EU/EEA countries, an incidence rate of 2 per 100 000. About 90% of UK cases are acquired abroad, mainly in south Asia: this appears to also be true for the EU as a whole from the limited data available.

Clinical features

The onset may be insidious and non-specific. Fever is usually the earliest symptom, rising over a period of two to three days, possibly in a stepwise fashion. Headache and abdominal pain/tenderness may occur next, followed by anorexia, myalgia and fatigue. The most common symptoms reported in outbreaks are fever, headache and malaise. Other symptoms reported by a substantial

minority of cases are diarrhoea, constipation, respiratory symptoms, abdominal pain, myalgia, vomiting and chills/rigours. Common signs include hepatomegaly, splenomegaly, rose spots, and relative bradycardia. Fever commonly lasts for more than one week and may persist for three weeks. Infection in children is often mild.

Untreated typhoid has a case-fatality rate of 10–15%; prompt treatment reduces this to less than 1%. Relapses occur in 8–25% of cases, despite antibiotic treatment. Enteric fever should be considered when patients returning from an endemic or epidemic area develop a febrile illness.

Laboratory confirmation

Typhoid fever is caused by *Salmonella enterica* subspecies *enterica* serotype Typhi, more usually shortened to *S.* Typhi, a serogroup D *Salmonella*. Blood, stool, urine, rose spots, bone marrow and gastric or intestinal secretions can be cultured. Blood, urine and faeces culture are usually the first line: faeces are usually positive after the first week of illness and provisional results should be available in 72 hours. The sensitivity of blood culture is about 60%. PCR testing of faeces or stool may also be available in some laboratories: ideally PCR positives should be followed up with stool culture. In low-resource settings the anti-*Salmonella* Typhi/Paratyphi IgA-secretion assay ('TPTest') may be helpful.

Antibiotics may suppress *Salmonella* below detection levels for several weeks after completion of the course. However, bone marrow culture has 90% sensitivity, even after five days of antibiotic therapy. The Widal test on acute and convalescent sera may provide a retrospective diagnosis. Vi phage typing may be available for unexplained clusters: the most common in the UK are E1 and E9. Genotyping may also be available from reference laboratories (e.g. WGS in England).

Transmission

Humans are the only reservoir for *S.* Typhi. Typhoid is spread from person to person via the faeco-oral route. Transmission can occur via contaminated food or water. In developed countries, transmission is predominantly from the consumption of foods contaminated by a human case or carrier. Fruit and vegetables washed in water contaminated by sewage may be a vehicle; the food vehicle may have been imported from abroad. Attack rates of about one third have been reported from some food-borne outbreaks. Secondary spread can occur in households. Direct person-to-person spread is rare, but is possible in poor hygienic conditions, and spread can also occur via direct oro-anal contact.

Acquisition

The incubation period ranges from 3 to 56 days and varies with the size of the infecting dose. The average incubation period in outbreaks is about 14 days; 96% of cases who have a travel history develop symptoms within 28 days of return from an endemic area.

Cases are likely to be infectious for as long as faecal excretion continues. The ID_{25} is probably about 10^5 organisms and the ID_{50} is about 10^7 organisms; carriers often excrete $>10^5$ organisms g^{-1} stool. Half of cases are still excreting the organism after two weeks, despite treatment, 15% excrete for at least four weeks and 1–5% become chronic carriers. Prolonged asymptomatic carriage with intermittent detection in stool specimens may occur, particularly in those with existing gallbladder pathology. Five consecutive negative faecal samples gives near certainty of microbiological clearance, although about 95% of excretors are detected by three samples. Chronic urinary carriage of *S.* Typhi may occur, but is rare.

Repeated exposure (e.g. in endemic areas) leads to the development of natural immunity. However, immunity is not absolute.

Prevention

- Sanitation, clean water, handwashing and food hygiene.
- Advice on personal, food and water hygiene to travellers to affected countries.
- Two modern typhoid vaccines are available. Vaccine is usually recommended for travellers from low risk countries who are visiting higher incidence countries, especially where hygiene and sanitation may be poor.

Surveillance

- Typhoid is notifiable in most countries, including the UK. Some countries (e.g. England) may have national enhanced surveillance systems.
- Report on clinical suspicion to local public health authorities.

Response to a case

- Usually requires antibiotics: check antibiotic resistance of isolate.
- Advice on good personal and food hygiene to cases, carriers and contacts, especially handwashing.
- Enteric precautions for cases; consider isolation if hospitalised.
- National guidance documents for dealing with cases and contacts may be available (e.g. detailed evidence-based guidance is available via PHE website).
- Obtain food and travel history for the four weeks prior to onset of illness: a standard national enhanced surveillance may be available to assist this (e.g. via PHE website).
- Cases who have not visited an endemic country in the four weeks before onset should be investigated to determine the source of infection: this should include possible contact with those who have recently travelled to an endemic country.
- Cases, excretors and carriers who are higher risk for spreading infection (see Box 2.2.1) should be excluded from high-risk activities, until no longer excreting the organism. This can be defined (as in UK guidance) as three consecutive negative samples taken at least 48 hours apart (faecal sampling should not start until one week after completion of antibiotic therapy). Cases not in high-risk groups need only excluded until clinically well for 48 hours with formed stools and hygiene advice has been given.
- Contacts, such as co-travellers, household and other close (including sexual) contacts should be identified and questioned about whether they have suffered any symptoms compatible with typhoid and whether they are in a higher risk group for further transmission. All contacts should receive comprehensive hygiene advice. A faecal sample should be obtained from symptomatic contacts; co-travellers with similar exposure history who are in a higher-risk group of onward transmission; and household and other close contacts of non-travel associated cases. The ongoing risk assessment process may identify other cases suitable for screening. Symptomatic contacts in higher-risk groups should be excluded whilst awaiting the result of the screening sample.
- Antibiotic clearance, under the care of an appropriate specialist, can be considered for chronic carriers.

Investigation of a cluster

- Investigate to ensure that secondary transmission has not occurred.
- Most clusters in developed countries will result from exposure to a common source abroad, or transmission within close family groups.
- Obtain microbiological typing (e.g. WGS) from reference laboratory.

Control of an outbreak

- Outbreaks should be investigated as a matter of urgency.
- All cases and contacts should be investigated to identify the source of the outbreak.

- Consider contact with a chronic carrier, with faecal material, or with contaminated food, milk, water or shellfish.
- Contacts should be observed and investigated if they develop symptoms suggestive of typhoid, after appropriate specimens are taken.

Suggested case-definition for an outbreak

Confirmed: a clinically compatible case that is laboratory-confirmed (and with same phage/genotype if available).
Probable: a clinically compatible case epidemiologically linked to a confirmed case in an outbreak.

3.81 *Vibrio parahaemolyticus* infection

Vibrio parahaemolyticus causes a gastrointestinal infection that is particularly associated with consumption of contaminated seafood.

Suggested on-call action

If other cases are known to you or the reporting clinician/microbiologist, consult the local outbreak plan or SOP.

Epidemiology

Vibrio parahaemolyticus food poisoning is rare in north and west Europe (e.g. about 60 cases p.a. are reported in the UK), but incidence is slowly increasing (possibly related to climate change) and it may be more common in southern Europe (but subject to underdiagnosis). It is responsible for a significant proportion of food-borne disease in summer months in coastal areas of East, South East and South Asia, and in the USA. Most cases in the UK are in travellers returning from warmer countries, but outbreaks from seafood have occurred in Spain and France. All ages are affected.

Clinical features

Characterised by explosive watery diarrhoea, usually accompanied by abdominal cramps. Nausea, vomiting, and headache are common. Fever and chills occur in a minority of cases, as may bloody diarrhoea. The illness usually lasts one to seven days (median of three days). Death is rare but may occur, often associated with septicaemia, in very young children or elderly people with underlying disease.

Other non-cholera vibrios may also cause illness. *Vibrio vulnificus* usually causes non-gastrointestinal illness, such as septicaemia, wound infections and eye or ear infection. Those with chronic liver disease, immunosuppression or diabetes are at risk of severe or fatal infection.

Laboratory confirmation

Diagnosis is dependent upon isolation of the organism from culture on selective media of stool specimens or rectal swabs (warn the laboratory if organism suspected). PCR testing is also available. Almost all pathogenic *V. parahaemolyticus* produce a haemolysin, but most environmental isolates (and *Vibrio cholerae*) do not. Serotyping by O and K antigens is useful for outbreaks and molecular typing is available from reference laboratories. The organism may also be cultured from food and the level of contamination can be estimated. Isolates from both food and faeces often contain a mixture of serotypes.

Transmission

Vibrio parahaemolyticus (and *Vibrio vulnificus*) is ubiquitous in coastal waters of temperate and tropical countries. During the warm

season (water at least 10 °C, preferably over 22 °C), the organism is found in salt water, fish and shellfish.

Transmission to humans is food-borne via consumption of raw or undercooked seafood, for example oysters, clams, crab, scallops and shrimps (which may be imported), or food contaminated after cooking, for example by washing with seawater. The organism multiplies rapidly at room temperature (growth range 5–43 °C, optimum 37 °C): most outbreaks appear to involve food being held for several hours without refrigeration.

Skin infection has been reported following exposure of an open wound to contaminated seawater. Rarely, outbreaks of skin, eye or ear infections due to vibriosis may be reported.

Acquisition

The incubation period is dependent upon the ingested dose: extremes of 2–96 hours have been reported, with the median for most outbreaks being 13–23 hours. The organism is non-communicable between humans.

Prevention

- Care with seafood: maintain cold-chain (storage at less than 5 °C prevents multiplication), minimise time until consumption and cook thoroughly (e.g. boil oysters for three to five minutes after shells open).
- Avoid cross-contamination from raw seafood in kitchen. Do not use raw seawater to wash food.
- Immunocompromised patients should avoid swimming in potentially contaminated seas.

Surveillance

Not statutorily notifiable in most countries, but reporting to local public health departments and to national surveillance systems encouraged.

Response to a case

- Obtain details from case on foods consumed in 96 hours before onset, (especially seafood) and any history of travel.
- Although person-to-person transmission unusual, UK guidelines suggest cases in risk groups (Box 2.2.1) be excluded from work/school for 48 hours after first normal stool.

Investigation of a cluster

- Plot epidemic curve: if all cases within 48 hours then single exposure likely. If more than 96 hours, assume continuing source as secondary spread unlikely.
- Obtain food (especially seafood) and travel/recreation history for 96 hours before onset of each case.
- Organise laboratory testing of suspect foods.

Control of an outbreak

- Identify and rectify any of the following faults:
  - undercooking of seafood,
  - cross-contamination from raw seafood,
  - consumption of raw seafood after inadequate temperature control,
  - use of raw seawater.
- Reinforce food hygiene and handwashing.
- Report any suspected commercially produced food to relevant food safety authority.

Suggested case–definition for an outbreak

Confirmed: diarrhoea or abdominal cramps with *V. parahaemolyticus* identified in stool sample.

Clinical: watery diarrhoea and abdominal pain with onset 4–96 hours after exposure to suspect meal.

3.82 Viral haemorrhagic fevers, including Ebola

Viral haemorrhagic fevers (VHF) are severe, life-threatening viral infections caused by RNA viruses from several viral families.

Epidemiology

Each of the viruses grouped together has a different epidemiology and geographical distribution (Table 3.82.1). The risk of infection depends upon the vector and host ranges, which are largely found in rural areas. The importance lies in their propensity to spread following exposure to body fluids. Large human outbreaks can result from person-to-person transmission in the community as well as in healthcare facilities.

VHFs are endemic in Africa, South America and some parts of Asia, the Middle East and Eastern Europe. VHF may cause both sporadic cases and larger outbreaks. In the large 2014 West Africa Ebola outbreak, altogether 28 652 cases and 11 325 deaths were reported. Except for Crimean-Congo haemorrhagic fever (CCHF), which is endemic in the Balkans, Europe does not support the natural reservoirs or vectors for these diseases, and VHF is therefore restricted to occasional imported cases and a few nosocomial infections. The risk of epidemic spread in the general population is negligible.

Clinical features

The disease syndromes are characterised by fever, malaise, vomiting, mucosal and gastrointestinal bleeding, oedema and hypotension. There is often multi-organ involvement and the case fatality rate is high (Table 3.82.1).

Laboratory confirmation

Laboratory confirmation is mostly done by RT-PCR on body fluids and/or serology. Due to the risk of VHF transmission in healthcare settings, good laboratory practice guidelines must be in place and specimens must be taken and examined by experienced staff in laboratories with appropriate biosecurity level. Following the 2014 West Africa Ebola outbreak, all EU countries have national guidelines for safe handling of specimens and dedicated laboratories or agreements with laboratories in another country. Frontline staff should always consult their national reference centre before any sampling.

Transmission

Person-to-person spread is through contact with infected body fluids of ill or deceased patients. Zoonotic spread may occur from contact with other host species, such as bats or consumption of 'bushmeat' (Ebola, Marburg); consumption of raw milk or meat from infected animals (Congo-Crimean haemorrhagic fever, Rift Valley fever); contact with infected rodents or their excreta (arenaviruses, Hantaan, Omsk and Kyasanur Forest disease); insect vectors, mosquitoes (Rift Valley fever) or ticks (Congo-Crimean haemorrhagic fever, Omsk and Kyasnur Forest disease). See also Table 3.82.1.

Prevention

Primary prevention depends on transmission routes. Tick repellents, covering clothes, and skin inspection for protection against tick-borne VHF. Farm and abattoir workers should avoid unprotected contact with blood, tissues and fluids from possibly infected animals in endemic areas. Avoid bushmeat in areas endemic for Ebola and Marburg. Vaccines are available for some VHFs (Table 3.82.1).

Prevention of person-to-person transmission of highly contagious VHF rests on avoidance of contacts with bodily fluids from ill and deceased patients. Counselling and practice of safer sex with condoms for surviving Ebola patients with risk for sexual transmission (repeated monthly semen tests for male survivors). Possibly exposed persons should, under supervision of health authorities, monitor their health for at least three weeks

Table 3.82.1 Viral haemorrhagic fevers

Virus family	***Arenaviridae***
Diseases	Old World (LCM/Lassa complex): Lassa fever; lymphocytic choriomeningitis (LCM). New World (Tacaribe complex): Junin (Argentine haemorrhagic fever), Machupo (Bolivian haemorrhagic fever), Guanarito (Venezuelan haemorrhagic fever), Sabia (Brazilian haemorrhagic fever) and other recently recognised viruses (Chapare, Flexal).
Natural distribution	Lassa fever: rural areas of West Africa. Lujo haemorrhagic fever, LCM: Europe and Americas. Others: South America.
Route of infection and transmission	Exposure to rodent urine through inhalation, ingestion or contact with broken skin; nosocomial transmission through droplet and contact (Lassa, Machupo, Lujo).
Clinical features	Lassa fever: Often asymptomatic or mild symptoms (fever, malaise, headache). Twenty per cent progress to severe disease with generalised haemorrhages, pulmonary distress, vomiting, facial swelling and shock. There is a 1% overall case fatality (5–15% in hospitalised patients and even higher in third-trimester pregnant women). Deafness is a common complication both of mild and severe cases. Lassa responds to early treatment with ribavarin. Lujo: Similar to Lassa fever.
Incubation and infectious periods	Incubation period: Lassa 6–21 days; Lujo: 7–13 days; LCM 8–13 days; Tacaribe complex 6–14 days. Lassa: Virus is present in body secretions, including the pharynx during the acute illness, and may be excreted in semen and urine for 2–3 months. Sexual intercourse must be avoided for 3 months.
Virus family	***Bunyaviridae***
Disease	Rift Valley Fever (RVF) (*Phlebovirus*)
Natural distribution	Widespread in (mostly Sub-Saharan) Africa, Arabia. Recent epidemics occurred in Kenya, Somalia, Tanzania, Saudi Arabia and Yemen. Outbreaks in Egypt, Madagascar, Mauritania.
Route of infection and transmission	Mosquitoes (various), slaughter or consumption of infected livestock. RVF is most commonly associated with mosquito-borne epidemics during years of unusually heavy rainfall. No person-to-person transmission.
Clinical features	May be mild illness associated with fever and liver abnormalities or progress to haemorrhage, encephalitis and retinitis. 1–10% patients get permanent vision loss. 1% case fatality.
Incubation period	2–6 days
Disease	Crimean-Congo haemorrhagic fever (CCHF) (*Nairovirus*)
Natural distribution	The Balkans, Ukraine, Turkey, Russia, Middle East, Central Asia and large parts of Africa.
Route of infection and transmission	Hard ticks (*Hyalomma*), slaughter or consumption of infected animals, usually domestic livestock. Nosocomial transmission often occurs.
Clinical features	Sudden onset of headache, high fever, back pain, joint pain, stomach pain, vomiting, red eyes, red throat and palatal petechiae. Haemorrhagic features on fourth day. Case fatality in hospitalised patients 10–50%.
Incubation period	Incubation: 3–13 days
Disease	Haemorrhagic fever with renal syndrome (HFRS) (see Chapter 3.27) Hantavirus pulmonary syndrome (HPS) (see Chapter 3.27)

Table 3.82.1 (*Continued*)

Virus family	***Arenaviridae***
Virus family	***Filoviridae***
Disease	Ebola Marburg
Natural distribution	Ebola: Outbreaks in Liberia, Guinea, Sierra Leone, Senegal, Mali, (2014 West Africa outbreak), Nigeria, Uganda, Republic of Congo, Gabon, South Sudan, Democratic Republic of Congo, Côte d'Ivoire. Marburg: Outbreaks in Uganda, Kenya, Democratic Republic of Congo, Angola and South Africa.
Route of infection and transmission	Blood or body fluids (e.g. vomit, diarrhoea) from sick or dead patients (very high viral load in acutely ill patients); nosocomial transmission; contact with infected fruit bats or monkeys; ingestion of 'bushmeat'; possibly via semen from recovered Ebola patients. Aerosol transmission of Ebola has not been demonstrated in humans. Several Ebola vaccines are under trial, but none on the market (August 2016).
Clinical features	Sudden onset, malaise, fever, myalgia, diarrhoea. Hypotension and shock. 50–90% case fatality rate for hospitalised cases.
Incubation and infectious periods	2–21 days Virus is present in body secretions, including the pharynx during the acute illness, may be excreted in semen for 3–4 months (Ebola).
Virus family	***Flaviviridaes***
Disease	Dengue haemorrhagic fever (see Chapter 3.19) Yellow fever (see Chapter 3.86) Omsk haemorrhagic fever (OHF) Kyasanur Forest disease (KFD) Alkhumra haemorrhagic fever (AHF) (virus closely related to KFD)
Natural distribution	OHF: Western Siberia (Omsk, Kurgan, Tyumen and Novosibirsk oblasts) KFD: Southern India (Karnataka, Tamil Nadu and Kerala) with 40–500 cases per year. AHF: Saudi Arabia and Egypt.
Route of infection and transmission	KFD: Tick bites or rarely after contact with infected monkeys. Vaccine available in endemic areas. OHF: Tick bites or by contact with urine, faeces or blood of muskrat host. No human-to-human transmission but lab contamination has been described. TBE vaccine confers some cross-protection. AHF: Tick bites (soft and hard ticks); contacts with livestock and infected animals. No human-to-human transmission.
Clinical features	Biphasic course with initial fever, headache and muscle pain followed by bleeding and gastrointestinal symptoms after 3–4 days. Case fatality 0.5–3% (OHF); 3–5% (KFD).
Incubation period	3–8 days

following exposure and seek medical care immediately if symptoms develop.

Infection control precautions to prevent nosocomial transmission rests on caring for patients in specialised hospitals/units with strict barrier nursing by staff using proper personal protective equipment (PPE), single room isolation with a log of all persons entering the room, dedicated medical equipment, limiting the use of punctures and other invasive procedures, safe injection practices, avoidance of aerosol-generating procedures, proper hand hygiene and proper routines for cleaning and handling of garbage.

Surveillance

Highly contagious VHFs are notifiable in all EU countries. Local and national public health authorities should be informed of cases immediately on clinical suspicion.

Response to a case

All EU countries have specific guidelines for handling suspected cases as well as national preparedness plans for handling suspected and confirmed cases, based on a health-system approach. VHF should always be considered in patients with symptoms compatible with VHF that have visited endemic areas within the last three weeks or had contacts with confirmed or suspected VHF cases. Further management should be based on a proper risk analysis, for example the UK Advisory Committee on Dangerous Pathogens (ACDP) algorithm and guidance on management of patients with viral haemorrhagic fever: https://www.gov.uk/government/publications/viral-haemorrhagic-fever-algorithm-and-guidance-on-management-of-patients. For any moderate- or high-risk patient, further management, including referral and transportation, should be done under guidance of the health authorities and specialists in management of highly contagious patients. It is important not to delay diagnosis and treatment of other serious or life-threatening conditions such as malaria.

3.83 Warts and verrucae (and molluscum contagiosum)

Warts are caused by infection of the epidermis with human papillomavirus (HPV). Various HPV genotypes affect different sites influenced by environmental and host factors.

For Molluscum contagiosum lesions, see Box 3.83.1

Suggested on-call action
Usually none required.

Epidemiology

Most people will have warts at some time in their life. The prevalence increases during childhood, peaks in adolescence and declines thereafter. The prevalence in children and adolescents in the UK is 4–5%. Warts are more common in white ethnic groups. Warts clear spontaneously over time.

Clinical features

Various wart morphologies are recognised (See Table 3.83.1).

Laboratory confirmation

The diagnosis can be confirmed histologically.

Transmission

Warts spread by direct contact or indirectly via contact with fomites or contaminated floors and surfaces. The attack rate is thought to be low. Auto-inoculation occurs as a result of scratching and shaving. Sexual transmission occurs.

Acquisition

The incubation period ranges from one month to two years. A person with warts is infectious for as long as the warts persist. Warts are more common in immunocompromised people.

Box 3.83.1 Molluscum contagiosum

Molluscum contagiosum (MC) is a skin infection caused by a poxvirus (MCV) which replicates in epidermal cells to produce characteristic smooth-surfaced white or translucent papules 2–5 mm in diameter.

Epidemiology: MC more common in boys than in girls. Incidence peaks at age 10–12 years of age and again in young adults due to sexual transmission. It is more common in people who are immunocompromised and prevalence rates of 5–18% have been reported in persons with HIV infection.

Clinical features: MC may occur on any part of the body but in adults it often affects the anogenital area. There are usually about 20 lesions but they may be more extensive in HIV infection and atopic eczema. The lesions resolve spontaneously after 6–9 months (occasionally up to 24 months) and treatment is only justified on cosmetic grounds or if there is discomfort. If necessary, diagnosis can be confirmed by the typical appearance of the contents of the lesions on light microscopy or by electron microscopy. PCR testing may be available.

Transmission and acquisition: Transmission is by direct contact, both sexual and non-sexual, from human cases. Indirect spread can occur as a result of contaminated objects and environmental surfaces. Autoinoculation also occurs as a result of scratching. The incubation period is usually two to seven weeks (occasionally longer) and a person will remain infectious as long as the lesions persist. Transmission is thought to be higher in families than in other community settings such as schools.

Response to a case: Normal personal and environmental hygiene should be observed. There is no need for an affected person to stay away from work or school.

Table 3.83.1 Wart morplhologies

Clinical type	Appearance	HPV type
Common warts (verrucae vulgaris)	Flesh-coloured or brown, keratotic papules	1, 2, 4, 57
Plane or flat warts (verrucae planae)	Smaller, flat topped, non-scaling, papules, cluster on hands, neck or face	3, 10
Plantar warts (verrucae plantaris)	Grow inwards and are painful, common in adolescents and children	1, 2, 4, 57
Condylomata acuminata (genital warts)	Occur in the genital tract, transmitted sexually (see Chapter 3.26)	6, 11

Prevention

- Health education, environmental hygiene in swimming pools and other communal areas and avoiding direct contact with warts where practicable may reduce spread.
- Case reporting is not necessary.
- No single treatment is completely effective. Spontaneous regression is common and warts may be left untreated unless painful or unsightly.
- Children with warts do not have to stay away from school. Affected children can go swimming. Plantar warts should be covered if practicable in swimming pools, gymnasia and changing rooms.

Genital warts

Genital warts are caused by the human papillomavirus (HPV) and are the most frequently diagnosed viral STI in the UK. Most genital warts are caused by low-risk HPV types 6 and 11 and diagnosis is usually based on clinical appearance. Usually, they are self-limiting

within two years. Treatment options are podofyllotoxine, cryotherapy, electrocoagulation, laser, application of 5-fluorouracil cream, cidofovir cream and imiquimod. The success rate varies from 33 to 88%. However, asymptomatic HPV infections are also common. Also, asymptomatic infected individuals can be infectious. Only 1% of infections lead to genital warts. Immunocompromised people can develop serious invasive destructive tumours (no metastases). (NB children with genital warts can be infected through towels/hands and not necessarily by sexual abuse.)

Cervical cancer

HPV are implicated in the aetiology of cervical cancer, anogenital and head and neck cancers. In many areas of the world these diseases are a major cause of morbidity and mortality. For example, globally each year there are >500 000 new cases of cervical cancer and >260 000 deaths. Most of these cases occur in developing countries where early detection by screening is not available. HPV type 16 and type 18 cause about 70% of cervical cancers. Two HPV vaccines have been available since 2006 and are being introduced in immunisation programmes in many high-income and some middle-income countries. These vaccines may prevent 90% of precancerous cervical lesions caused by the vaccine-related HPV types. The quadrivalent vaccine also prevents 90% of anogenital warts due to HPV type 6 and type 11. Both vaccines are safe and the WHO has recommended that they should be included in national immunisation programmes, where it is feasible, affordable and cost effective. Consider vaccinating both girls and boys for reducing transmission and elimination in certain populations. Carcinoma is a rare event, as about 80% of females are infected at least once in their lifetime. Cervical intraepithelial neoplasia (CIN) lesions, which are a potentially premalignant transformation of cells of the cervix, occur in only 20% of infections; 90% of CIN lesions disappear spontaneously.

3.84 West Nile virus

West Nile virus (WNV) is a mosquito-borne flavivirus that is maintained in an enzootic cycle between mosquitoes and birds. Humans and horses are incidental dead-end hosts. West Nile virus can cause encephalitis, which can be serious.

Suggested on-call action
None usually needed.

Epidemiology

WNV is transmitted through mosquito bites (mainly of the genus Culex). The disease is present in Africa and the Middle East. First reported in the USA in 1999, the virus has now spread into Canada, Central America and the West Indies. In recent years there has been an increase of cases in Southern and Eastern Europe (The Balkans, Czech Republic, France, Hungary, Romania, Spain, Italy, Portugal) with significant outbreaks in some of the countries. In Greece there was a large outbreak in 2010, with 262 reported cases, with neuroinvasive disease in 197 cases and 35 deaths. Neuroinvasive disease has been seen in adults of all ages, with a dominance of persons >50 years.

Clinical features

Usually a mild infection, with 80% of cases being asymptomatic. The most common symptoms are a flu-like illness with fever, headache and myalgia, sometimes accompanied by nausea and a maculopapular or morbilliform rash. Severe disease, seen in less than 1% of cases, includes aseptic meningitis or acute encephalitis, sometimes with flaccid paralysis and coma. Ataxia, cranial nerve abnormalities, myelitis, eye pain, polyradiculitis and seizures have also been described,

and in some outbreaks myocarditis, pancreatitis and fulminant hepatitis. Case fatality rates of 10–15% if hospitalised (higher in elderly people).

Laboratory confirmation

- Virus-specific IgM can be detected in most cerebrospinal fluid (CSF) and serum specimens at the time of clinical presentation. Paired serum samples should be tested. False positive results may be seen if recently exposed (vaccination or infection) to related flaviviruses (e.g. yellow fever, Japanese encephalitis, dengue). The test should always include other closely related flaviviruses for comparison.
- Viral detection with RT-PCR can be performed on blood, CSF and postmortem brain biopsies. Viraemia is short and limited to the early phase of disease.

Transmission

WNV is spread by the bite of a mosquito infected by feeding on an infected bird. Transmission through blood transfusion, transplantation, breast milk and transplacentally have been described. No person-to-person spread.

Acquisition

The incubation period is 2–14 days and depends on the species, route of transmission and infective dose, which may be as low 10–100 organisms. The duration of acquired immunity is uncertain.

Prevention

- Blood safety measures with deferral or the implementation of systematic nucleic acid testing (NAT) screening of blood donors in affected areas. ECDC provides a weekly updated overview of affected areas in order to support this activity.
- Avoidance of mosquito bites, especially for the elderly during periods of transmission.
- No vaccine is available.

Surveillance

WNV is a notifiable disease at the EU level.

Response to a case

- If the first case, clinicians should be alerted to the presence of circulating WNV.
- Ensure public health advice about avoiding mosquito bites.

Response to a cluster and control of an outbreak

- Primarily mosquito control.
- Further details available on ECDC website.

3.85 Whooping cough

Whooping cough (pertussis) is an acute bacterial respiratory infection caused by *Bordetella pertussis* (a related organism, *Bordetella parapertussis*, also causes a pertussis-like illness). Its public health importance lies in the severity of the disease, particularly in young infants, and its preventability by vaccination.

Suggested on-call action

- Start antibiotic treatment (erythromycin, azithromycin or clarithromycin) to reduce infectiousness for vulnerable contacts if within three weeks after onset of case.
- Exclude from nursery or school for five days from starting antibiotic treatment.

Epidemiology

Pertussis is well controlled in countries with good immunisation coverage, although there have been recent outbreaks in highly vaccinated populations. Where coverage is low, the disease has a cyclical pattern, with epidemics occurring at three to four yearly intervals. These epidemics affect young children; infants under six months are particularly at risk. In highly vaccinated populations most clinical cases are caused by infection with *B. parapertussis*.

The incidence of pertussis varies widely across Europe and has changed over time in many countries. In 2015, 40 195 cases of pertussis were reported to ECDC in Europe. The overall notification rate was 9.0 per 100 000; highest rates were reported from Norway (36.8 per 100 000), the Netherlands (36.6 per 100 000), Denmark (16.7 per 100 000) and Spain (14.8 per 100 000). Variations in notification rates reflect different vaccine coverage and schedules, but also differences in reporting and awareness of the disease. Even in countries with the highest reporting rates underreporting is considerable. There were 13 deaths recorded in Europe in 2015, a case fatality rate of 0.3 per 1000 overall; 12 of the deaths were in infants below three months of age. Enhanced surveillance using new laboratory methods such as PCR diagnosis has significantly improved detection rates.

There has been an increase in reported pertussis in Europe and many other countries in recent years, despite high vaccination coverage. Reasons for this include waning of vaccine-induced immunity, changes in circulating strains, and enhanced surveillance.

Clinical features

The initial illness starts with cough, cold and a fever. Over the next week, the cough gradually becomes paroxysmal; there are bouts of coughing that are terminated by the typical whoop, or by vomiting. The cough often lasts for two to three months. Young infants do not usually whoop, and coughing spasms may be followed by periods of apnoea. Adults and vaccinated children have a milder illness that lasts two to three weeks. Pertussis is being increasingly recognised as a cause of chronic cough in adults, who in Europe are estimated to have five to six lifetime episodes of prolonged cough due to *B. pertussis*

Laboratory confirmation

The classical method is culture from a pernasal swab, although the organism is difficult to grow, so sensitivity is low (although specificity is high). The sensitivity has been greatly improved by the availability of PCR diagnosis. Serology (EIA) is also available.

Transmission

Humans are the only reservoir. Transmission is by droplet spread from an infectious case, often an older sibling or parent. Carriers do not exist, but mild or subclinical cases among vaccinated individuals are also a source of infection.

Acquisition

The incubation period is 7–10 days, but may occasionally be up to 3 weeks. A case is highly infectious during the early stage of the illness, before the typical cough; infectiousness then decreases and the case is normally no longer infectious three weeks after the onset of paroxysmal cough, although in a proportion of cases (up to 20%) infectivity may persist for up to six weeks. The period of communicability may be shortened by antibiotic treatment. An attack of pertussis usually confers immunity, although second cases do occur.

Prevention

- Immunisation is highly effective at preventing illness, although its role in limiting transmission is less clear. Pertussis vaccine

has also been shown to reduce the incidence of sudden infant death syndrome.
- There are two types of pertussis vaccine: killed whole-cell preparations and subunit acellular vaccines. Acellular vaccines are the standard of care in Europe because of the lower incidence of side-effects. The vaccines are usually given in combination with diphtheria, tetanus, polio, hepatitis B and Hib antigens. Three doses are given in the first years of life, with booster doses are various ages. The recent increase in pertussis has prompted expansion of vaccine recommendations in many countries, including boosters for adolescents and adults, vaccination of healthcare workers and pregnant women ('cocooning strategy'). It is important that pertussis vaccine is not delayed in infants, and that older siblings and parents are fully vaccinated. The only true contraindication is a severe reaction to a previous dose.

Surveillance

- Pertussis is notifiable in most European countries.
- Laboratories should also report all clinically significant infections to local and national surveillance centres.
- Serotyping should be performed in the national reference unit; surveillance of serotypes is important to monitor vaccine efficacy.

Response to a case

- Isolate, with respiratory precautions, in hospital.
- Start antibiotic treatment (macrolide antibiotic) and exclude from nursery or school for two days after treatment has started. Healthcare workers with pertussis should also receive antibiotics and be excluded from work for two days after treatment has started.
- Arrange for laboratory confirmation.
- Check vaccination status of case and household contacts, and arrange for vaccination if any are unvaccinated; report vaccine failures to the national surveillance unit.
- Antibiotic prophylaxis is recommended for unvaccinated household contacts of suspected or confirmed pertussis cases, particularly infants under six months of age, if given within 21 days of onset of case. Prophylaxis should also be considered for contacts who are at risk of transmitting the disease to high-risk individuals, that is healthcare workers and pregnant women after 32 weeks gestation.
- The antibiotics of choice for treatment and prophylaxis of pertussis are clarithromycin (seven days) and azithromycin (three days); clarithromycin is preferred in neonates. For pregnant women, erythromycin (seven days) is preferred. Co-trimoxazole (seven days) is an alternative for those allergic to macrolides but is not licensed for this purpose.

Investigation of a cluster

- Obtain laboratory confirmation, including serotyping.
- Check vaccination status of cases.
- Look for links to populations with low vaccine coverage. Consider potential sources of infection, for example unvaccinated adults.

Control of an outbreak

- Look for unvaccinated individuals and consider community-wide vaccination if coverage is low (NB three doses of vaccine are required for protection, so vaccination is a long-term outbreak control measure).
- Treatment of cases and macrolide prophylaxis for unvaccinated contacts as above.
- Look for undiagnosed cases.
- Outbreaks in institutions can be controlled by a combination of case-finding, antibiotic treatment and case exclusion.
- Detailed guidance on the public health management of pertussis, including in health care settings, is available on the Public Health England website (updated December 2016).

Suggested case-definitions for an outbreak

Clinical: 14 days or more of cough plus, *either* epidemiological link to a confirmed case, *or* one of paroxysms, whoop or post-cough vomiting.

Confirmed: Compatible symptoms with *B. pertussis* infection confirmed by culture, PCR or serology.

3.86 Yellow fever

An imported acute viral haemorrhagic fever caused by the yellow fever virus.

Epidemiology

Yellow fever is endemic in Central Africa and parts of South and Central America. Forty-seven countries are either endemic for, or have regions that are endemic for, yellow fever. The WHO estimates for 2013 approximately 84 000–170 000 severe cases and 29 000–60 000 deaths. Underreporting is common due to misidentification and inadequate surveillance systems.

The insect vector is absent from Europe. Travellers to endemic areas are at risk. Imported cases are rare in Europe.

Clinical features

Cases are classified as inapparent, mild, moderately severe or malignant. Onset is sudden, with fever of 39–40 °C. An initial tachycardia becomes a relative bradycardia given the fever. In mild cases, the illness ends after one to three days. In moderately severe and malignant cases, the fever falls suddenly two to five days after onset, a remission ensues of several hours or days; the fever recurs, albuminuria and epigastric tenderness with haematemesis appear, oliguria or anuria may occur and petechiae and mucosal haemorrhages are common. In malignant cases, delirium, convulsions and coma occur terminally.

Mortality of clinically diagnosed cases is up to 10% overall, but as many infections are undiagnosed it is much lower in practice.

Laboratory confirmation

Diagnosis is confirmed by virus isolation from blood, by a rising antibody titre (in absence of recent immunisation and after excluding cross-reactions to other flaviviruses) or at autopsy. There is a growing use of RT-PCR in the early stages of infection to detect viremia.

Transmission

In sylvatic (jungle) yellow fever, the virus is acquired from wild primates and transmitted by forest canopy mosquitoes. In urban yellow fever, the virus is acquired from a viraemic patient within the previous two weeks and transmitted by the *Aedes aegypti* mosquito.

Acquisition

Incubation lasts three to six days.

Prevention

- Active immunisation with the 17D live attenuated vaccine effectively prevents cases.
- Vaccination requirements vary by country; information and vaccination centres' addresses can be obtained from public health authorities.
- Eradication of urban yellow fever requires widespread mosquito control and mass immunisation.

Surveillance

Yellow fever is notifiable and should be reported to local public health authorities and to the WHO.

Response to a case

- The case should be reported urgently to the WHO (via national centre) and the country of origin.
- The case should be transferred to suitable isolation facilities and strict procedures such as those laid down by the Advisory Committee on Dangerous Pathogens (UK) and other European advisory groups followed.
- In an area where there is potential for further mosquito transmission, patients should be isolated in a screened room sprayed with residual insecticide.
- Hospital and laboratory personnel should be aware of the risk of transmission from inoculation.

Investigation of a cluster and control of an outbreak

Not usually relevant to Europe, but verify if cases have been to an infected area in the week before onset. Control of an outbreak is through mass immunisation and vector control.

Suggested case-definition for an outbreak

Clinically compatible illness with fourfold rise in antibody titres or demonstration of virus, antigen or genome.

3.87 Yersiniosis

Non-plague yersiniosis is a zoonotic, often foodborne, cause of intestinal disease. *Yersinia enterocolitica* (YE) causes predominantly enterocolitis, whereas *Yersinia pseudotuberculosis* (YP) mainly causes an appendicitis-like illness.

Suggested on-call action

- Exclude symptomatic cases in high-risk groups.
- If you or the reporting microbiologist/clinician know of other cases, consult the outbreak control plan or SOP.

Epidemiology

About 6700 cases a year of yersiniosis are reported in EU/EEA states, a rate of 1.8 per 100 000, although there will be considerable underascertainment in countries that do not routinely test for *Yersinia*. Over 95% of reports are YE. Rates are significantly higher in northern countries such as Finland and Lithuania. About 60 cases a year are reported in the UK, a rate of 0.1 per 100 000. All ages are susceptible, but rates are highest in children, particularly those under five. Infection may be more common in rural areas and amongst those exposed to pigs or their carcasses.

YP has a worldwide distribution, but is more commonly reported from Europe. Most cases are aged 5–20 years and males are more commonly affected. Peak incidence is in winter.

Clinical features

YE enteritis commonly causes diarrhoea, abdominal pain and fever, but some cases may also have vomiting or blood in stools. The duration of illness is usually two to three weeks, slightly longer than for most enteric pathogens. Sequelae include reactive arthritis and erythema nodosum. Other presentations include pharyngitis, appendicitis-like syndrome in older children, and septicaemia in the infirm.

YP usually presents as mesenteric adenitis causing fever and right lower abdominal pain. Many cases result in appendicectomy.

Erythema nodosum may occur, but enteritis and septicaemia are less common.

Carriage of *Yersinia* species in studies of asymptomatic individuals ranges from 0 to 2.9%.

Laboratory confirmation

Serological diagnosis is available for both species. YE can be diagnosed by stool culture, but grows slowly on routine culture media and may not be routinely ascertained by many laboratories. If yersiniosis is suspected, then enrichment and highly selective media can be used, but this takes several days. Small numbers of organisms may continue to be excreted for four weeks.

YE are divided into six biotypes, of which type 1A is considered to be non-pathogenic, and over 50 serotypes, of which O3 is the most common in Europe. Molecular typing is possible and may be available from reference laboratories for potential outbreaks.

YP may be confirmed by isolation from an excised mesenteric lymph node. There are 15 different O serotypes; most human cases are serotype 1. Genotyping is available in some countries.

Transmission

The most important reservoir of YE in Europe is asymptomatic carriage in pigs. Other hosts are rodents, rabbits, sheep, goats, cattle, horses, dogs and cats. YP is found in a number of mammals and birds, particularly rodents and poultry.

Humans usually acquire the infection orally via food. Sporadic cases are more likely to have consumed raw or undercooked pork products than controls and outbreaks have been linked to pork, milk, salad and vegetables. Pork is easily contaminated with YE in the abattoir and if eaten raw or undercooked may cause illness; refrigeration offers little protection as the organism can multiply at 4 °C. Milk has also been implicated in YE and YP outbreaks, probably due to contamination after pasteurisation or the use of unpasteurised milk. Vegetables such as tofu or bean sprouts have become contaminated from growing in contaminated water. Outbreaks have been linked to mixed salad (YE), carrots (YP), and lettuce (YP). The optimum temperature for growth is 22–29 °C. Raw or undertreated water may also be a risk.

Person-to-person spread is probably uncommon, but it may have contributed to some outbreaks in nurseries, schools and hospitals. Respiratory transmission from cases with pharyngitis appears unlikely. Human cases have been reported after contact with sick puppies and kittens.

Contaminated blood in blood banks has led to severe disease and several deaths in recipients. Not all donors were unwell. The ability of the organism to replicate in refrigerators is likely to be relevant.

Acquisition

The incubation period is usually 3–7 days with extremes of 1–14 reported for YE and 2–18 for YP. The infectious dose is likely to be high, perhaps 10^9 organisms. Secondary infection appears to be rare, but it may be best to assume that the infectious period extends until 48 hours after the first normal stool. Natural infection confers immunity, although the extent and duration is unclear. Maternal antibodies protect the newborn.

Prevention

- Avoidance of consumption of raw meats, particularly pork products.
- Reduction of contamination of raw pork by improved slaughtering methods, improved husbandry, or irradiation of meat.
- Avoidance of long-term refrigeration of meat (maximum four days). Growth should not occur at freezer temperatures under –2 °C.
- Pasteurisation of dairy products and subsequent separation from unpasteurised milk-handling processes.

- Chlorination of drinking water.
- Washing of salad items to be eaten raw.
- Exclusion of blood donors with recent history of diarrhoea or fever.
- General measures to protect against gastrointestinal infection, including handwashing, safe disposal of human and animal/pet faeces, food hygiene and exclusion of cases with high risk of onward transmission.

Surveillance

- Cases of yersiniosis should be reported to local public health departments and to national surveillance systems: statutorily notifiable in some countries (notify as suspected food poisoning in UK).
- Clinicians should inform the local public health department of any increase in cases of mesenteric adenitis or appendicectomy.

Response to a case

- Give hygiene advice to case (enteric precautions).
- Exclude case and symptomatic contacts if in risk group (Box 2.2.1) until 48 hours after first normal stool. No microbiological clearance necessary.
- Obtain history of consumption of pork or pork products, raw or undercooked meat, milk, salad, raw vegetables or water. Ask about sick pets, blood transfusions and exposure to animals/carcasses.

Investigations of a cluster

- Discuss case finding with local laboratory: need to change testing policy for routine specimens?
- Discuss further microbiological investigations of existing cases to discover if all one serotype or genotype.
- Conduct a hypothesis-generating study. Questionnaire should include consumption of pork and pork products; consumption of raw or undercooked meats; salad and raw vegetable items; source of milk; source of water; all other food consumed in last 11 days; contact with other cases; blood or blood product transfusions; hospital treatment; occupation; contact with animals (wild, agricultural or pet).

Control of an outbreak

- Exclude symptomatic cases in high-risk groups and ensure enteric precautions followed.
- Reinforce food hygiene and handwashing.
- Look for ways in which food could have become contaminated (especially cross contamination from raw pork), undercooked or stored too long in a refrigerator. Check that pasteurised milk could not become contaminated in dairy.
- Prevent use of unpasteurised milk. Prevent use of raw vegetables grown in untreated water, unless subsequently cleaned adequately.

Suggested case-definition for outbreak

Clinical: diarrhoea, or combination of fever and right lower abdominal pain, with onset three to seven days after exposure.

Confirmed: isolate of outbreak strain or serological positive, with one of diarrhoea, fever, abdominal pain or vomiting, beginning 1–12 days after exposure.

3.88 Zika virus infection

Zika virus is an RNA virus from the Flaviviridae family, identified in 1947 with two lineages; the African and the Asian. The recent spread in the Pacific and Americas is caused by the Asian lineage.

Epidemiology

Before 2007, Zika virus infection was endemic in Sub-Saharan Africa and Southeast Asia.

In 2007, a large outbreak in Yap Island, Micronesia, was the first outbreak outside Africa and Asia. Since then the virus has, similarly to chikungunya virus, spread very rapidly, with significant outbreaks and widespread transmission in the Pacific Region, and since 2015, also in South and Central America and Southeast Asia, and more local transmission in parts of southern Florida. Many imported cases to Europe have been reported, but as of January 2017 no autochthonous transmission. Maps showing Zika virus transmission in the past nine months are provided on the ECDC website to aid medical practitioners assess returning travellers.

Clinical features

Zika virus infection is a mostly mild and self-limiting infection of two to seven days duration, with circa 80% of the cases being asymptomatic. The main symptoms include a maculopapular rash (with or without pruritus), often starting on the face before spreading across the body. Other symptoms may include mild fever, myalgia, arthralgia, headache and conjunctivitis, and more rarely retro-orbital pain and gastro-intestinal symptoms. Co-infection with dengue fever or chikungunya occurs occasionally. Zika virus infection in pregnant women can cause abortion, congenital microcephaly as well as other malformations of the central nervous system (highest risk during first and second trimester). There is also an association between infection with Zika virus and Guillain-Barré syndrome.

Laboratory confirmation

Laboratory diagnosis of Zika virus infection is based on the detection of viral RNA from bodily fluids, such as blood (first three to five up to seven to eight days after onset of symptoms), urine (two to three weeks after symptom onset) and semen (up to two months after symptom onset). Virus has also been detected in saliva, CSF, amniotic fluid and breast milk. Diagnosis by serology (fourfold IgM antibody titre increase in paired sera) may also be available. Always consult a specialised laboratory when considering testing.

Transmission

The virus is transmitted to humans by *Aedes* mosquitoes, especially by the *Aedes aegypti* species (present also in Madeira and the Black Sea Region), but also other *Aedes*, including *Aedes albopictus* (present also along the Mediterranean coast of Europe), are considered as potential vectors for Zika virus, although with low vector competence. The *Aedes* mosquitoes bite throughout daylight hours with peaks of activity in the early morning and late afternoon. Zika virus can also transmit from mother to child through the placenta and during delivery.

Sexual transmission, both male-to-female and female-to-male, have been described as late as five to six weeks after onset of symptoms, and Zika virus has been identified in semen for as long as six to eight months.

A person should be considered potentially infectious if residing in an affected area, or having recently been in an affected area (women in the past eight weeks and men in the past six months) or recently (eight weeks for women or six months for men) having had unprotected sex with a potentially infectious person as defined above.

There is also a risk of virus transmission via blood transfusion and organ transplantation, while there is no increased risk of Zika virus infection for recipients of plasma-derived or urine-derived medicines. The risk of transmission via saliva cannot currently be assessed.

Acquisition

The incubation is 3–12 days after the bite by an infected mosquito.

Prevention

- Reduce the proximity of mosquito vector breeding sites to human habitation in affected areas.

- Mosquito protection (see Chapter 1.3) when visiting areas with transmission.
- Pregnant women or women planning to be pregnant should postpone non-essential travel to areas with widespread transmission and consider postponing travel to areas with sporadic transmission.
- In areas with presence of competent vectors, returning travellers from areas with transmission should practice mosquito protection for at least three weeks.
- Prevent sexual transmission (abstaining from sexual contact or consistently using barrier methods during sexual contact) from partners returning from affected areas for at least eight weeks if the returning partner is a woman and six months if a man.
- Practicing safe sex (including use of condoms) is advisable throughout the pregnancy if the partner of the pregnant woman has been visiting an area with transmission.
- The possibility of Zika virus transmission via blood donations calls for preventive safety measures to be applied to donors returning from affected areas. Blood safety authorities need to be vigilant regarding the epidemiological situation in outbreak areas.

Surveillance

- Zika virus infection is mandatory notifiable in most of the European countries.
- Timely reporting of autochthonous cases is essential in areas with presence of competent vectors (ECDC is performing surveillance of the competent vector in Europe).

Response to a case

- Case investigation is indicated in pregnant women exposed since the beginning of pregnancy, persons with neurological symptoms exposed in the past four weeks, and for clusters of cases with Zika-like symptoms in areas with competent vectors.
- Treatment is directed primarily at relieving the symptoms, including pain relief and anti-histamines for pruritic rash.
- Rapid implementation of vector control measures around each case identified in areas with presence of the competent vector (see Chapter 1.3).

ECDC interim case definition for surveillance

ECDC interim case definition (from 17 March 2016, accessed 23/03/18) is based on *clinical criteria* (rash with or without fever, and at least one of arthralgia or myalgia or non-purulent conjunctivitis/hyperaemia), *epidemiological criteria* (history of exposure in an area with transmission of Zika virus within two weeks prior to onset of symptoms or sexual contact with a male having been confirmed with a Zika virus infection in the past four weeks or sexual contact with a male who had been in an area with Zika virus transmission in the past four weeks) and *laboratory criteria* (for a probable case detection of Zika specific IgM antibodies in serum and for a confirmed case and at least one of the following: detection of Zika virus nucleic acid in a clinical specimen; detection of Zika virus antigen in a clinical specimen; isolation of Zika virus from a clinical specimen; detection of Zika virus specific IgM antibodies in serum sample(s) and confirmation by neutralisation test; seroconversion or fourfold increase in the titre of Zika specific antibodies in paired serum samples). On this basis, the following categories of cases are to be reported: a *probable case* (a patient meeting both the clinical and epidemiological criteria; or a person meeting the laboratory criteria for a probable case) and *confirmed case* (a person meeting the laboratory criteria for a confirmed case).

3.89 Other organisms

This section does not cover infections featured in the main Section 3 chapters (consult book index).

3.89.1 Bacteria

Key features of *Bartonella* and *Burkholderia* infections are given in Table 3.89.1.

3.89.2 Rickettsia, including typhus and ehrlichia

The order Rickettsiales includes the Rickettsiae, and Ehrlichiae, small Gram-negative intracellular parasites. Typhus refers to a number of illnesses caused by Rickettsiae.

Transmission is by an arthropod vector; the natural host is typically a rodent. The epidemiology of disease depends upon the interaction of people with the vector; disease may result from conditions of poverty and poor hygiene, occupational exposure or with leisure and walking (Table 3.89.2).

Prevention

Prevention is by reducing the incidence of vector bites through both personal and public health measures:

Avoiding tick bite: wear long trousers, tucked into socks, and use repellents (permethrin can be sprayed on boots and clothing, DEET (n, n-diethyl-m-toluamide) can be applied to the skin). Conduct body checks and remove ticks found using fine-tipped tweezers or fingers shielded with a tissue, paper towel, or rubber gloves. Grasp the tick close to the skin and pull upward steadily, twisting may break off the mouthparts. (If this happens, remove with tweezers). The tick (saliva, haemolymph, gut) may contain infectious organisms therefore do not squeeze or handle with bare hands. Following removal, disinfect the bite site and wash hands with soap and water.

In an epidemic of louse-borne disease, delousing measures with changing of clothes and impregnation with insecticide may be necessary.

Public health action

There is no person-to-person spread. Notifiable in many countries.

Review the need for intervention if louse-borne disease related to poor sanitation. Consider education campaigns for those exposed to vectors (e.g. information to walkers about ticks).

Clinical features

The clinical features depend upon the infecting organism. In typhus, following an infected arthropod bite, replication of the organism at the site may give rise to a characteristic skin lesion, a small painless ulcer with a black centre (an 'eschar'). The infection then becomes generalised with fever; which in severe infections is high and unremitting. If there is a rash, it appears around the fourth or fifth day of illness and may have either a dusky macular appearance or be petechial. In the most serious infections multiple organ damage may develop, usually towards the end of the second week.

Investigation

Rickettsial infection should be considered if there is fever, with either the typical rash or an eschar, and an appropriate travel history.

Diagnosis is usually clinical. Treatment decisions must be based on epidemiologic and clinical clues, and should not await laboratory confirmation. To confirm serologically, use assays that detect antibodies to rickettsial antigens, such as the indirect fluorescence antibody test. Increased IgM titres are usually seen by the end of the first week of illness. Diagnostic levels of IgG antibody generally do not appear until 7–10 days after the onset of illness.

Table 3.89.1 Main diseases caused by a selection of rare bacterial organisms

Disease and *organism*	Epidemiology	Clinical	Incubation period (days)	Vector/Mode of transmission	Laboratory diagnosis	Prevention and control
Bartonella						
These are vector-borne infections caused by a group of Gram-negative bacteria that are now considered re-emerging pathogens and are capable of causing chromic bacteraemia.						
Carrion disease (Oroya fever and verruga peruana) *Bartonella bacilliformis*	Case are mostly in young people aged >14 years. Outbreaks occur occasionally in endemic areas. Found in Andes mountains region of South America (Peru, Ecuador and Colombia)	Biphasic illness: Acute phase (Oroya fever): fever, pallor, jaundice, hepato-splenomegaly, lymphadenopathy, severe haemolytic anaemia and transient immunosuppression. Late phase (verruga peruana or Peruvian wart): cutaneous rash produced by a proliferation of new blood vessels. High case fatality if untreated.	21–90	Vector: sand fly Reservoir: Humans	Direct examination of Giemsa stained blood films (*B. bacilliformis*) or silver impregnated (Warthin–Starry staining) tissue samples (*Bartonella* spp.) Culture is possible but slow & difficult. Serology to detect antibodies against *Bartonella*. PCR based typing methods are useful for epidemiologic purposes.	Effective antibiotic treatment exists. Avoid arthropod vectors and cat scratches; treat body lice infestations and cat flea infestations.

(*Continued*)

Table 3.89.1 (*Continued*)

Disease and *organism*	Epidemiology	Clinical	Incubation period (days)	Vector/Mode of transmission	Laboratory diagnosis	Prevention and control
Cat-scratch disease *Bartonella henselae*	Worldwide distribution with peak incidence in autumn and winter.	Usually causes self-limited cutaneous papule or pustule and regional lymphadenopathy. Musculoskeletal symptoms may occur and encephalopathy is rare. Fever of unknown origin and endocarditis Bacillary angiomatosis: vascular proliferative disorder in immuno-compromised persons	3–10	Vector: cat flea Host: domestic and feral cats Transmission is via inoculation of faeces of arthropod vectors into non-intact skin		
Trench fever *Bartonella quintana*	Found worldwide but endemic in Eastern Europe, North Africa, Russia, and China. Clusters are associated with poor sanitation and poor personal hygiene; seen in homeless persons and those with AIDS.	Recurrent fever (5-day fever), headache, malaise; pain or tenderness in the shin. Rash may be macular or maculopapular. Chronic bacteraemia, endocarditis, lymphadenopathy, and bacillary angiomatosis may also occur.	15–25	Vector: human body louse Reservoir: humans		

Burkholderia *These are Gram-negative aerobic bacteria*						
Glanders *Burkholderia mallei*	It has been eradicated from most countries but remains endemic in parts of Africa, Asia, the Middle East and Central and South America. It primarily affects horses and other solipeds. Natural infection in humans is rare, but occasional cases occur from veterinary and laboratory exposures.	*Burkholderia mallei* and *B. pseudomallei* can cause acute or chronic infection. Clinical manifestation includes a localised, pus-forming, cutaneous infection with lymphadenopathy, fever and malaise. Pneumonia, pulmonary abscess, and septicaemia. Reactivation of latent infection can occur.	1–2 but may be as long as several months	Percutaneous transmission following contact with tissues or body fluids of infected animals. Transmission can also occur following inhalation of contaminated aerosols or dust. Sporadic cases have been documented in veterinarians, horse caretakers and those who work in laboratories.	Culture to isolate *B. mallei* from blood, sputum, urine, or skin lesions. (*Note: may be misidentified as pseudomonas*)	Identification and elimination of glanders in the animal population. Cases of glanders should be isolated. During clusters and outbreaks, consider the possibility of deliberate release. Cases should be reported to the public health authorities. Follow extant guidelines for managing laboratory exposure. Cystic fibrosis patients should consider avoiding travel to high-risk areas

(*Continued*)

Table 3.89.1 (*Continued*)

Disease and *organism*	Epidemiology	Clinical	Incubation period (days)	Vector/Mode of transmission	Laboratory diagnosis	Prevention and control
Melioidosis *Burkholderia pseudomallei*	Common in South-East Asia and northern Australia with increasing reports of cases in the South Pacific, Africa, India and the Middle East. Cases are rare in Europe and are imported, mostly from travel to South-East Asia.	Most cases are asymptomatic. Clinical features include skin ulcers or abscesses, chronic pneumonia and septicaemia. Mortality from melioidosis is 20–50% even with treatment. Antibiotic resistance is common. Reactivation of latent infection can occur.	1–21	*B. pseudomallei* is found in the soil, rice paddies, and stagnant water. Acquisition is via percutaneous inoculation, inhalation or ingestion of contaminated water and soil. Person-to-person transmission is very rare.	Culture to isolate *B. pseudomallei*. (*Note: may be misidentified as pseudomonas*) Molecular methods (PCR), latex agglutination assay, and rapid immunofluorescence are available.	

Table 3.89.2 *Rickettsia, Ehrlichia* and *Anaplasma* infections

Disease, *Organism*	Incubation Period (days)	Mode of Transmission and Epidemiology	Clinical
Rickettsiae: Typhus Group			
Epidemic (louse-borne) typhus *Rickettsiae Prowazekii*	7–14	Vector: Dog Tick Host: humans. Human-to-human transmission: human body louse. Principally a disease of tropical highlands such as Ethiopia and the Andes. Infestation occurs where poverty and a cold climate coincide.	Relatively mild in children, mortality increases with age; untreated, about 50% of 50-year-olds will die. There is no eschar, usually a rash, often petechial. The high fever may be associated with severe headache, vomiting and epistaxis. Complications include diminished consciousness, pneumonia and renal failure.
Murine typhus *Rickettsiae typhi*	7–14	Vector: Flea, Host: Rat. Found worldwide, particularly in tropical Asia.	Resembles epidemic typhus, but milder.
Rickettsiae: Spotted Fever Group			
Rocky Mountain Spotted Fever *Rickettsiae rickettsii*	3–14	Vector Dog Tick. Various hosts; rodents most significant. North American disease, occurs widely in the Eastern USA as well as in the Rocky Mountains.	Severe illness. The rash is typically petechial and complications, including pneumonia and myocarditis, are common. Untreated, the mortality is around 20%.
Boutonneuse fever, *Rickettsiae conorii, Rickettsiae slovaca*	5–8	Vector: Tick. Similar syndromes, occur in the Mediterranean, Asia, Australia and Brazil.	An eschar is usual, sometimes with regional lymphadenopathy, and a macular rash may occur; rarely fatal.
Rickettsial pox *Rickettsiae akari*	7–14	Vector: Mite. Found in S and E Asia and in parts of Queensland, Australia. Also reported from Russia, Eastern USA and South Africa.	Disseminated vesicular rash, may be confused with chickenpox. Fatality is low.
Spotted fever rickettsiae have been found on all continents except Antarctica. Those causing human rickettsioses include *R. africae* (African tick bite fever), *R. japonica* (Japanese spotted fever), *Rickettsiae sibirica* (North Asian tick typhus), *Rickettsiae helvetica* (p erimyocarditis), *Rickettsiae australis* (Queensland tick typhus) and *Rickettsiae honei* (Flinders Island spotted fever).			

(*Continued*)

Table 3.89.2 (*Continued*)

Disease, *Organism*	Incubation Period (days)	Mode of Transmission and Epidemiology	Clinical
Rickettsiae: Scrub Typhus Group			
Scrub typhus *Orientia. tsutsugamushi*	6–21	Vector: Mite Occurs in many parts of the world, including Japan, China, the Philippines, New Guinea, Indonesia, other southwest Pacific islands, SE Asia, northern Australia, India, Sri Lanka, Pakistan, Russia and Korea.	Only fever, headache, and swollen lymph nodes and in some cases myalgia, gastrointestinal complains, or cough. Mortality about 5% untreated.
Ehrlichia and Anaplasma: intracytoplasmic bacteria that infect mononuclear cells and granulocytes. In contrast to spotted fevers rash is rare and not petechial.			
Human monocytic ehrlichiosis *Ehrlichia chaffeensis – Ehrlichia canis* group	3–16 days – may be longer	Vector: deer ticks. Found in the USA and Thailand.	Illness similar to Rocky Mountain Spotted Fever but milder: acute fever (97%), headache (80%), muscle (57%) and joint pains (41%), general fatigue, vomiting (30%), rash (30%).
Human granulocytotropic anaplasmosis *Anaplasma phagocytophilum (formerly Ehrlichia phagocytophia – Ehrlichia equi group)*		Vector: tick. Host small mammals, deer. Found in N America, Europe (reported from Sweden, Norway, Germany, Switzerland, UK, Belgium, The Netherlands and Portugal).	Illness similar to human monocytic ehrlichiosis: acute fever, headache, muscle and joint pains, general fatigue, vomiting (30%). No rash.

Ehrlichiosis can be confirmed using serology (IFA), PCR may be available. Clusters of *Ehrlichia* (morulae) can be seen in infected cells.

3.89.3 Viruses

Person-to-person spread is rare with these viruses; however, it may occur in some (e.g. monkeypox). Public health action comprises identifying the mode of transmission and reducing exposure (Table 3.89.3). Expert advice should be sought.

3.89.4 Protozoa

Protozoa are unicellular eukaryotic microorganisms and is a sub-kingdom of the *Protista* kingdom. Some can cause human disease. For *Entamoeba* (amoebiasis) see Chapter 3.1; for *Cryptosporidium* see Chapter 3.16; for *Cyclospora* see Chapter 3.17; for *Giardia* see Chapter 3.24; for *Plasmodium* (malaria) see Chapter 3.45; for *Toxoplasma* see Chapter 3.77; and for *Trichomonas* see Chapter 3.26.

Leishmaniasis

Leishmania are flagellate protozoan parasites transmitted by the bite of sand flies. Cutaneous leishmaniasis (CL) is the most common form of disease, visceral leishmaniasis (VL) occurs when parasites have migrated to vital organs.

There are a number of species of *Leishmania*, these include the *Leishmania donovani* complex; the *Leishmania mexicana* complex; *Leishmania tropica*; *Leishmania major*; *Leishmania aethiopica*; and the subgenus *Viannia*. The different species are not distinguishable morphologically, but can be differentiated by DNA sequence or monoclonal antibodies (Table 3.89.4a).

Trypanosomiasis

There are three trypanosomes pathogenic to humans: the causes of African trypanosomiasis, *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense*, and *Trypanosoma cruzi*, the cause of South American trypanosomiasis (Table 3.89.4b).

Babesiosis

Infection with bovine or rodent *Babesia* spp. causes a malaria-like illness (Table 3.89.4c).

Acanthamoebiasis

Acanthamoebae are free-living trophozoites in moist environments that can cause keratitis. The microorganism can survive in the space between lens and the eye, especially in people using contact lenses (Table 3.89.4d). Several species of *Acanthamoeba* can cause granulomatous amoebic encephalitis, a chronic fatal disease of the CNS associated with immunocompromised patients. Acanthamoebae may serve as a reservoir in the environment for pathogenic bacteria such as *Legionella* species, and are an important factor in water management preventing Legionnaire's disease.

Naegleriasis

Naegleria fowleri is a thermophilic free-living amoeba, found in warm fresh water. It can cause primary amoebic meningoencephalitis, a rare but rapidly fatal hemorrhagic necrotizing infection of the CNS, which generally occurs in previously healthy children and young adults with a history of swimming and other recreational activities in warm fresh water (Table 3.89.4e).

Pneumocystis carinii

Pneumocystis carinii was renamed *Pneumocystis jirovecii*. It used to be classified as a protozoan, but is now considered a fungus (see Chapter 3.89.6).

Table 3.89.3 Rare potentially imported viral infections. The table does not cover infections with their own chapters or viral haemorrhagic fevers (Chapter 3.82)

Viral family	Infection / agent	Clinical	Incubation period	Vector/transmission	Geographical spread
Arenaviridae	Lymphocytic choriomeningitis virus (*Mammarenavirus*)	Meningoencephalitis	8–13 days	Rodents such as the common house mouse, hamster, cell lines	USA, South America, Europe
Bunyaviridae	Bunyamwera virus (*Orthobunyavirus*)	Fever, headache, non-specific	3–12 days	Mosquitoes (*Aedes* spp.)	All continents except Australia and Antarctica
	Bwamba virus (*Orthobunyavirus*)	Fever, headache, arthralgia, local as well as generalised pain, and rash. Often mistaken for malaria.	3–12 days	Mosquitoes (*Anopheles* spp.)	Widespread in Africa
	Oropouche (*Orthobunyavirus*)	Fever, headache, non-specific	3–12 days	Mosquitoes (*Aedes* and *Culex* spp.), midges (*Culicoides*)	Central and South America
	California encephalitis (*Orthobunyavirus*)	Meningoencephalitis	5–15 days	Mosquitoes (*Aedes* spp.)	USA, Canada
	La Crosse virus (*Orthobunyavirus*)	Meningoencephalitis	5–15 days	Mosquitoes (*Aedes triseriatus*)	Midwestern, mid-Atlantic and south-eastern USA
	Toscana virus/Sandfly fever (*Phlebovirus*)	Fever, headache, retro-orbital pain, non-specific	3–12 days	*Phlebotomus* flies and mosquitoes	Africa and some parts of Asia and Mediterranean
	Bhanja virus (*Phlebovirus*)	Fever, photophobia, vomiting, meningoencephalitis	3–12 days	Ticks (*Dermatocenter* spp. in Europe, *Haemaphysalis intermedia* in India, *Hylaomma* spp. in Africa)	Europe (Italy, Croatia, Bulgaria, Romania, Eastern Slovakia), Africa, Asia.
Flaviviridae	Powassan virus (*Flavivirus*)	Fever, encephalitis	7–28 days	Ticks (*Ixodes* spp.)	USA, Canada, Russia
	Louping ill (*Flavivirus*)	Fever, encephalitis	7–14 days	Ticks (*Ixodes ricinus*)	UK, Ireland, Norway
	St. Louis encephalitis (*Flavivirus*)	Mostly asymptomatic, rarely encephalitis	5–15 days	Mosquitoes (*Culex* spp.)	Americas from Canada to Argentina
Paramyxoviridae	Hendra virus (*Henipavirus*)	Fever, flulike symptoms, encephalitis	9–21 days	Horses, bats	Eastern Australia
	Nipah virus (*Henipavirus*)	Respiratory disease, meningoencephalitis	5–14 days	Bats, pigs, person-to-person	Southern and south-eastern Asia

Poxviridae	Monkeypox virus (*Orthopoxvirus*)	Fever, skin lesions similar to smallpox	5–21 days	Monkeys, squirrels, prairie dogs	Central Africa, USA
	Cowpox virus (*Orthopoxvirus*)	Nodular skin lesions	7–21 days	Cats, rodents, cattle	Europe, Western Asia
	Orf virus disease (*Parapoxvirus*)	Nodular skin lesions	3–7 days	Sheep, goats, cattle	Worldwide
	Pseudocowpox virus (*Paravacciniavirus*)	Nodular skin lesions (milker's nodules)	5–14 days	Cattle	Worldwide
Reoviridae	Colorado tick fever (*Coltivirus*)	Meningoencephalitis, systemic symptoms, rash	1–14 days	Ticks (*Dermatocenter* spp.)	USA (Rocky Mountain area)
	Eyach virus (*Coltivirus*)	Meningoencephalitis, systemic symptoms, rash	1–14 days	Ticks (*Ixodes* spp.)	Germany, France; Netherlands, Czech Republic, Slovakia
Togaviridae	Eastern equine encephalitis (*Alphavirus*)	Systemic symptoms or encephalitis	4–10 days	Mosquitoes (*Aedes, Coquillettidia,* and *Culex* spp.)	Eastern and central USA
	Western equine encephalitis (*Alphavirus*)	Mostly asymptomatic, systemic symptoms, rarely severe encephalitis	5–10 days	Mosquitoes (*Culex, Aedes* and *Psorophora* spp.)	North and South America
	Venezuelan equine encephalitis complex (*Alphavirus*)	Systemic symptoms or encephalitis	2–6 days	Mosquitoes (*Aedes, Culex, Psorophora,* and *Ochlerotatus* spp.)	South and central America, USA (Florida only for Everglade EE)
	Barmah Forest virus (*Alphavirus*)	Fever, arthritis, myalgia, rash	3–11 days	Mosquitoes (*Aedes* and *Culex* spp.)	Australia
	Ross River virus (*Alphavirus*)	Fever, arthritis, myalgia, rash	3–21 days	Mosquitoes (*Aedes* and *Culex* spp.)	Australia, South Pacific
	Sindbis virus (*Alphavirus*)	Fever, arthritis, myalgia, rash	3–11 days	Mosquitoes (*Culex* and *Culiseta* spp.)	Widespread in Europe (with outbreaks in Sweden and Finland), Africa, Asia, Australia
	Semliki Forest virus (*Alphavirus*)	Malaria-like symptoms	Unknown	Mosquitoes (*Aedes*)	Africa, India, southeast Asia
	O'nyong'nyong (*Alphavirus*)	Fever, arthritis, myalgia, rash	>8 days	Mosquitoes (*Anopheles* spp.)	East Africa with large outbreaks

Table 3.89.4a Leishmaniasis

Incubation period	Cutaneous (CL): a few days to more than 6 months. Visceral (VL): usually 2–4 months, may be prolonged (10 days–10 years).
Infectious period	As long as there are parasites present, this may be many years. Person-to-person spread is reported.
Epidemiology	Tropical and subtropical areas of the Mediterranean, Middle East, Indian subcontinent and South America.CL over 1 million annually; highest incidence in Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia, Syria.VL 300 000 cases, 20 000 deaths annually; highest incidence in Bangladesh, India, Nepal, Sudan and Brazil. In Europe slowly spreading in northern direction, first autochtonous cases reported from southern Germany. Leishmania HIV-co-infections seen in Spain, Portugal, Southern France and Italy.
Clinical	Cutaneous (CL): the lesions begin as a small itching papule with increasing infiltration of the dermis. The lesion becomes crusted which, when scratched, produces a shallow discharging ulcer. Mucocutaneous (espundia): progressive involvement of destructive cutaneous lesions. Visceral (kala azar, VL): a primary lesion resembling cutaneous leishmaniasis may occur. The onset is usually insidious. Patients present with anorexia, malaise and weight loss, and may complain of abdominal discomfort due to splenic enlargement. Anaemia and cachexia are present and the liver and spleen are enlarged. Fever is intermittent and undulant with often two spikes in 1 day. Untreated patients undergo a slow decline and die usually from secondary infections after about 2 years. More severe clinical features in patients with impaired cellular immunity (e.g. HIV infection).
Investigation	Amastigotes of *Leishmaniasis donovani* may be found by direct microscopy of slit skin smears (cutaneous disease), bone marrow or splenic aspirate. Occasionally, amastigotes may be demonstrated in the buffy coat cells. PCR (not yet standardised).VL: serology (DAT, ELISA, IFAT), dip-stick.
Mode of transmission	Transmitted to humans by the bite of a sand fly. Infective blood meals may come from another human or an animal reservoir host. This may be a fox, wolf, dog or rodent, depending on the species of *Leishmania* (hares in Spain).
Public health action	Measures to break transmission cycle. Prevent insect bites using repellants (DEET) and appropriate clothing, impregnated mosquito nets. Reduce dog reservoir with impregnated collars, repellant droplets. Cover the cutaneous lesion. No isolation required. VL: direct person-to-person spread through blood transfusion, sharing needles (IDU), rarely mother to child.

Table 3.89.4b Trypanosomiasis

Disease and organism	African human trypanosomiasis. *Trypanosoma brucei gambiense.* *Trypanosoma brucei rhodesiense.*	South American trypanosomiasis Chagas' disease *Trypanosoma cruzi*
Incubation period	*T.b. gambiense*: few days to months *T.b. rhodesiense:* few days to 2–3 weeks	1–2 weeks for acute disease. Many years for chronic
Epidemiology	Control efforts have reduced the estimated numbers to below 20 000 per year. *T.b. gambiense*: West and Central Africa, river and lakeside areas. Humans are the main reservoir. *T.b. rhodesiense:* Southern and Eastern Africa, wild antelope (particularly the bushbuck) is reservoir.	Estimates of 6–7 million people infected in Continental Latin America. Increasingly diagnosed in USA, Canada, and European and Western Pacific countries

Table 3.89.4b (*Continued*)

Clinical	*T.b. gambiense*: chronic course and can last several years. *T.b. rhodesiense*: acute, untreated infection can cause death in a few months and usually before 1 year. Initial sign is a papule that develops into an indurated nodule (chancre) at the bite site. The diagnosis should be suspected in a patient with fever and lymphadenopathy who has recently resided in an endemic area. Death occurs as a result of encephalitis, which may be insidious.	In many instances acute infection is asymptomatic or unrecognised. A local inflammatory reaction at the site of the bite with regional lymphadenopathy, generalised adenopathy and hepatomegaly may also be found. Acute infection is complicated by myocarditis in about 15% of cases, and most deaths are due to this complication. The latent stage follows and this asymptomatic period may last for up to 25 years. The final stage, Chagas' disease, is characterised by cardiomyopathy and intractable congestive cardiac failure.
Investigation	Parasites may be demonstrated by Giemsa-stained films of the peripheral blood during the early stages of infection, in the CSF, and sometimes in a lymph node aspirate. Serological tests are largely useful for screening; the wb-CATT may be useful in diagnosis.	Examination of peripheral blood for parasites. Parasites may be concentrated by centrifugation and lysis of the red cells. *T. cruzi* may be cultured *in vitro* or in mice. In xenobiotic culture laboratory-reared triatomid bugs are fed on the patient with suspected disease. After 30 days trypomastigotes are sought in the insect's gut. An antibody ELISA is available, this is most useful in excluding Chagas' disease in those from endemic areas and in sero-epidemiological surveys. PCR may be available.
Mode of transmission	Bite of the tsetse fly. Mother-to-child transmission, laboratory infection, and sexual transmission are reported.	Infective organisms, excreted in the faeces of biting triatomid bugs (living in cracks in poorly constructed houses, active at night when feeding on human blood) are inoculated into the bite when the victim scratches. Transfusion of blood and blood products may cause transmission. Food contaminated with faeces or urine of infected bugs can transmit *T. cruzi*. Mother-to-child transmission and laboratory infections reported.
Public health action	Vector control and elimination. There are no control implications outside endemic areas.	Improve the quality of housing construction. Spraying houses with residual insecticide. No control implications outside endemic areas.

Table 3.89.4c Babesiosis

Incubation period	1–4 weeks, may be up to 9 weeks
Epidemiology	USA (Long Island, Massachusetts), Ireland, UK, France, Japan, Korea, China, Mexico, South Africa and Egypt.
Clinical	Most cases are asymptomatic or mild fever. May be similar to malaria, with fever, chills and severe haemolytic anaemia with organ failure. Splenectomised patients are at increased risk.
Investigation	Blood film, PCR.
Mode of transmission	Tick-bite. Similar transmission and epidemiology to Lyme disease and ehrlichiosis. Transfusion associated.
Public health action	Avoid tick bites.

Table 3.89.4d Acanthamoebiasis

Epidemiology	The microorganism is ubiquitous and lives in moist environments (freshwater, tapwater, soil). In the industrialised world keratitis is rarely seen, only in people using contact lenses. The reference lab in Austria reports less than 10 cases per year. In other parts of the world keratitis is also seen in people without contact lenses.
Clinical	Acanthamoeba invading the cornea of the eye results in keratitis, ultimately leading to permanent visual impairment or blindness.
Investigation	Culture of lens, PCR.
Mode of transmission	Insufficient cleaning of lenses.
Public health action	Follow hygienic instructions for using and cleaning contact lenses. Remove contact lenses before swimming or surfing.

Table 3.89.4e Naegleriasis

Incubation period	1–7 days.
Epidemiology	Underdiagnosed and underreported. European data are unknown. In the USA the estimated number of fatal cases is 16 per annum (8 male, 8 female).
Clinical	Meningoencephalitis, cerebral oedema. Survival is reported, but most cases are diagnosed post mortem.
Investigation	CSF microscopy, PCR.
Mode of transmission	The microorganism enters the nose and subsequently invades the brain. The majority of reported cases have a history of swimming in warm fresh water. Infection after nasal irrigation with non-sterile water is reported.
Public health action	Follow hygienic instructions in nasal irrigation. Early diagnosis and treatment might influence survival.

3.89.5 Helminths

For schistosomiasis see Chapter 3.67; for threadworms (pinworms) see Chapter 3.74; and for *Toxocara* see Chapter 3.76.

Intestinal roundworms

Most intestinal nematodes are not passed directly from person to person and so spread is rare in developed countries (Table 3.89.5a). Control is based on enteric precautions and early treatment of cases. The main exception is threadworm infection (see Chapter 3.74).

Filariae

Filariae produce larvae called microfilariae directly without an egg stage. Their life cycle involves an arthropod intermediate host, usually a biting insect which acts as a vector for the dissemination of the disease. At least 10 species infect humans. The incubation period is prolonged and may be more than a year. There is no person-to-person spread; individuals remain infectious for the insect vector if microfilariae are present. The endemic range of the diseases is determined by the insect vector (Table 3.89.5b).

Tapeworms

Humans are the only definitive host for the tapeworms *Taenia saginata* and *Taenia solium* and may also be accidental intermediate hosts for *T. solium*, giving rise to cysticercosis, and for *Echinococcus granulosus*, giving rise to hydatid disease.

Eggs, or whole detached segments (proglottids), are evacuated in the faeces of the definitive host and disseminate in the environment. Following ingestion by a suitable intermediate

Table 3.89.5a Intestinal roundworms

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Ascariasis *Ascaris lumbricoides*	Non-infective eggs excreted in faeces, become infectious after 2–3 weeks in soil and may survive for many months. Infective eggs ingested from soil or foods contaminated by soil. Eggs hatch in the duodenum. Larvae migrate in blood and lymphatics to lung and oropharynx where swallowed to develop into adult worms in small intestine. Adults live 6–12 months.	Migrating larvae may produce an eosinophilic pneumonia. Asymptomatic patient may pass an adult worm by vomiting or per rectum. Heavy infection may produce abdominal cramps and may cause intestinal obstruction. Even moderate infections can lead to malnutrition in children.	Identification of the eggs in faeces. Occasionally, adult worms are passed in the stool or vomited.	Worldwide but concentrated in tropical and subtropical areas with poor sanitation. Estimated that more than 1 billion persons are infected making ascariasis the world's most prevalent intestinal helminth infection. Uncooked and unwashed vegetables should be avoided in areas where human faeces (night soil) is used as fertiliser. There is no risk of transmission from a case in Europe if basic hygienic precautions are taken.
Whipworm infection *Trichuris trichiura*	Non-infective eggs excreted in faeces to develop in soil over 10–14 days. Ingested from soil or via contaminated food or water. No migration to other tissues. Adult worms may live 7–10 years.	Infection is often asymptomatic. Heavy infection causes abdominal pain, anorexia and diarrhoea and may retard growth. Rarely, weight loss, anaemia, and rectal prolapse may occur.	Identification of the eggs in faeces.	The parasite is found principally in the tropics and subtropics. Prevention rests upon adequate sanitation and good personal hygiene.
Hookworm infection *Ancylostoma duodenale* or *Necator americanus*	Eggs passed in human stool hatch in 1–2 days and release larvae, which mature over 5–8 days and may then penetrate human skin (often foot), migrate to the lungs via blood vessels, ascend to epiglottis and are swallowed. Adult worms may live 2–10 years. Occasionally, cat or dog hookworms may infect humans.	Most cases are asymptomatic. Migration of larvae may cause an eosinophilic pneumonia. Adult worms in the intestine may cause colicky pain and non-specific symptoms. Chronic infection may lead to iron deficiency anaemia and hypoproteinaemia.	Identification of the eggs in faeces.	*A. duodenale* is widely distributed in the Mediterranean, India, China, Japan and South America. *N. americanus* is the predominant hookworm of Central and South Africa, Southern Asia, Melanesia, the Caribbean and Polynesia. About 25% of the world's population is infected with hookworms. Preventing defecation where others may come into contact with the stool. Avoiding direct skin contact with the soil. Wearing shoes. Periodic mass deworming may be effective in high risk populations.

(*Continued*)

Table 3.89.5a (*Continued*)

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Strongyloidiasis *Strongyloides stercoralis*	Adult worms live in the duodenum and jejunum. Released eggs hatch immediately and larvae are then passed in faeces. After a few days the larvae can penetrate the skin of humans, migrate through the lungs, and reach the intestine, where they complete maturation in about 2 weeks. Filariform larvae can bypass the soil phase and directly penetrate the colon or the skin. Transmission is often due to exposure of bare skin to larvae in contaminated soil in unsanitary conditions. Faeco-oral transmission may occur in mental institutions and daycare centres. Self-reinfection may occur and can result in extremely high worm burdens (hyperinfection syndrome).	Most cases are asymptomatic. There may be non-specific abdominal symptoms. An enteritis, protein losing enteropathy, urticaria and pulmonary symptoms are seen less frequently. Larva currens, a serpiginous, migratory, urticarial lesion, is pathognomonic. The hyperinfection syndrome and disseminated strongyloidiasis are usually seen in persons with impaired immunity. Immunosuppression may lead to overwhelming hyperinfection in persons with previously asymptomatic infection. Hyperinfection produces serious gastrointestinal symptoms including haemorrhage, pulmonary infiltration, hepatitis and may involve the CNS. Even with treatment the mortality is over 50%.	Larvae can be identified in stool 25% of the time. Repeat examination of concentrated stool is necessary. Antibody detection (EIA)	Endemic throughout the tropics and subtropics. Prevention of primary infections is as for hookworms. To prevent hyperinfection syndrome, patients with possible exposure to *Strongyloides* (even in the distant past), should undergo several stool examinations and, if necessary, a string test or duodenal aspiration before receiving immunosuppressive therapy including steroids.

Trichinosis *Trichinella* sp, especially *T. spiralis*	Infectious cysts are acquired from eating undercooked meat from infected carnivores or omnivores (pigs). Larvae develop in the small intestine, penetrate the mucosa, and become adults in 6–8 days. Mature females release larvae for 4–6 weeks, before dying or being expelled. Larvae pass though the intestinal wall and travel to striated muscle cells, where they encyst over 1–3 months. The cycle continues when encysted larvae are ingested by another carnivore.	Gastrointestinal symptoms are absent or mild; nausea, abdominal cramps and diarrhoea may occur during the first week. The characteristic syndrome of periorbital oedema, myalgia, fever and subconjunctival haemorrhages and petechiae appears in weeks 2–3. Soreness may affect the muscles of respiration, speech, mastication, and swallowing. Heavy infection may cause severe dyspnoea, multisystem disease, or fatal myocarditis. Most symptoms and signs resolve by the third month.	There are no specific tests for the intestinal stage. Eosinophilia peaks 2–4 weeks after infection. Muscle enzymes are elevated in 50% of patients. A muscle biopsy may disclose larvae, inflammation and cysts. Serology can give false negative results, especially if performed early. They are of most value if initially negative and turn positive.	Trichinosis occurs worldwide. The life cycle is maintained by animals that are fed on (e.g. pigs) or that hunt (e.g. bears) and other animals whose striated muscles contain encysted infective larvae (e.g. rodents). There have been outbreaks in Europe associated with imported horsemeat. Trichinosis is prevented by cooking meat thoroughly (55 °C (140 °F) throughout). Larvae can also be killed by freezing at −15 °C (5 °F) for 3 weeks or −18 °C (0 °F) for 1 day. Meat should be inspected before being sold. There is no person-to-person spread. Investigate clusters for a common contaminated food source.
Intestinal capillariasis *Capillaria philippinensis*	Larvae acquired from gut of undercooked fish. Mature and multiply in human gut.	Gastrointestinal symptoms: weight loss, diarrhoea, abdominal pain; may be fatal.	Faeces microscopy. Intestinal biopsy.	Philippines. Avoid raw whole fish.
Hepatic capillariasis *Capillaria hepatica*	Eggs are present in soil or food contaminated with faeces of infected rodents. Larvae migrate to and mature in liver.	Fever, eosinophilia, hepatomegaly.	Liver imaging and biopsy.	Found on all continents in rodents, rare in humans.
Pulmonary capillariasis, Lung worm *Capillaria aerophila*	Similar to *C. hepatica except* host is often dog or cat and final maturation is in lung.	Cough, wheeze.	Eggs in nasal or tracheal lavage.	Found on all continents, rare in humans.

Table 3.89.5b Filariae

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Lymphatic filariasis (elephantiasis), *Wuchereria bancrofti*, *Brugia malayi*	Adult worms inhabit the lymphatics; the microfilariae, which have a strong diurnal periodicity, appear briefly in the peripheral blood around midnight when they can be ingested by mosquitos, which are the vectors.	Cause of elephantiasis. Fever and lymphangitis may occur early in the disease; the most serious consequences are the chronic sequelae of lymphatic damage caused by dying worms. Gross lymphoedema, most often of the legs or genitals, and chyluria are typical features.	Definitive diagnosis is by recognition of the microfilariae (in a midnight sample of blood for *W. bancrofti)*. Rapid antigen test is often used in elimination programmes. Serology provides supportive evidence, but there may be cross-reactions with other nematode infections.	*W. bancrofti* has a widespread distribution in South Asia, the Pacific islands, tropical Africa and some parts of South America. Two species of *Brugia*, restricted to South-East Asia, give rise to a similar syndrome. Eliminating vector breeding sites.
Onchocerciasis (river blindness), *Onchocerca volvulus*	Microfilariae in the skin are ingested by a black fly of the genus *Simulium*.	The adult *Onchocerca* lives in the subcutaneous tissues. Clinical consequences are caused by the inflammation resulting from death of the microfilariae. In the skin this causes a chronic dermatitis. Most significant is damage to the eye. The inflammatory process may involve all the structures between the cornea and the optic nerve. Blindness occurs after 20 years or more of heavy infection.	Diagnosis depends on detecting microfilariae in superficial snips of skin.	Primarily an African disease although there are some foci in Central America. Eliminate vector breeding sites.

Loiasis: *Loa loa* (African eye worm)	Human reservoir. Spread by bites of *Chrysops* spp (deer fly). Adult *Loa loa* are migratory and roam widely in the subcutaneous tissues and may become visible on passing under the conjunctiva of the eye. The microfilariae appear with a diurnal periodicity in the blood around midday.	Many cases asymptomatic, symptoms include 'Calabar swellings', diffuse areas of subcutaneous oedema, usually distally on the limbs, which last a few days.	Diagnosis is by recognising the microfilariae in midday blood.	Rainforests of West and Central Africa Eliminate vector breeding sites.
Dracontiasis Dracunculiasis *Dracunculus medinensis* (Guinea worm)	The disease is acquired by drinking water containing *Cyclops* ('water fleas') which harbour larvae. The larvae invade into the body cavity mature and mate. The gravid female, about 60 cm long, then makes her way to the lower extremities where she penetrates to the surface, giving rise to an irritating ulcer. Contact with water causes her to release larvae through this defect where they may be able to infect new *Cyclops*.	The chronic ulceration, and associated secondary infection, may be a severe problem in conditions of poor hygiene. Death of the worm causes intense inflammation.	Recognition of larvae or adult worm.	Now only Sudan, Ghana, Mali and Ethiopia. Eradication planned. Provision of clean drinking water. Filtering drinking water. Treat water with larvicides.

host they develop into invasive larvae in the gut, migrate through the tissues, and settle as cysts at sites determined by the tropism of the parasite. When the intermediate host is eaten by a definitive host, allowing the cysts to develop into adults, the life cycle is completed (Table 3.89.5c).

Trematodes, flukes

Most flukes' life cycles involve molluscs; infection is acquired from an intermediate host, from cysts on water plants or direct penetration of skin. Human disease results either from the reaction to the eggs (schistosomes), obstruction (liver flukes) or inflammation at the site of attachment of intestinal flukes, which may lead to malabsorption. Chronic infection may result in malignancy. There is no person-to-person spread (Table 3.89.5d).

3.89.6 Fungi and actinomycetes

For ringworm (tinea), including onychomycosis, see Chapter 3.62.

Fungi can be divided in yeasts (e.g. *Candida* and *Cryptococcus*) and filamentous fungi or moulds (e.g. *Aspergillus*, *Trychophyton*). Some have both forms and are called 'dimorphic' (e.g. *Histoplasma*).

Infections can be broadly classified according to the site and severity of infection:

- Superficial mycoses: confined to the outer layers of skin, hair and nails (ringworm, athlete's foot, tinea capitis, onychomycosis),
- Mucosal infection: oral and oesophageal (*Candida* vaginitis or thrush),
- Allergic fungal disease (allergic bronchopulmonary aspergillosis [ABPA], severe asthma with fungal sensitization [SAFS]),
- Chronic lung or deep tissue infection,
- Invasive fungal infections (cryptococcal meningitis, aspergillosis, candidemia, pneumocystis pneumonia).

Opportunistic fungal pathogens such as *Aspergillus, Candida, Cryptococcus, Rhizopus* and *Pneumocystis jiroveci* are distributed worldwide and constitute the majority of invasive fungal infections (IFIs). Dimorphic fungi such as *Histoplasma capsulatum*, *Coccidioides* spp., *Paracoccidioides* spp., *Blastomyces dermatiditis*, *Sporothrix schenckii*, *Talaromyces (Penicillium) marneffei*, *and Emmonsia* spp. are geographically restricted to their respective habitats and cause endemic mycoses.

Life-threatening fungal infection has increased due to the rising prevalence of immunocompromise, resulting from disease (HIV, cancers) or immunosuppressive treatments – this is particularly due to opportunistic mycoses, fungi of low inherent virulence (Table 3.89.6). A number of primary monogenic immunodeficiency disorders have been identified that cause increased susceptibility to fungal infections. In addition, changing patterns of behaviour are bringing larger populations in contact with potentially pathogenic fungi.

Diagnostic methods have increased with molecular techniques and mass spectrometry (Matrix-assisted Laser Desorption/Ionisation Time of Flight: MALDI-TOF) and treatment options have improved. Treatment of serious fungal disease is complex and should be undertaken in collaboration with an infectious disease specialist/microbiologist.

3.89.7 Bites, stings, and venoms

Epidemiology

Although Western Europe has few indigenous venomous species, the pet trade has increased the likelihood of exposure to exotic animals that may bite or sting.

Bites

Human, dog and cat

These bites frequently become infected. The sharp teeth of cats are especially risky as they can cause punctures with deposition of saliva deep in the tissues, with a wound that initially

Table 3.89.5c Tapeworms (cestodes)

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Taeniasis *Taenia saginata,* *Taenia solium*	Infection is acquired by eating undercooked infected pork or beef.	Adult *T. saginata* (beef tapeworm) may grow to 10 m and *T. solium* (pork tapeworm) to 4 m. However, infection is usually asymptomatic. Abdominal pains are sometimes reported. Detached motile segments (proglottids) of *T. saginata* may be noticed as they emerge from the anus.	Taeniasis infections are usually diagnosed because of eggs or proglottids in the faeces	Occurs in most countries where beef or pork is eaten undercooked. Rare in North-West Europe. Basic hygienic precautions. Exclusion of cases of pork tapeworm in risk groups 1–4 (see Box 2.2.1) until treated. Regular deworming of pets.
Dwarf tapeworm *Hymenolepsis nana*	Eggs excreted in human faeces are infectious. May spread faeco-orally or via contaminated food. May be auto-infection.	Asymptomatic or mild abdominal discomfort. May be anorexia, dizziness, diarrhoea.	Identification of characteristic eggs in faeces.	Occurs in Asia, South-East Europe, Africa, Latin America. Occasionally found in institutions or the immunocompromised. Basic hygiene precautions. Exclusion of risk groups (Box 2.2.1) until treated. Consider screening household.
Fish tapeworm *Diphyllobothrium latum*	Acquired by eating undercooked fish.	Causes B_{12} deficiency.	Identification of eggs in faeces.	Worldwide, rare in North-West Europe. Avoid raw, smoked or undercooked fish.
Cysticercosis Due to the larval stage of pork tapeworm (*T. solium)*	If eggs excreted by a human carrier of the pork tapeworm are ingested by other humans, the cysticerci preferentially settle in skeletal muscle and central nervous system, where they act as space-occupying lesions. Auto-infection possible.	Clinical features may include epilepsy, raised intracranial pressure and chronic basal meningitis.	Diagnosis has been much advanced by modern imaging techniques, which may be supported by serology or by evidence of cysticerci in other tissues. Definitive identification of parasite segments and eggs, and serology is available from reference laboratory	Cysticercosis occurs in most countries where pork is eaten undercooked and person-to-person transmission occurs. Rare in North-West Europe. Treatment of Cysticercosis should be undertaken by specialists. Poor hygiene, close contact with tapeworm cases and contaminated water/food are all risk factors. Treatment of infected animals and humans. Safe disposal of faeces.

(*Continued*)

Table 3.89.5c (*Continued*)

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Hydatid disease Due to the dog tapeworm *Echinococcus granulosus*, or *Echinococcus multilocularis*	Humans acquire hydatid cysts, the metacestodes of *Echinococcus* sp. by ingesting eggs excreted in the faeces of an infected dog.	The most common sites for hydatid cysts are liver, lung and bone. The cysts expand slowly over several years. Occasional leaks may cause hypersensitivity phenomena such as generalised urticaria and can seed further cysts at distant sites. Symptoms are most often due to the mass effect of the lesion.	An appropriate imaging technique, such as ultrasound of the abdomen, will reveal the diagnosis, and may be supported by serology.	Hydatid is found in most sheep and cattle raising parts of the world. Treatment of Hydatid disease should be undertaken by specialists. Poor hygiene and close contact with infected animals are risk factors.
Sparganosis Infection by larvae of *Spirometra* tapeworm *Spirometra*	Exposure to contaminated water or to flesh of an infected frog used as poultice (South-East Asia).	Larvae develop into cysts in subcutaneous tissue.	Microscopy of lesion.	Avoid frog poultices. Water sanitation.

Table 3.89.5d Flukes (trematodes)

Disease and *organism*	Mode of transmission	Clinical	Investigation	Epidemiology and public health action
Lung fluke *Paragonimus westermani*	Eating uncooked crustaceans (e.g. prawns, crabs).	Cough, wheeze.	Sputum examination. Serology.	Asia, South America.
Liver fluke *Fasciola hepatica, Fasciola gigantia*	Eating contaminated water plants (e.g. watercress); ingesting contaminated water. Main hosts are cattle and sheep; snails are intermediate hosts.	Fluke may obstruct biliary ducts. Fever, abdominal pain, malaise, weight loss, eosinophilia, hepatomegaly may occur.	Stool examination. Serology.	Worldwide, including Portugal, France and Spain. Avoid water plants in contaminated areas.
Oriental liver fluke, Clonorchiasis *Clonorchis sinensis* Opisthorchiasis *Opisthorchis* spp	Eating undercooked or raw fish.	Bile duct infestation. Chronic liver disease. Cholangiocarcinoma.	Stool/duodenal aspirate examination for eggs. Serology, antigen detection, PCR. CT/MRI.	Clonorchiasis: China, South-East Asia, E Russia. Opisthorchiasis In Europe (Russia, former USSR) and Asia. Cook fish, educate public.
Intestinal flukes *Fasciolopsis buski* There are large *numbers* of intestinal flukes fasciolipsis is shown as an exemplar.	Eggs in human faeces contaminate fresh water. These hatch into miracidia which infect snails. A maturation cycle produces cercariae which encyst on plants which are consumed by humans.	Most infected people are asymptomatic. Large numbers of worms provoke mucous discharge and may cause obstruction. Mucosal damage causes complications.	Eggs in faeces or vomitus.	Endemic in Far East, South-East Asia.

For an overview on laboratory identification of parasites see also the overview from the US-CDC (https://www.cdc.gov/dpdx/az.html).

Table 3.89.6 Fungal infections

Disease, organism, epidemiology, investigation and public health relevance	Clinical
Actinomycosis *Actinomyces israelii, gerencseriae, graevenitzii, meyeri, neuii, turicensis,* etc. (25 species described from human material) Actinomycetes are bacteria formerly classified with fungi as they can be grown on fungal media and form long branching chains. Species of *Actinomyces* are among the causes of mycetoma (see below) Occurrence: worldwide Investigation: microscopy. Identify Gram-positive filaments, sulphur granules. 16S rRNA sequence analysis, MALDI-TOF mass spectrometry Transmission: endogenous organism. Public health relevance: none.	An indolent slowly progressing chronic suppurative, granulomatous disease. May present with jaw/tooth abscess, abscesses may also be found in the thorax and abdomen. Lesion often drains pus. In the last decade, using advanced molecular methods *Actinomyces* species are increasingly being associated with infections at many body sites (e.g. brain, eye, ear/nose/throat, urosepsis).
Aspergillosis *Aspergillus fumigatus, A. flavus* Occurrence: worldwide Incubation period: days to weeks. Investigation: serum precipitins, microscopy of sputum. Culture confirmation. Serum and BAL galactomannan antigen positivity. Transmission: inhalation of organism found in damp hay, decaying vegetation, soil, household dust, building materials, ornamental plants, food and water. Public health relevance: clusters may occur where the immunocompromised are gathered together: Leukaemia and transplant centres should perform regular surveillance of cases of invasive mould infection. Environmental investigation should be carried out to determine the source. Nosocomial infection may be associated with dust exposure during building or renovation works. Occasional outbreaks of cutaneous infection traced to contaminated biomedical devices. High-risk patients should avoid gardening, spreading mulch (compost), and close exposure to construction or renovation.	Chronic pulmonary disease. Invasive disease in the immunocompromised, most frequently involves the lungs and sinuses. May disseminate and involve brain, bones and other organs. Also causes allergic sinusitis and allergic bronchopulmonary disease. If severe granulocytopaenia persists, mortality rate can be very high (up to 100% in patients with cerebral abscesses). Patient outcome depends on resolution of granulocytopaenia and early institution of effective antifungal drug therapy.

Blastomycosis

Blastomyces dermatitidis

Occurrence: temperate climates in Central and South-East USA, Central and South Africa, India, Near and Middle East.

Incubation: weeks to many months.

Investigation: microscopy, culture, serology.

Transmission: inhalation, exposures to warm wooded sites and moist soil enriched with decomposing organic debris (farmers, forestry workers, hunters and campers at risk).

Public health relevance: identify likely exposure – often not determined.

Asymptomatic in (majority of) immunocompetent individuals.

Picture similar to TB. Symptomatic infection (50% of cases) usually presents as a flu-like illness with fever, chills, productive cough, myalgia, arthralgia and pleuritic chest pain.

Skin involvement at inoculation site (nodules, lymphangitis, gummata, ulcers, abscesses).

Some patients fail to recover and develop chronic pulmonary infection or widespread disseminated infection (affecting the skin, bones and genitourinary tract). Occasionally affects the meninges. Mortality rate is about 5%.

Rarely related to acquired immunodeficiencies.

Candidiasis

Candida albicans is the most common species (50%), followed by *C. glabrata* (northern hemisphere) and *C. parapsilosis* (southern hemisphere); other less frequent species associated with specific hosts (*C. dubliniensis* in HIV-infected) and susceptibility patterns. *C. glabrata* an *C. krusei* are less virulent

Occurrence: worldwide, invasive disease 250 000 new cases per year, 50 000 deaths despite antifungal treatment.

Investigation: microscopy and culture, Candida mannan antigen and antimannan antibody, β-D-glucan, PCR.

Transmission: endogenous organisms.

Public health relevance: none unless contaminated devices considered. Antifungal prophylaxis only in specific high-risk ICU patients.

New drugs are developed, but resistance to all drug regiments is reported (0–12%).

Candidiasis may be classified as superficial or invasive.

Superficial: candidiasis of the mouth and throat, also known as a 'thrush' or oropharyngeal candidiasi or vulvovaginal candidiasis (VVC). Women with VVC usually experience genital itching or burning, with or without a 'cottage cheese-like' vaginal discharge. Males may have an itchy rash on the penis.

Risk factors: pregnancy, diabetes mellitus, broad-spectrum antibiotics, corticosteroids, and immunosuppression.

Invasive: mostly in neonates and old age. Candidaemia is the most common manifestation, but deep seated blood-culture-negative infection of other organ systems is reported frequently. The alimentary tract and intravascular catheters are the main routes of entry for candidaemia and visceral candidiasis. The main predisposing factors are prolonged courses of broad-spectrum antibiotics, vascular catheters, abdominal surgery, cytotoxic chemotherapy and corticosteroids. A number of single-nucleotide polymorphisms (SNPs) are identified with increased susceptibility to candidemia.

(*Continued*)

Table 3.89.6 (*Continued*)

Disease, organism, epidemiology, investigation and public health relevance	Clinical
Chromoblastomycosis *Chromomycosis. Fonsecaea* spp. (>50%), *Cladophialophora* spp. (<25%) and *Phialophora* spp. (<25%) are the most frequent etiological agents. Occurence: rural areas in tropical or subtropical climates. Investigation: microscopy (histopathology: 'sclerotic bodies', 'medlar bodies', or 'muriform cells', in KOH mount and HE staining). Transmission: found in soil and decaying plant debris, including wood. Inoculation of contaminated soil, penetrating foreign bodies (splinters, thorns). Public health relevance: occupational risk in agriculture and outdoor activities.	A chronic progressive localised infection of the skin and subcutaneous tissue following the implantation of the aetiological agent. Lesions start as solitary papules, over years slowly progressing to (ulcerating) verrucous nodules and plaques. The mycosis usually remains localised with keloid formation. Metastasis to lymph nodes, brain, lung is reported. Many different fungi may cause this disease.
Coccidioidomycosis *Coccidioides immitis* and *C. posadasii* Occurrence: semi-desert areas in North and South America (esp. Arizona, California in USA). Incubation: weeks to years. Investigation: microscopy (spherules) and culture of tissue and respiratory secretions, serology: EIA, ID, CF (Antibodies appear to be detrimental rather than protective), PCR experimental. Transmission: inhalation after disturbance of contaminated soil. Occupational exposure in farmers, etc. Present in pigeon and chicken droppings. Public health relevance: anti-dust measures in endemic areas. Risk groups: persons in areas with endemic disease who are exposed to dust (construction or agricultural workers and archaeologists). High risk: African-Americans and Asians, pregnant women during third trimester and immunocompromised persons. AIDS-defining condition	Asymptomatic in 60%, 40% develop respiratory illness. Symptomatic infection usually presents as flu-like illness and rash '(Valley fever)'. 5% of symptomatic patients develop chronic pulmonary infection and 1% widespread disseminated infection (affecting meninges, soft tissues, joints and bone). Attack rates are higher in outbreak situations, presumably related to high dose exposure. Severe pulmonary disease may develop in HIV-infected persons, patients on anti-TNF-alpha, chemotherapy, organ transplants, diabetes, cardiopulmonary disease, pregnancy. Meningitis may lead to permanent damage. Mortality high in HIV-infected persons with diffuse lung disease.

Cryptococcosis

Cryptococcus neoformans

Occurrence: worldwide.

Investigation: culture, direct microscopy with Indian ink staining; antigen detection (LA, EIA, LFA) is more sensitive.

Transmission: inhalation of air-borne yeast cells, isolated from the soil, usually in association with bird droppings.

Less common *C. neoformans var. gattii* isolated from eucalyptus trees (and 50 other species including Douglas Fir) in tropical and subtropical regions (primarily Australia and New Guinea, but also Africa, Asia, Europe, Mexico, South America, USA).

Public health relevance: none. Resistance to antifungals is increasing

Principally a disease of the immunosuppressed and occurs most commonly in AIDS. Initial pulmonary infection is often asymptomatic. Most patients present with disseminated infection, especially meningoencephalitis. Resembles tuberculous meningitis with subacute onset and similar CSF findings. Meningitis may lead to permanent neurologic damage. Mortality rate is about 12%.

Symptoms for *C. neoformans var. gattii* same as *C. neoformans*, but more often in the immunocompetent. Surgical removal of 'cryptococcomas' (fungal growths in various organs) often required.

Histoplasmosis

Histoplasma capsulatum

Incubation: weeks to years.

Occurrence: tropical regions, *H. capsulatum* in North and South America (Ohio and Mississipi river valleys), *H. capsulatum* var. *duboisii* Africa, India and South-East Asia.

Investigation: culture (may take 6 weeks), microscopy, skin testing, serology: EIA on urine/serum/CSF/BAL. Antibody appears late, antibody tests less useful (ID, CF). PCR experimental.

Transmission: found in soil and in bird and bat droppings. Infection is acquired by the inhalation of spores; spreading chicken manure and bat caves have been identified.

Public health relevance: identify likely exposure (walking on contaminated grounds, setting up tents, clearing bird roosting sites) – often not determined. Disseminated histoplasmosis is an AIDS-defining condition

Mostly acquired as asymptomatic infection in childhood.

Symptomatic infection usually presents as a self-limiting flu-like illness with fever, cough, headaches and myalgias. Illness may resemble acute pneumonia, chronic, apical, chest infection mimicking tuberculosis or in the immunocompromised (HIV, anti-TNF-alpha, cancer chemotherapy, organ transplant) a fulminant disseminated infection.

Resolution may leave multiple miliary calcifications on the chest X-ray.

Some patients develop chronic pulmonary infection or widespread disseminated infection.

Mycetoma, Madura foot, Actinomycosis

Diverse microorganisms: fungal mycetoma (eumycetoma) in Africa, bacterial (actinomycetoma) in other parts. *Madurella mycetoma*

Occurrence: 'Mycetoma Belt' from Mexico and Venezuela, to Mauretania, Senegal, Chad, Sudan, Ethiopia, Somalia, and Yemen to India.

Investigation: microscopy, culture, biopsy. Radiology is used in evaluating the extent of disease.

Transmission: not elucidated. Inoculation most likely.

Public health relevance: none. Avoid percutaneous injury (shoes and clothing) and clean and disinfect wounds.

Localised chronic granulomatous infections with multiple discharging sinuses and slowly progressive destruction of underlying structures including bone, occur in many tropical countries and are known collectively as mycetomas.

They may be caused by true fungi such as *M. mycetoma,* or by actinomycetes such as *Streptomyces somaliensis* or *Nocardia brasiliensis*. Organisms typically inoculated through the skin by thorns. After some delay, a painless swelling appears which subsequently breaks down and discharges pus. A network of sinuses and chronic inflammatory tissue extends over a period of months, destroying surrounding structures. Bacterial secondary infection commonly exacerbates the problem. The most common site is the foot. *Actinomyces israelii* typically causes multiple abscesses around the mouth, in the chest, or at the terminal ileum. Drug treatment depends upon the organism, so microbiological diagnosis is essential.

(*Continued*)

Table 3.89.6 (*Continued*)

Disease, organism, epidemiology, investigation and public health relevance	Clinical
Mycotic keratitis Occurrence: worldwide. Investigation: slit lamp, microscopy. Transmission: may be iatrogenic. Public health relevance: investigate for contaminated contact cleaning fluid and iatrogenic transmission.	Corneal infection caused by fungi or yeast. The risk factors include trauma, contact lens usage, chronic ocular surface diseases, surgery and corneal anaesthetic abuse. Fungal keratitis is a serious condition that requires prolonged treatment and close follow-up.
Nocardiosis *Nocardia asteroides, N. brasiliensis* Occurrence: worldwide. Investigation: microscopy. Transmission: soil organisms. Endogenous in sputum. Public health relevance: none.	Causes severe systemic opportunistic infections, brain abscess and occasionally chronic chest infections in the immunocompetent.
Paracoccidioidomycosis *Paracoccidioides brasiliensis* South American blastomycosis Occurrence: tropical regions in Central and South America. Incubation: up to 20 years. Investigation: microscopy, serology. Transmission: from acid soil in coffee sugar cane plantations. Public health relevance: none.	Asymptomatic in (majority of) immunocompetent individuals. Chronic granulomatous disease of mucous membranes, skin and pulmonary system. Classic triad of symptoms: pulmonary lesions, edentulous mouth, cervical lymphadenopathy. Organism invades mucous membranes of the mouth causing the teeth to fall out. White plaques are found on the buccal mucosa. Women show fewer symptoms, as oestrogens inhibit conidial transformation to yeast cells. HIV-infection predisposes to disseminated disease.
Pityriasis versicolor *Malassezia furfur Pityrosporum ovale*) and other related species Investigation: view scrapings under Wood's lamp. Public health relevance: avoid sharing of towels, etc.	*M. furfur* colonises oily areas of the skin, especially the scalp, back and chest causing characteristic discoloured or depigmented lesions of the skin '(raindrops)' especially after sun exposure. Young people around puberty are most commonly affected.
Pneumocystis pneumonia (PCP) *Pneumocystis carinii* has been renamed *Pneumocystis jirovecii.* It was thought to a protozoon, but is now classified as fungus. Investigation: microscopy respiratory secretions, biopsy, PCR, β-D-glucan. Transmission: air-borne person to person, healthy carriers of the fungus. Public health relevance: AIDS defining disease. Chemoprophylaxis for high-risk patients (TMP/SMX)	An estimated 20% of adults carry the fungus and get rid of the fungus without developing symptoms in several months. Respiratory illness with fever in patients with HIV/AIDS developing over weeks, in other immunocompromised patients developing over days.

Sporotrichosis

Sporothrix schenckii complex (*albicans, brasiliensis, globosa, luriei, Mexicana* and *schenckii*)
Occurrence: worldwide, most cases in Central and South America, found in sphagnum moss, in hay, in other plant materials and in the soil.
Incubation: 1–12 weeks.
Investigation: microscopy of swab, biopsy.
Transmission: enters the skin through small cuts or punctures from thorns, barbs, pine needles or wires.
Public health relevance: outbreaks have occurred among nursery workers handling sphagnum moss, rose gardeners, children playing on baled hay, and greenhouse workers.
Wearing gloves and long sleeves when handling materials that may cause minor skin breaks. Avoid skin contact with sphagnum moss.

Skin infection with often spontaneous resolution.
Usually starts with a small, painless, red, pink, or purple nodule resembling an insect bite. This appears where the fungus entered through a break on the skin.
Infection may progress to chronic cutaneous and deeper infection. Additional nodules follow; these ulcerate and are slow to heal.
Disseminated disease (joint, lung and CNS involvement) can occur in the immunocompromised (HIV, immunosuppression, DM, cirrhosis, malnutrition).

Talaromycosis/Penicilliosis

Talaromyces marneffei
Occurrence: Southeast Asia
Incubation period: considered two weeks
Investigation: microscopy, culture of available clinical specimens. Culture of skin biopsy, blood and bone-marrow have highest yield.
Transmission: soil, particularly burrows of bamboo rats
Public health relevance: high-risk patients avoid recreational soil exposure during rainy season, occupational hygienic measures. AIDS-defining disease

Asymptomatic in (majority of) immunocompetent individuals.
Localised umbilicated skin lesion and lymphadenitis at inoculation site.
Pneumonia.
In acquired immunodeficiencies (HIV and other), disseminated disease with hepatosplenomegaly, bone marrow, osteoarticular and neural involvement. Mortality (under antifungal therapy) up to 30%.

Zygomycosis/Mucormycosis

Rhizopus, Rhizomucor, Absidia, Mucorales
Occurrence: up to 11% of filamentous fungal infections in leukaemia are mucormycosis.
Investigation: microscopy, biopsy. 'Reverse halo' is an early radiographic feature.
Transmission: inhalation of spores.
Public health relevance: none. Clusters of cutaneous and mucormycosis seen after Tsunami and tornado type events.

Invasive sinopulmonary infections such as the rhinocerebral syndrome, which occurs in diabetics with ketoacidosis, present with pain, fever, orbital cellulitis and proptosis. The palate, the facial bones and nasal septum may be destroyed.
The other common site of infection is the lung.
Rarely, the skin and digestive system are involved.
Without treatment mortality is nearly 100%

(*Continued*)

Table 3.89.6 (*Continued*)

Disease, organism, epidemiology, investigation and public health relevance	Clinical
Opportunistic mycoses	
Public health relevance: ensure there are no clusters associated with contaminated preparations, building works, etc.	Fungal infection is associated with immunosuppression. Immunosuppression may be due to underlying disease (e.g. malignancy, diabetes mellitus, HIV) or pharmacological. Fungi account for about 10% of all nosocomial infections in the USA. The most common reported were *Candida* spp. (85.6%), followed by *Aspergillus* spp. (1.3%). *C. albicans* accounted for 76% of all *Candida* spp. infections. Other fungal pathogens (e.g. *Malassezia*, *Trichosporon*, *Fusarium*, and *Acremonium*) represented 11% of the nosocomial fungal pathogens. Fungal infection should be considered in all immunosuppressed patients with an unexplained fever. Diagnostic tests for fungi are improving; mycological advice should be sought early so that appropriate specimens are sent. *Candida* septicaemia in a transplant recipient or periorbital mucormycosis in a diabetic patient require prompt treatment if the patient is to survive.

looks innocuous. The bite should be cleaned and dead tissue removed. Infecting organisms are usually derived from the oral flora: these may include streptococci, *Pasteurella* and anaerobes. Antibiotics covering the likely organisms should be given if there is evidence of infection (and occasionally as prophylaxis, e.g. for human bite to hand). Tetanus prophylaxis should be given generously and always if any doubt of previous vaccine history. Consider rabies if exposure to imported animal or any animal bites in areas where the disease may be present in wildlife reservoirs.

Venomous snakes

Except for adders, there are few venomous snakes in Europe; however, bites may arise from imported exotic snakes. Venomous snakebites are medical emergencies; a poisons centre should be contacted. The symptoms and signs depend upon the species and size of snake, the volume of venom injected, the location of the bite (central bites tend to be more severe than peripheral), and the age, size and health of the victim. The victim should avoid exertion and be urgently moved to the nearest medical facility. Rings, watches, and constrictive clothing should be removed and the injured part immobilised in a functional position just below heart level. Tourniquets, incision, suction, or application of ice on the wound are contraindicated. Attempts should be made to identify the snake so that the appropriate antivenom can be provided.

Spiders

Venomous spiders may be introduced as novelty pets. In the event of a bite every attempt should be made to identify the spider and a poisons centre should be contacted.

Ticks

Ticks may transmit infection such as Lyme disease, tick-borne encephalitis, ehrlichiosis, tularaemia, relapsing fever and Crimean-Congo haemorrhagic fever. Tick paralysis is a rare ascending flaccid paralysis that may occur when toxin-secreting ticks remain attached for several days. The condition, which is more common in animals than in humans, is the only tick-borne disease that is not caused by an infectious organism. Symptoms and signs include anorexia, lethargy, weakness, incoordination and ascending flaccid paralysis. Tick paralysis may be confused with Guillain–Barré syndrome, botulism, myasthenia gravis or spinal cord tumour. Bulbar or respiratory paralysis may develop. Tick paralysis is rapidly reversible on removal of the tick (or ticks) and may require only symptomatic treatment.

Mites

Mite bites are common. Chiggers are mite larvae that feed in the skin, causing a pruritic dermatitis. There may be sensitisation.

Centipedes and millipedes

Some centipedes can inflict a painful bite, with some localised swelling and erythema. Lymphangitis and lymphadenitis are common. Millipedes may secrete a toxin that can cause local skin irritation and, in severe cases, marked erythema, vesiculation and necrosis. Some species can spray a secretion that causes conjunctival reactions.

Other arthropods

There are a large number of other biting arthropods: mosquitoes, fleas, lice, bed bugs, sand flies, horseflies; none of these are venomous. The lesions produced vary from small papules to large ulcers; dermatitis may also occur; bites can be complicated by sensitivity reactions or infection; in hypersensitive persons, they can be fatal.

Stings

Bees, wasps

The average person can tolerate about 20 stings kg^{-1} body weight. One sting can cause a fatal anaphylactic reaction in a hypersensitive

person. Stings may remain in the skin and should be removed. An ice cube will reduce pain, and an antihistamine will reduce itching and swelling. Persons known to be hypersensitive should carry epinephrine with them.

Scorpions

Stings from pet scorpions should be treated as potentially dangerous as the species may be difficult to determine. The victim should be observed. Information on antivenoms should be obtained from a poisons centre.

3.89.8 Chemical food-borne illness

Scombrotoxin fish poisoning

Caused by excess histamine, a consequence of inadequate refrigeration or storage of tuna, mackerel and other oily fish, leading to diarrhoea, flushing, headache and sweating, sometimes accompanied by nausea, abdominal pain, burning in the mouth, tingling and palpitations. Onset is 10 minutes to 2 hours after consumption; symptoms usually resolve over 12 hours. Antihistamines may reduce severity. Histamine level of fish can be tested.

Ciguatera

Poisoning caused by eating fish contaminated with toxins produced by dinoflagellates and associated with fish caught in tropical and sub-tropical reef waters. Ciguatoxin is very heat-resistant and not detoxified by conventional cooking. May occur in imported fish. Gastrointestinal and neurological symptoms occur: gastrointestinal symptoms usually start 0.5–12 hours after exposure and resolve within 28 hours; neurological symptoms can last up to six months and may become chronic in some patients.

Shellfish poisoning

Associated with consumption of filter-feeding bivalve shellfish or crustaceans (e.g. mussels, clams, oysters, scallops and crabs) that have consumed toxin-producing plankton, sometimes after 'red tides'. The various toxins can be measured in a specialist laboratory. The most common syndromes follow.

Paralytic

Caused by saxitoxins produced by certain algae. Causes neurological symptoms: dizziness, tingling, drowsiness and muscular paralysis. Severe cases may suffer respiratory failure and death. There may occasionally be gastrointestinal symptoms. Onset is 30 minutes to 2 hours after consumption.

Diarrhetic

Caused by okadaic acid and other toxins in algae. Causes diarrhoea, nausea, vomiting and abdominal pain, with onset 30 minutes to 12 hours after consumption. Illness lasts three to four days. Toxin may be detected in shellfish.

Amnesic

Caused by domoic acid; in addition to gastrointestinal symptoms, can cause short-term memory loss and brain damage.

Neurotoxic

Caused by brevetoxins, causes neurological (e.g. paresthesia of lips, face and extremities and slurred speech) as well as gastrointestinal symptoms.

Phytohaemagglutinin poisoning

Caused by inadequate preparation of pulses such as red kidney beans, butter beans, and lentils. Causes nausea and vomiting, followed by abdominal pain and diarrhoea, with onset 30 minutes to 12 hours after consumption.

Mushroom poisoning

Due to cyclopeptides and amatoxins consumed in *Amanita phalloides* (death cap), *Amanita verna*, *Amanita virosa* and some *Galerina* and *Lepiota* species. Causes colic, nausea, vomiting and diarrhoea, which – after apparent recovery – may be followed by liver or kidney failure with appreciable mortality. The advice of a specialist poisons centre is vital for both investigation and treatment.

Others

- Gastrointestinal illness caused by heavy metal poisoning (e.g. from food containers).
- Intoxication (alcohol-like) caused by mushrooms.
- Gastrointestinal, liver and renal illness caused by aflatoxins (e.g. fungal contamination of cereals).
- Neurological illness caused by pesticides.
- Puffer fish poisoning (Japan, Thailand).
- Ricin poisoning from castor beans.

Section 4
Services and organisations

4.1 Surveillance of communicable disease

The effective public health and clinical management of infectious diseases depends on good surveillance, which has been defined as the continuing scrutiny of all aspects of the occurrence and spread of a disease through the systematic collection, collation and analysis of data and the prompt dissemination of the resulting information to those who need to know so that action can result. There are two types of public health surveillance – event-based surveillance and indicator-based surveillance. Event-based surveillance gathers unstructured information about health events that are or could be a serious risk to public health in order to detect and report events that might signal an outbreak. Indicator-based surveillance involves structured reports of specific diseases from health care providers to public health officials. The account of surveillance in this section is based on indicator-based surveillance activities in the UK, but similar arrangements can be found in most other European countries.

Purpose of surveillance

- Surveillance allows individual cases of infection to be identified so that action can be taken to prevent spread.
- Surveillance measures the incidence and prevalence of infectious disease. Changes in incidence may signal an outbreak, which may need further investigation and the introduction of generic and targeted control measures.
- Surveillance tracks changes in risk factors of infectious disease and can indicate if sections of the population are at increased risk of infection as a result of environmental or behavioural factors. This allows appropriate interventions to be targeted at those groups.
- Surveillance allows existing prevention and control measures, programmes and policies to be evaluated, and if changes are introduced, continuing surveillance will allow their effectiveness to be assessed.
- Surveillance enables the epidemiology of infections to be described and generates hypotheses about aetiology, risk factors and possible interventions.

Principles of surveillance

A good surveillance system primarily aims to meet the needs of the prevention and control programme or activities and consists of the following key elements:

- There should be a clear statement of the surveillance objectives.
- There should be a case-definition, which includes clinical and/or microbiological criteria that enables the standardisation of case reporting.
- Cases of infection are identified from a variety of sources including reports from clinicians and laboratories. The case or an informant, who may be a relative, friend or clinician, is contacted by telephone, visit, letter or email, depending on the degree of urgency. A dataset is collected for each case. The data that are collected depend on the nature of the infection. For all infections, consider the following minimum data set: name; date of birth; gender; address; ethnic group; place of work; occupation; name of general practitioner (GP); recent travel; immunisation history; date of illness; clinical description of illness. For food-borne infections, food histories and food preferences may be recorded. For infections that are spread from person to person, the

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

names and addresses of contacts may be requested, and for infections with an environmental source such as Legionnaires' disease, places visited and routes taken may be recorded. For some infections where public health intervention is required, additional data are collected. For example, in the case of meningococcal infection the names of close household contacts may be recorded so that chemoprophylaxis and immunisation may be offered. For rare or novel infections, or where there is a need to find out more about the epidemiology, an *enhanced dataset* may be collected or there may be a request for laboratory data to confirm the diagnosis. An example of this is the serological confirmation of clinical reports of measles using salivary antibody testing.

- Data are recorded on specially designed data collection forms and collated in a computerised database. Increasingly, data may be entered directly into an online database or automatically downloaded from databases used for patient management, for example emergency department electronic health records.
- One of the first uses of the data is to ensure that the cases satisfy the case-definition. The data is then analysed to produce summary statistics including frequency counts and rates, if suitable denominators are available. This permits the epidemiology of the infection to be described in terms of person, place and time and the detection of outbreaks using statistical exceedance algorithms. Local data can be shared and merged to produce anonymised data sets at national or even international level.
- Interpretation of the data and summary statistics leads to information on trends and risk factors, which are disseminated so that action can be taken. Dissemination can take place in a variety of ways. Increasingly, anonymised data are available online, but may also be found in local and national newsletters and journals (see Section 5 chapters for country-specific details).
- Feedback to local data providers is important. It demonstrates the usefulness of the data and creates reliance on it. This in turn will lead to improvement in case ascertainment and data quality. Local data may be sent to GPs, hospital clinicians, microbiologists, environmental health professionals and health service managers.
- Evaluation of the surveillance system should be undertaken at defined intervals as part of quality assurance and continuous quality improvement.

Sources of surveillance data

Several data sources are available for the surveillance of infectious diseases. Subclinical cases of infection can only be measured by serological surveys while clinical infection that does not lead to a medical consultation can be measured by population surveys or calls to a telephone helpline, for example NHS 111 in England.

Cases that are seen by a clinician may be reported via a primary care reporting scheme or statutory notification system. Cases that are investigated by laboratory tests are usually reported via a laboratory reporting system, and those that are admitted to hospital will be captured in the hospital electronic health records. Finally, the small proportion of infections that result in death will be detected by the death notification system. When designing a surveillance system it is important to ensure that the most appropriate data source is utilised. For example, it is not sensible to rely on laboratory reports for the surveillance of pertussis, which is only rarely diagnosed by the laboratory.

Statutory notifications are an important way of monitoring trends in infectious disease, such as whooping cough, where diagnosis is rarely confirmed by laboratory test. The list of notifiable diseases varies by country and over time may also change as new infections emerge or existing infections attain new levels of importance (see Table 5.34.1 for list of notifiable diseases in England).

In England, any clinician suspecting these diagnoses is required to notify the proper officer of the local authority, who is usually the Consultant in Communicable Disease

Control (CCDC) or Consultant in Health Protection (CHP). The proper officer sends a weekly return to Public Health England (PHE) by email and the data are collated and published on their website. New UK regulations also require the notification of other infections (such as those caused by new or emerging diseases) or contamination, such as with chemicals or radiation, that may pose a significant risk to public health. Data that are received by PHE are collated, analysed and published regularly in reports such as the Notification of Infectious Diseases (NOIDs) report and the *Health Protection Report* which are available weekly on the PHE website.

European Surveillance

All European Union (EU) Member States are obliged to report to the European Centre for Disease Prevention and Control (ECDC) some 50 infectious diseases and 3 special health conditions, using commonly agreed case definitions (Table 4.1.1). This indicator-based surveillance rests on commonly agreed case definitions (https://ecdc.europa.eu/en/all-topics-z/surveillance-and-disease-data/eu-case-definitions). The surveillance data is collated in the European Surveillance System (TESSy), and accessible both as an interactive surveillance atlas and as annual epidemiological

Table 4.1.1 Diseases under mandatory EU surveillance

Diseases preventable by vaccination
- Diphtheria
- Infections with *Haemophilus influenzae* group B
- Influenza – including influenza A(H1N1)
- Measles
- Mumps
- Pertussis
- Poliomyelitis
- Rubella
- Smallpox
- Tetanus

Sexually transmitted diseases
- Chlamydia infections
- Gonococcal infections
- HIV infection
- Syphilis
- Viral hepatitis
- Hepatitis A
- Hepatitis B
- Hepatitis C

Food- and water-borne diseases and diseases of environmental origin
- Anthrax
- Botulism
- Campylobacteriosis
- Cryptosporidiosis
- Giardiasis
- Infection with enterohaemorrhagic *Escherichia coli*
- Leptospirosis
- Listeriosis
- Salmonellosis
- Shigellosis
- Toxoplasmosis
- Trichinosis
- Yersiniosis

Diseases transmitted by non-conventional agents
- Transmissible spongiform encephalopathies
- Variant Creutzfeldt–Jakob's disease

Air-borne diseases
- Legionnaires' disease
- Invasive meningococcal disease
- Invasive pneumococcal disease
- Tuberculosis
- Severe Acute Respiratory Syndrome (SARS)

Zoonoses (other than those listed above)
- Avian influenza in humans
- Brucellosis
- Echinococcosis
- Q fever
- Rabies
- Tularaemia
- West Nile virus infection
- Serious imported diseases
- Cholera
- Malaria
- Plague
- Viral haemorrhagic fevers

Vector-borne diseases
- Tick-borne encephalitis

Special health issues
- Nosocomial infections
- Antimicrobial resistance
- Antimicrobial consumption

reports per disease (https://ecdc.europa.eu/en/surveillance-and-disease-data). The reports on measles and rubella are published monthly. Surveillance of tuberculosis, HIV/AIDS and seasonal influenza is done jointly by ECDC and WHO Euro; the two former are published as joint annual reports, while seasonal influenza is reported on a weekly basis on a joint website: http://flunewseurope.org.

The results and analysis from ECDC event-based surveillance (epidemic intelligence) is disseminated through weekly communicable disease threat reports (CDTR), and ad hoc epidemiological updates and risk assessments (https://ecdc.europa.eu/en/threats-and-outbreaks).

Laboratory reporting system

A main source of surveillance data is from laboratory diagnoses and each country has a system to monitor key diagnoses of interest. Although the data are usually specific and of high quality, they are limited to infections for which there is a suitable laboratory test and infections that are easy to diagnose clinically tend to be poorly covered. Trends may be difficult to interpret, because the data are sensitive to changes in testing or reporting by laboratories (for example, antimicrobial resistance data). In addition, because data are usually based on place of treatment rather than place of residence, denominators are not usually available and because negatives are not usually reported, neither the number of specimens tested nor the population at risk is known with certainty.

In England, PHE laboratories, National Health Service (NHS) hospital laboratories and private laboratories should be able to offer a full diagnostic service for all common pathogenic microorganisms. If the laboratory is unable to carry out the work, then specimens are forwarded to a suitable reference laboratory. Medical microbiologists ensure that results of clinical significance are notified to the requesting clinician. In the UK, the 2010 Health Protection (Notification) Regulations also require diagnostic laboratories to notify PHE within seven days when certain causative agents are detected in human samples. Reports of microorganisms of public health significance should also be reported to the local Health Protection Team (HPT) so that public health action can be taken. This should be in accordance with previously agreed arrangements covered by a written policy. Typical arrangements for reporting to the HPT are shown in Table 4.1.2. Ideally, results should be sent

Table 4.1.2 Laboratory reporting of infectious diseases to the HPT: statutory list in England

Infection	Likely to be urgent?
Viral infections	
Viral haemorrhagic fever (CCHF, Ebola, Lassa, Marburg)	Yes
Chikungunya virus, dengue, Hanta, Zika	No, unless thought to be UK acquired
Viral hepatitis (all forms)	All acute cases and any chronic cases who might represent a high risk to others, such as healthcare workers who perform exposure-prone procedures
Influenza virus	No, unless known to be a new subtype of the virus or associated with known cluster or closed communities such as care homes
Measles	Yes
Mumps	No
Polio virus	Yes
Rabies virus	Yes
Rubella virus	No
SARS coronavirus	Yes

Table 4.1.2 (*Continued*)

Infection	Likely to be urgent?
Varicella zoster virus	No
Variola virus	Yes
West Nile virus	No, unless thought to be UK acquired
Yellow fever virus	No, unless thought to be UK acquired
Bacterial infections	
Bacillus anthracis	Yes
Bacillus cereus	No, unless part of a known cluster
Bordetella pertussis	Yes, if diagnosed during acute phase
Brucella spp.	No, unless thought to be UK acquired
Burkholderia mallei/pseudomallei	Yes
Campylobacter spp.	No, unless part of a known cluster
Chlamydia psittaci	Yes, if diagnosed during acute phase or part of a known cluster
Clostridium botulinum	Yes
Clostridium perfringens	No, unless known to be part of a cluster
Clostridium tetani	No, unless associated with injecting drug use
Corynebacterium spp.	Yes
Coxiella burnetii	Yes, if diagnosed during acute phase or part of a known cluster
Francisella tularenis	Yes
Haemophilus influenzae	Yes
Legionella spp.	Yes
Listeria monocytogenes	Yes
Mycobacterium tuberculosis	No, unless healthcare worker, or infectious in congregate setting, or suspected cluster or multidrug-resistance
Neisseria meningitidis	Yes
Salmonella spp	Yes, if *S.* Typhi or *S.* Paratyphi or suspected outbreak or food handler or closed communities such as care homes. No, if sporadic case of other *Salmonella* serovar
Shigella spp.	Yes, except *Shigella sonnei* unless suspected outbreak or food handler or closed communities such as care homes
Streptococcus pneumoniae	No, unless part of a known cluster
Streptococcus pyogenes	Yes
Shiga-toxin producing *Escherichia coli* (STEC)	Yes
Vibrio cholerae	Yes
Yersinia pestis	Yes
Protozoan infections	
Cryptosporidium	No, unless part of a known cluster, known food handler or evidence of increase above expected numbers
Entamoeba histolytica	No, unless known to be part of a cluster or known food handler
Giardia lamblia	No, unless part of a known cluster, known food handler or evidence of increase above expected numbers
Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and *Plasmodium knowlesi*	No, unless thought to be UK acquired

CCHF, Congo–Crimean haemorrhagic fever; SARS, severe acute respiratory syndrome.

Table 4.1.3 Data to be included in laboratory reports when available (to CCDC/HPTs in England)

Epidemiological features/risk factors	Clinical/syndrome features
Recent travel abroad, dates, places	Died
Country of birth, dates of arrival	Bacteraemia
Outbreak	Conjunctivitis
Hospital acquired	Bronchiolitis
Sexual orientation	Arthritis
Animal contact	Meningitis
Transplant recipient	Invasive
Blood recipient	Pneumonia
Vaccine status	Croup
Immunocompromised	Enteric fever
Pregnancy	Haemolytic uraemic syndrome (HUS)
Injecting drug use	Asymptomatic
Congenital infection	
Food source, vehicle	
Transmission (person to person, water-borne, animal, food-borne)	

electronically within 24 hours but infections requiring immediate public health action should be reported urgently by telephone. The dataset that the laboratory forwards to the public health authority will depend on the data that are included on the request form by the requesting clinician and is often limited. If additional clinical and epidemiological data are available (Table 4.1.3) then the inclusion of these data in reports from laboratories is welcomed.

Microbial genome sequencing

Increasingly, whole genome sequencing techniques are being employed to identify and characterise microbes of public health importance. This rapid diagnostic tool represents a paradigm shift in the surveillance of certain gastrointestinal infections (e.g. *Salmonella* and *Shigella*) and respiratory infections (e.g. tuberculosis) through gains in the timeliness and resolution of outbreak detection, and elucidation of epidemiologic linkages and transmission patterns. The ongoing development of molecular diagnostic tools and their increasing integration into routine clinical and public health practice will raise challenges around quality assurance, privacy and ethical issues interpretation and integration with data from traditional surveillance systems.

Reporting from primary care

There are 340 million GP consultations per year in England and around 30% of consultations will be for an infection. A number of European countries have surveillance systems that capture data from a sample of general practices. The data can be related to a defined population, so that rates can be calculated for a selection of common diseases that are not notifiable, for which laboratory confirmation is not usually obtained and that do not usually result in admission to hospital. Primary-care data are particularly useful in the surveillance of seasonal influenza and influenza-like illness. In England, the Royal College of General Practitioners (RCGP) Weekly Returns Service is a network of over 250 general practices covering a combined population of over 1.7 million that collect data on consultations and episodes of illness diagnosed in general practice. A comparable and larger syndromic surveillance system based on routine computerised GP data (PHE GP in-hours surveillance) is operated by PHE and data from both systems can be accessed via the PHE website.

Syndromic surveillance

Syndromic surveillance is the (near) real-time collection, analysis, interpretation and dissemination of health-related data to enable the early identification of the impact, or absence of impact, of potential threats. Syndromic surveillance is different to traditional public health surveillance systems in that it monitors non-specific clinical signs, symptoms and proxy measures for health; it does not monitor confirmed diagnoses or laboratory reports. The main role of syndromic surveillance in health protection is to provide early warning of infectious disease activity, detect currently unknown or emerging threats, provide reassurance over lack of impact and provide 'situational awareness' to quantify and monitor the health impact during an identified public health threat.

Syndromic surveillance data are generally anonymised and, although capturing data on individual episodes of illness, they are mostly sentinel national systems. In general, therefore, they are not suitable for detecting or monitoring small and sub-regional outbreaks of disease. In England, a wide range of health data is currently utilised for syndromic surveillance: emergency department attendances, general practitioner consultations (in and out of hours), telehealth calls (NHS 111), and ambulance call outs. Other data sources that are currently being assessed to determine whether they might provide any additional benefit to existing syndromic surveillance systems include: over-the-counter pharmacy sales of medications, internet search and social media data.

The growth of the internet has led to new opportunities and methods for infectious disease surveillance through the use of web-based data sources such as internet search data (for example Google®) and social media data (for example Twitter®). These data sources present a low-cost, near real-time option for infectious disease surveillance for conditions such as seasonal influenza, dengue and norovirus and have been shown to both complement and supplement traditional surveillance systems. However, the nature of the data, concerns about privacy and the sensitivity of these datasets to external stimuli (example: media reports) make their use challenging and complex. Research, development and evaluation are ongoing to determine the utility of web-based data to improve the early detection of emerging threats.

Hospital data

Data are available from hospital information systems on infectious diseases that result in admission to hospital. This is a useful source of data on more severe diseases likely to result in admission to hospital, although the data are often not sufficiently timely for some routine surveillance functions. In England, another type of hospital data is collected via the emergency department syndromic surveillance system and ongoing changes to the national emergency care datasets have improved access to and the use of near-real-time emergency care information.

Death certification and registration

Mortality data on communicable disease are of limited use because in high income countries, communicable diseases rarely cause death directly. Exceptions are deaths due to influenza, AIDS and TB. However, not all deaths due to infection are coded as such, and data may not be sufficiently timely for all surveillance functions.

Other sources of data

Data may be collected by organisations or sources that do not have specific communicable disease control duties. One example is the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health that co-ordinates active surveillance of uncommon paediatric conditions. An electronic reporting card (orange card) is sent each month to over 3300 consultant paediatricians and other specialists in the UK. They indicate if they have seen a case that month and return the card. An investigator then

contacts the paediatrician for further information. In 2018, conditions of infective origin that are listed in the orange card include HIV/AIDS, congenital rubella, congenital Zika infection, and listeriosis.

4.2 Managing infectious disease incidents and outbreaks

An infectious disease incident may be defined in one of the following ways:

- Two or more persons with the same disease or symptoms or the same organism isolated from a diagnostic sample, who are linked through common exposure, personal characteristics, time or location.
- A greater than expected rate of infection compared with the usual background rate for a particular place and time.
- A single case of a rare or serious disease such as for example diphtheria, rabies, viral haemorrhagic fever or polio.
- A suspected or actual event involving exposure to an infectious agent (e.g. HIV infected healthcare worker, white powder incident, failure of decontamination procedures).
- Actual or potential microbial or chemical contamination of food, water or air.

The first two of these categories may also be described as an outbreak. The control of an outbreak of infectious disease depends on early detection followed by a rapid structured investigation to uncover the source of infection and the route of transmission. This is followed by the application of appropriate control measures to prevent further cases. Outbreaks of infectious disease are usually investigated and managed by an informal team comprising of epidemiologists (e.g. from the local health authority), microbiologists (e.g. a medical microbiologist from the local hospital) and environmental health (e.g. an environmental health officer [EHO] from the local authority).

Consideration should be given to convening an outbreak control team to oversee management if:

- the outbreak affects a large number of people,
- it involves a serious infection,
- it affects a wide geographical area, or
- there is significant public or political interest.

A written *outbreak control plan* detailing the steps that should be taken is an essential requirement: multiagency plans are necessary for larger or more serious outbreaks, which include the pre-agreed responsibilities of the various agencies and specialists. Incident management may be more effective if an incident control room is established. Accommodation that can be used as an incident room within local authority or health premises and access to the necessary resources should be identified in the outbreak control plan. In circumstances where there are likely to be significant numbers of enquiries from members of the public, for example during a look-back exercise following identification of a healthcare worker infected with hepatitis B, a dedicated telephone helpline may be established. Telephone helplines can deal with large numbers of people needing information, counselling or reassurance and they can be used for case finding. Setting up an incident room is a useful part of an outbreak exercise or simulation (Box 4.2.1).

Box 4.2.1 The incident room

- Dedicated use.
- 24-hour access and security.
- Large enough for the incident team their equipment and files.
- Sufficient telephone lines and teleconferencing facilities.
- Sufficient computers with internet access and access to a common server for filing.
- Access to photocopying facilities.
- Filing systems for storing all communications, minutes of meetings, notes of decisions, etc.

Detection

An outbreak can be identified by case reports, complaints or as a result of routine surveillance.

An outbreak of haemorrhagic colitis due to consumption of cold turkey roll contaminated with Escherichia coli O157 was discovered when several people who had attended the same christening party were admitted to the infectious disease ward at a local hospital.

An outbreak of gastroenteritis due to Salmonella Panama infection due to the sale of contaminated cold meats from a market stall was detected when the local public health laboratory isolated this unusual organism from several faecal samples sent in by General Practitioners (GPs) from patients with diarrhoea.

An outbreak of food-borne viral gastroenteritis affecting people who had attended a wedding reception at a hotel came to light when affected guests complained to the local environmental health department.

An outbreak due to the common strain of Salmonella Enteritidis PT4 was uncovered when environmental health officers questioned several people, initially reported as sporadic cases by clinicians and laboratories, with this infection in a Midlands town. They all reported buying and eating bakery products from a mobile shop. Further investigations revealed that custard mix used in the preparation of trifle had become contaminated with raw egg.

Systematic investigation

The reasons for investigating an outbreak are to identify and control the source of infection and route of transmission to prevent further cases, to identify others at risk, to prevent similar outbreaks in the future, to describe new diseases and learn more about known diseases, to teach and learn epidemiology, to address public concern and to gather evidence for legal action.

A systematic approach to the investigation of an outbreak consists of nine stages.

Confirm that a problem exists

A report of an outbreak of infection may be mistaken. It may result from increased clinical or laboratory detection of cases, changes in reporting patterns, changes in the size of the at-risk population or false positive laboratory tests.

Recent increases in the number of cases of tuberculosis after many years of decline may be due to increases in the size of certain population subgroups that are at increased risk of tuberculosis. These would include the elderly, the homeless, and those who have migrated from areas of the world where the incidence of tuberculosis remains high.

An outbreak of cryptosporidiosis was due to false positive laboratory tests. The microbiology technician mistook fat globules for oocysts of the protozoon Cryptosporidium parvum in faecal smears.

Apparent clusters may be identified by ascertainment issues, such as batch reporting of results from a laboratory (check onset or specimen dates) or introduction of a new test with higher sensitivity (e.g. polymerase chain reaction [PCR] for faecal samples). Others disappear when further typing of isolates is undertaken that show that the organisms are unrelated. Other pseudo-outbreaks due to laboratory contamination were recognised because cases, despite having identical microbiological results, had no detectable epidemiological links, inconclusive clinical diagnoses and were only reported by one laboratory.

Confirming the diagnosis

Cases can be diagnosed either clinically or by laboratory investigations. At an early stage it is important to produce and adhere to a clear case-definition. This is particularly important with previously unrecognised diseases in which proper definitions are needed before epidemiological studies can proceed.

An investigation was started into an outbreak of atypical pneumonia affecting men of working age in the Birmingham area. Four weeks elapsed before the laboratory confirmed the diagnosis as

Q fever and progress could be made with the epidemiological investigation. Cases of Q fever were defined as patients with onset of an acute febrile illness between 27 March and 3 July and a fourfold rise in titre of complement fixing antibodies to phase II antigen of Coxiella burnetii, a sustained phase II titre of ≥256, or the presence of specific IgM on an indirect immunofluoresence test.

Different levels of case definition can be set to represent the level of certainty of the diagnosis (e.g. 'Confirmed', 'Probable' and 'Possible'). Case definitions can be set to be highly specific (e.g. to ensure that cases used in an analytical study are unlikely to be false positives and so reduce the power of the study) or highly sensitive (e.g. to ensure that all cases are identified for investigation and follow up).

Immediate control measures

Control measures involve controlling the source of infection, interrupting transmission or protecting those at risk. Often a set of general control measures can be instituted based on the information available at the time, such as general assessment and improvement of food hygiene or infection control at an affected premises or advice to those affected on how to limit onward transmission. These can be modified later in the outbreak as more detailed information is obtained: an example is the generic measures given for an outbreak of gastrointestinal illness in Chapter 2.2.2.

Case finding

In an episode of infection, the cases that are first noticed may only be a small proportion of the total population affected and may not be representative of that population. Efforts must be made to search for additional cases. This allows the extent of the incident to be quantified, it allows a more accurate picture of the range of illness that people have experienced, it allows individual cases to be treated and control measures to be taken, and it provides subjects for further descriptive and analytical epidemiology. There are several ways of searching for additional cases:

- Notifications of infectious disease,
- Requests for laboratory tests and reports of positive results,
- People attending their GP, the local accident and emergency department, hospital inpatients and outpatients,
- Reports from the occupational health departments of large local businesses,
- Telephone helplines,
- Reports from schools of absenteeism and illness,
- Household enquiries,
- Appeals through TV, radio and local newspapers,
- Screening tests applied to communities and population subgroups.

In a local outbreak of Salmonella Panama infection, a message was sent to all microbiologists in the region asking them to report isolates of Salmonella Panama to the investigating team.

In an outbreak of Q fever, local GPs were telephoned and local occupational health departments were contacted to enquire about cases of atypical pneumonia or unexplained respiratory disease.

Collection of data

A set of data is collected from each of the cases. This includes name, age, sex, address, occupation, name of GP, recent travel, immunisation history, date of illness and clinical description of illness, including onset date and time, and direct questioning on presence or absence of key symptoms that might help reach a provisional diagnosis and can be used to define cases. Data should also be collected about exposure to possible sources of the infection, including the exact date and time of the exposure. In the case of a food-borne infection this would include a recent food history. In the case of infection spread by person-to-person contact, the case would be questioned about contact with other affected persons. In the case of an infection spread by the air-borne route, cases would be questioned about places they had visited.

It is preferable to collect these data by administering a detailed semi-structured questionnaire in a face-to-face interview. This allows the interviewer to ask probing questions which may sometimes uncover previously unsuspected associations between cases. Telephone interviews or self-completion questionnaires are less helpful at this stage of an investigation. Some questionnaires from routine public health investigation of individual cases may already be available and can be reviewed.

In an investigation of a possible national outbreak of Salmonella Newport infection that was thought to be food-borne, very detailed questioning was undertaken about the food that had been consumed in the seven days prior to illness. This included asking specifically what food items had been eaten at each meal. In addition, respondents were asked if they had eaten particular food items and if so, where these had been purchased and the brand that had been purchased.

In the investigation of an outbreak of Legionnaires' disease thought to have an environmental source, cases were asked to indicate on a map the exact places they had visited in the 10 days prior to illness. In addition, they were asked specifically if they had visited particular locations that had been mentioned by other respondents.

It may be necessary to re-interview early cases to ask about possible exposures that are reported by later cases.

In the investigation of the Salmonella Panama outbreak, it was not until the seventh case was interviewed that the market stall was mentioned for a second time. The early cases were questioned again and all but one reported buying or receiving items that could be traced to this stall.

Descriptive epidemiology

Important data items on each case are summarised in a table often called a *line listing* in which each column represents an important variable and each row represents a different case. This format ensures key information on each case is available and allows updating and the addition of new cases. Cases are described by the three epidemiological parameters of time, place and person. Describing cases by person includes clinical features, age, sex, occupation, ethnicity, food history, travel, leisure activity. Describing cases by place includes home address, work address, and travel. Describing cases by time involves plotting the epidemic curve, a frequency distribution of date or time of onset. This may allow the incubation period to be estimated which, with the clinical features, may give some clues as to the causative organism (see Table 2.2.1). The incubation period should be related to events that may have occurred in the environment of the cases and which may indicate possible sources of infection.

In a national outbreak of Salmonella Ealing infection, those affected were mainly infants. This suggested a connection with a widely distributed infant food. Dried baby milk was subsequently found to be the source of infection.

A national outbreak of Salmonella Napoli infection affecting mainly children was found to be due to contaminated chocolate bars.

In another nationwide outbreak of S. Enteritidis, the review of the routine Salmonella questionnaires revealed that most of the cases owned snakes (the source was contaminated feeder mice for the snakes).

Figure 4.2.1 shows the epidemic curve that would occur in a milk-borne *Campylobacter* outbreak due to delivery and consumption of contaminated milk on one particular day (point source outbreak). Figure 4.2.2 shows the epidemic curve in a similar outbreak in which contaminated milk was consumed at the school over several days (continuing source outbreak). Figure 4.2.3 shows the epidemic curve in a community outbreak of measles where the infection is spread from person to person (propagated outbreak). There is a smooth epidemic curve with distinct peaks at intervals of the incubation period.

Generating a hypothesis

A detailed epidemiological description of typical cases may well provide the investigators

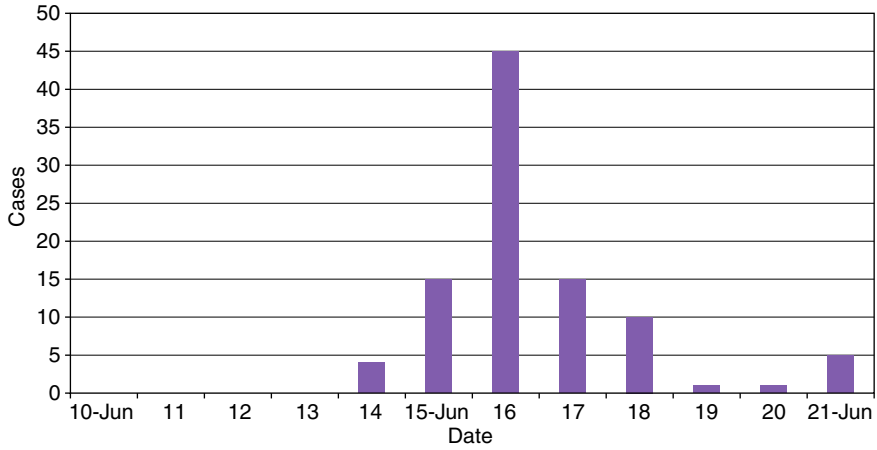

Fig. 4.2.1 Outbreak of *Campylobacter* gastroenteritis associated with consumption of unpasteurised milk at a boarding school (point source).

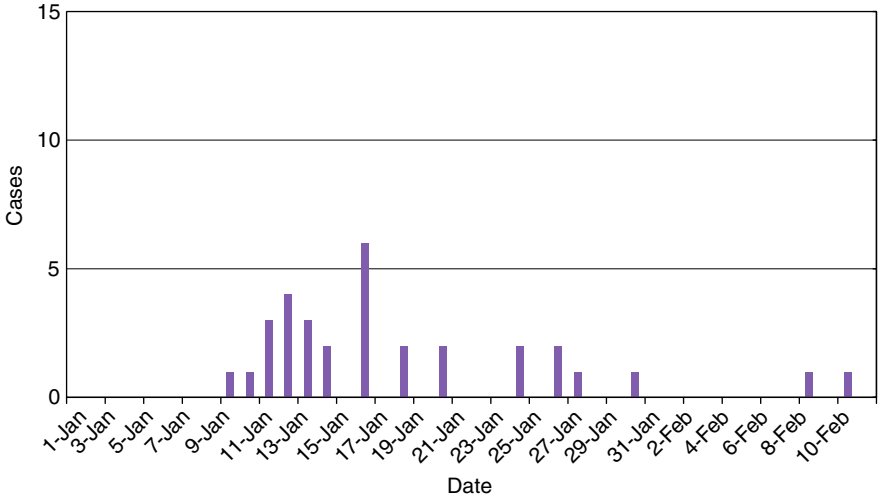

Fig. 4.2.2 Outbreak of *Campylobacter* gastroenteritis associated with consumption of unpasteurised milk at a boarding school (continuing source).

with a hypothesis regarding the source of infection or the route of transmission. A description of atypical cases (e.g. geographical outliers) may also be helpful. Sometimes it is helpful to develop a number of competing hypotheses and consider what further information might be needed to strengthen or weaken the evidence for each one. It can also be helpful in some outbreaks to consider hypotheses in a hierarchical or contingent fashion, for example:

In an outbreak of E. coli O157 PT54, the hierarchical hypotheses were: the cases are all linked; the cases have all attended the same large park; cases had all been exposed to an area of the park that could be contaminated by animals; cases

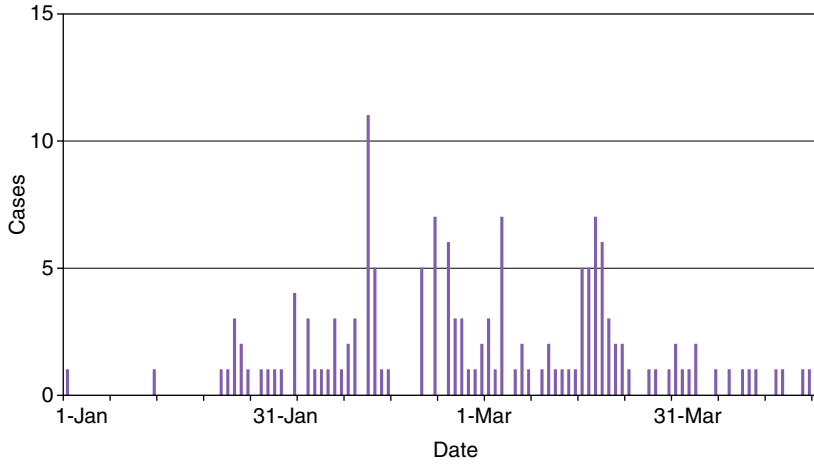

Fig. 4.2.3 Outbreak of measles in a community (propagated outbreak).

had all been exposed to mud or faeces in that area (competing hypotheses included exposure to one of the food outlets); that the free range cattle in this area were the source of the organism. These hypotheses were investigated by detailed case interviews and re-interviews (to obtain a detailed breakdown of activity in the park and to exclude other sources, such as the food outlets), environmental testing (including animal faeces) and molecular typing of human and animal strains to show that they were linked.

Testing the hypothesis

Finding that consumption of a particular food, visiting a particular place, or being involved in a certain activity is occurring frequently among cases is only a first step. These risk factors may also be common among those who have not been ill. To confirm an association between a risk factor and disease, further microbiological or environmental investigations may be required, or an analytical epidemiological study may be necessary. This can be either a cohort study or a case–control study.

- *Case–control study*: a case–control study compares exposures in people who are ill (the cases) with exposure in people who are not ill (the controls). Case–control studies are most useful when the at-risk population cannot be accurately defined (e.g. when cases are laboratory reports of infection in the general population). Controls can be selected from a GP's practice list, from the primary care trust's patient register, from the laboratory that reported the case, from people nominated by the case or from neighbours selected at random from nearby houses. Recently controls have become available from commercially organised market research panels: these can provide much more rapid response than conventional means.

A variant on the case–control study is the *case–case study* where controls are replaced by people who are known to have a different infection: this has been used to analyse data already collected in an enhanced surveillance system for Shiga-toxin producing *E. coli* (STEC), where the 'cases' were those with the STEC phage type (or whole genome sequence type) of interest and the 'controls' were those with other phagetypes: this approach has strengths (reliable data because data obtained nearer the potential exposure time and before a hypothesis was formed, avoiding bias; and speed of study as data already available)

and weaknesses (potential overmatching of controls and the existing data may not be specific enough to the precise hypothesis generated in the outbreak).

- *Cohort study*: a cohort study is a type of natural experiment in which a proportion of a defined population is exposed to a risk factor, while the remainder is not. The incidence or attack rate of infection among exposed persons is compared with the rate among non-exposed persons. For example, following a food poisoning outbreak at a social gathering, thought to be due to consumption of contaminated chocolate mousse, the cohort (all those who attended) is divided into those who ate the mousse (the exposed) and those who did not (the unexposed).
- *Collecting the data*: a defined set of data is collected from both cases and control or from the exposed and unexposed persons within the cohort. A case-definition should be agreed and sample size calculation should be performed to ensure that the study has adequate statistical power. To avoid any bias the data must be collected from each subject in exactly the same way. Usually this is done by questionnaire. Unlike the hypothesis-generating questionnaire, the questionnaire for an analytical study is often shorter, more structured and uses mostly closed questions. It may be administered by interview, by telephone or it may be a self-completion online or postal questionnaire. Questionnaires should be piloted before use. If several interviewers are to be used they should be adequately briefed and provided with instructions to ensure the questionnaire is administered in a consistent way.

  In an outbreak of STEC O157 PT34 linked to two premises with a common salad supplier, a questionnaire was constructed for the cohort that included questions on each menu item available. Data was also obtained from the chefs on the ingredients and garnishes for each dish, which allowed investigators to show that cases were statistically significantly more likely to have purchased food containing a specific salad leaf product and that no case had not done so.

- *Analysis*: In both cohort and case–control studies initial analysis, a bivariate analysis, is done using a 2×2 table. In cohort studies the ratio of incidence in exposed to incidence in unexposed is calculated. This is the relative risk or risk ratio. In case–control studies the odds of exposure in the cases is compared with the odds of exposure in the controls. This is the odds ratio, which usually approximates the relative risk. Confidence intervals for these estimates can be calculated and tests of statistical significance applied. Computer programs that will perform these calculations are freely available (e.g. Epi-Info, EpiData). Where more than one exposure is associated with illness, multiple regression analyses can help eliminate confounding variables.

  In an outbreak of cryptosporidiosis in England, the hypothesis was that infection was associated with the consumption of cold drinking water supplied by the local water company. This was tested using a case–control study. Cases were defined as people living locally who had had a diarrhoeal illness between 1 December 1990 and 31 January 1991, with oocysts present in a faecal sample. Cases were excluded if they had travelled abroad or if another household member had diarrhoea in the four weeks before the onset of their illness. The names and addresses of controls were obtained from the patient list held by the health authority. They were matched with the cases for sex, age group and GP or health centre. They were excluded if they had been abroad within four weeks of the onset of illness in their matched cases or if they themselves had diarrhoea since 1 December 1990. Five names and addresses of controls were obtained for each case. For each case and control a questionnaire was completed by a member of the investigating team during a telephone interview. The questionnaire asked about illness and consumption of various food items, including milk, salad, meat and cheese. Participants were also asked about the consumption of cold tap water both at home and outside the home, consumption of untreated, filtered or bottle water and exposure

Table 4.2.1 Cryptosporidiosis in England, December 1990. Odds ratios for exposure to selected factors

	Case		Control			
	Y	N	Y	N	Odds ratio[a]	95% CI on odds ratio
Unpasteurised milk	0	29	0	80	N/A	N/A
Lettuce	16	11	51	29	0.83	0.31–2.22
Fresh raw vegetables	2	6	56	23	1.51	0.5–5.12
Unpasteurised cheese	0	29	10	69	0	0–1.15
Contact with farm animals	0	27	0	80	N/A	N/A
Tap water Y = >1 cup day^{-1} N = <1 cup day^{-1}	19	7	33	47	3.87[b]	1.35–12.03[c]
Water consumed outside the home	15	10	23	51	3.33	1.18–9.49
Water filtered	0	29	8	72	0	0–1.57
Bottled water	0	29	16	64	0	0–0.63[d]
Swimming pool	5	23	16	64	0.87	0.22–2.87
Rivers	2	26	1	79	6.08	0.3–363

[a] The odds ratio is the odds of exposure in the cases divided by the odds of exposure in the controls. An odds ratio of one indicates no association.
[b] Consumption of tap water is nearly four times as likely in cases as in controls.
[c] The 95% confidence interval (CI) does not include 1, indicating that this is a significant association that is unlikely to be due to chance.
[d] Controls are significantly more likely than cases to have been exposed to bottle water (i.e. there is a protective effect).

to recreational water. The results are shown in Table 4.2.1. *There was a dose–response relationship with the quantity of tap water consumed.*

Evidence to support or refute a hypothesised source may also be obtained by one or more of:

- Iterative interviewing and re-interviewing of cases (as new potential sources identified by later cases) to show that all cases exposed to the same potential source – this is often helpful in community legionellosis outbreaks,
- Detailed microbiological typing of isolates taken from human cases and from a suspected food, water system, animal or environment,
- Food trace-back investigations, which can use specialist software (e.g. FoodChainLab) or control groups (e.g. 'venue based' analytical studies) – this is often helpful in outbreaks in which foods such as eggs or salad has been consumed from a variety of different retail premises to look for a common source,
- Social network analysis to find links between cases and potential common sources or 'super spreaders' – this approach has been found useful in tuberculosis (TB) or sexually transmitted infection (STI) outbreaks.

Further control measures and declaring the outbreak over

Once the source and route of transmission are known further control measures may be required (see disease specific chapters in Section 3). Surveillance to detect new cases and updating of the epidemic curve will allow the outbreak control team to set criteria for declaring the end of the outbreak and monitor the effectiveness of the intervention.

4.3 Community infection control

Introduction

The community is defined as all settings that are outside major hospitals. However, with growing interdependence in control activities, most public health authorities also have close collaboration with hospitals in infection control (Chapter 4.4), as transmission in hospital frequently affects individuals outside the hospital.

Care settings in the community are those that provide health and social care and include community hospitals, care homes, home-care services, schools, nurseries, day-care centres, and prisons. Other community settings are workplaces, leisure centres, hotels, restaurants, communal areas, specific businesses (e.g. tattoo shops) and individual homes. Many infectious diseases have the capacity to spread within community settings where people, some of whom may be particularly susceptible or vulnerable, share eating and living accommodation, and some settings have specific transmission risks (e.g. swimming pools, tattoo and piercing shops, brothels).

Prevention and control of infection in community settings has become important because of an increase in the number of services providing health and social care, the increase in the number of vulnerable individuals in the community and an increase in the scope and complexity of the interventions used.

Community infection control services have to prepare for balanced risk governance. This comprises surveillance/early warning, investigation and risk assessment, advice, stakeholder management, support and leadership on standard precautions, development and implementation of policies and guidelines, training, audit, advice on hygienic precautions, immunisation and decontamination, management of outbreaks and use of antimicrobials.

Sources of advice and guidance

Administrative arrangements

Prevention and control of infection in the community depends on joint working between many different agencies, companies and individuals including the local authorities' responsible health and social care services, the specialist health protection service, local health protection teams, local authorities, care homes, General Practitioners (GPs), hospitals and other independent providers of health and social care for adults and children. There is an even larger group of non-care-providing stakeholders, for example plumbers/engineers for *Legionella* control, farmers for zoonosis control, the food industry, forestry, and so on that can assist in advice and control. There are limited legislative possibilities to implement prevention and control measures, and less formal means, based on knowledge-based authority, is often needed to convince stakeholders: nationally agreed expert guidance documents are a vital tool in helping to achieve this.

The day-to-day work of enforcement is mainly the responsibility of Local Authority staff (e.g. Environmental Health departments in the UK), but for food production, specialist agencies (e.g. the Food Standards Agency in the UK) enforces some regulations. Water supply, sewage and waste management is regulated by the Government but provided by private companies. Supervision and control of fresh water ponds, lakes and rivers is mostly a mixed responsibility of landowners and the government (e.g. the Environment Agency in England); equally, prevention of directly transmissible zoonoses is a mixed responsibility of animal owners, handlers and the government. Regulations and codes of practice place obligations on businesses to ensure their activities are carried out in a hygienic way including arrangements governing food handlers' fitness to work. For food there are frequently additional regulations regarding staff handling food or working in a food handling areas to report diarrhoea and vomiting symptoms to the

management and managers should exclude staff with these symptoms from working with or around open food.

Measures in specific community settings

Specific national guidelines are available in many countries for control of infection in community settings. For example, the UK Department of Health has developed a Code of Practice for health and adult social care on the prevention and control of infections and related guidance. This is legally binding on all providers of health and social care.

Box 4.3.1 gives a checklist for the community infection prevention and control (CIPC) measures that should be in place in community settings. These settings include community hospitals, care homes, GP and primary care clinics, dental clinics, home-care services, schools, nurseries and prisons. Other settings include tattooists and body-piercing premises, swimming pools and gymnasia. Not all these measures will be relevant for every setting.

Box 4.3.1 Checklist for community infection prevention and control (CIPC) measures

- Clear management accountability for CIPC.
- CIPC is part of clinical governance and quality framework.
- Named person with operational responsibility for CIPC.
- Programme of policy review and updating, training and audit.
- Arrangements for seeking advice on risk assessment and application of appropriate control measures.
- Arrangements for surveillance, recording and reporting of cases of infection and outbreaks and incidents. Outbreaks and incidents should be reported to the Health Protection Team (HPT). The HPT will advise what action is required. An outbreak may be defined as symptoms in two or more residents which may indicate a possible outbreak such as cough and/or fever (e.g. influenza), diarrhoea and/or vomiting (e.g. *Clostridium difficile*/norovirus/food poisoning) and itchy skin lesion or rash (e.g. scabies).
- Handbook or procedure manual detailing.
  - **(a)** Standard precautions: hand hygiene; and use of personal protective equipment (gloves, aprons, masks, eye protection).
  - **(b)** Aseptic technique for clinical procedures to prevent contamination of wounds and other susceptible body sites (including minimising exposure of susceptible site, using a 'no-touch' approach if appropriate, hand decontamination, using sterile or non-sterile gloves as appropriate, use of disposable plastic apron, ensuring all equipment and materials are sterile, not re-using single-use items).
  - **(c)** Safe handling and disposal of sharps.
  - **(d)** Management of waste.
  - **(e)** Managing spillages of blood, vomit and diarrhoea.
  - **(f)** Collection and transport of specimens.
  - **(g)** Decontaminating equipment and the environment including cleaning, disinfection and sterilisation.
  - **(h)** Maintaining a clean and safe clinical environment including vaccine storage.
  - **(i)** Laundry and linen management.
  - **(j)** Placing patients with infections in appropriate accommodation including isolation.
  - **(k)** Circumstances where droplet, air-borne or contact precautions are required.

(*Continued*)

Box 4.3.1 (*Continued*)

- Arrangements for meeting the occupational health needs of staff.
  - **(a)** Prevention of occupational exposure to blood-borne viruses (BBV) including prevention of sharps injuries.
  - **(b)** Management of occupational exposure to BBVs and post-exposure prophylaxis.
  - **(c)** Management of exposure to rash illnesses.
  - **(d)** Health of pregnant staff.
  - **(e)** Pre-employment assessment (TB, HIV).
  - **(f)** Immunisation of staff (influenza, varicella, MMR, hepatitis B).
- Antibiotic formulary or equivalent to ensure appropriate use of antimicrobials.
- Information for patients, relatives, visitors and staff.
- Access to reference book or poster detailing the epidemiology and control measures for common infections of public health significance.
- Guidance on specific procedures and practices such as, in England, that published by Public Health England, the Department of Health and Social Care, the National Institute for Health and Care Excellence and professional bodies such as the Royal College of Nursing. This guidance covers management of urinary catheters, enteral feeding, peripheral and central vascular devices and respiratory support equipment.
- Arrangements for responding to outbreaks of infection including reporting, closure of care homes, wards, departments and premises to new admissions, restrictions on visitors, staff absenteeism and business continuity planning.

Guidelines for specific community settings and specific infections

A range of manuals, handbooks and guidelines have been developed by various national authorities covering selected community settings. In addition, specific infections are of particular importance in the community. In some cases, international consensus guidelines are available from the European Centre for Disease Prevention and Control (ECDC), WHO and others and some of these can be found at

https://ecdc.europa.eu/en/publications-data

Many useful community guidelines are available in the UK and these can offer guidance to professionals in other countries where local guidelines are not available. There are key infection prevention and control guidelines for the management in care homes with material to educate and motivate staff:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214929/Care-home-resource-18-February-2013.pdf

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214930/Care-Home-Resource-Summary-Feb14-2013.pdf

A list of useful guidance documents is given in the Appendix to this book.

Prevention

Activity to prevent infection can be directed at the host or the environment. Activities are directed at identifying and minimising or eliminating sources (human, animal, environment), reducing or stopping transmission, and protecting the susceptible host.

Host

Risk behaviour may be changed by health education campaigns. These may be national or local, and may be aimed at the general population or targeted at those who are particularly at risk. Infections that have been the subject of many national health education

campaigns include sexually transmitted infections (STIs) and HIV infection (safe sex, early testing, early diagnosis, early treatment), *Salmonella*, *Listeria*, and *Escherichia coli* Shiga-toxin producing *E. coli* (STEC) infection (food hygiene), influenza pandemic (hand hygiene and vaccination). Health services offer health education, diagnosis, screening, treatment, prophylaxis and immunisation. Examples are routine and selective immunisation (Chapter 4.7), services for STI diagnosis and treatment (Chapter 4.8), services for tuberculosis screening (Chapter 4.10), and other screening for newly arrived immigrants (Chapter 4.12).

Environment

Specified public agencies in most countries have legal powers to control aspects of the environment that could be a source of infection including supplies of food and water, disposal of sewage, waste management and pest control. In the UK, most of these powers rest with Local Authority environmental health departments.

Food safety

There are usually specific powers in relation to food safety; for example, in the UK, the Food Safety Act 1990 provides a framework for a range of regulations that govern the activity of food businesses, the composition and labelling of foods, chemical safety, food hygiene and the control of specific foodstuffs: guidance and enforcement under this Act is provided by the Food Standards Agency and local authority environmental health departments.

Zoonoses

Many microbes infect both animals and humans and prosper in the eco-system they live in. In the One Health approach multiple sectors (animal husbandry, medical, environmental) collaborate for better animal, human and environmental health. The One Health approach is particularly relevant in control of zoonoses, food safety and combatting antibiotic resistance. In these situations it is essential to share epidemiological data and laboratory information across sectors for effective control. Most human zoonotic disease results from exposure to companion and farm animals, less to exposure to wildlife (e.g. hantavirus, plague). Most prevention and control activities are directed at farm animals. Some countries have national Wildlife Health Centres, organising surveillance and sentinels of specific species. Hunters and the public are asked to send shot or found dead animals for investigation, adding to the knowledge of what diseases are prevalent in wildlife. The national agency in Great Britain is the Animal and Plant Health Agency (APHA)

Vector control

In well-organised countries, centres for monitoring of vectors are operational. Endemic vectors (e.g. mosquitos, ticks) are mapped and screened for prevalence of human pathogens. To prevent new vectors from establishing in an area, entomologists select high-risk locations for entry, where they monitor mosquito species periodically (using mosquito traps). If exotic species are detected and eliminated, a wider area is checked for presence of the respective species and further control. The public and veterinarians can be asked to send ticks for surveillance of new species and pathogens.

Control

Control measures for community infection can be directed at the source of infection, the route of transmission, or susceptible people can be offered protection with antibiotics, antivirals or immunisation. The measures may involve the person or case, his or her contacts, the environment and the wider community. Ideally, control measures should be evidence-based or at least based on consensus of stakeholders and best practice.

Person

The case is contacted by visit, telephone, or letter and details are recorded on a specific case report form. Diagnostic samples may be requested (e.g. faecal samples in the case of suspected gastrointestinal infections). Control measures are based on an assessment of the risk that the case may spread infection. Guidelines are available to assist with this risk assessment. For example, with gastrointestinal infections the case may be assigned to one of four higher risk groups: food handler; health, social care or nursery worker; child aged less than five years; or older child or adult with low standards of personal hygiene (Box 2.2.1). Factors such as type of employment, availability of sanitary facilities and standards of personal hygiene should also be considered. Chapter 1.3 discusses control measures and precautions for gastro-intestinal, blood-borne, and respiratory infections, such as isolation, exclusion from work, strict surveillance, restriction of contacts (with susceptible vulnerable high-risk persons), etc.

Measures restrict the personal freedom and privacy of persons and influence management of institutions and companies (infectious source). It is therefore essential to have juridical backup to impose measures (see Box 4.3.2 for UK example).

Box 4.3.2 Public health law: English example

In England, the Health Protection Regulations 2010 deals with notification of infectious diseases and gives local authority and justices of the peace (JPs) powers and duties to take action to protect public health from infection or contamination, if this cannot be done by voluntary cooperation. Examples of local authority powers are keeping a child away from school, requiring a head teacher to provide a list of contact details of pupils attending their school and disinfecting or decontaminating premises or articles. JPs can make orders to control things, premises and people. For example, a JP can require that a person is medically examined, detained in hospital or is disinfected or decontaminated.

Contacts

Contacts of a case of infectious disease may be at risk of acquiring infection themselves, they may risk spreading infection to others, or they may be the source of infection. It is important to have a definition of a contact and conduct a risk assessment. For example, a contact of a case of gastrointestinal infection is someone who has been exposed to the excreta of a case. With typhoid, this definition would be extended to those exposed to the same source as the case, such as those who were on the same visit abroad. A contact of a case of meningococcal infection is someone who has spent a night under the same roof as the case in the seven days before onset, or has had mouth-kissing contact.

Contacts may be subjected to clinical or laboratory examination. For example, in the case of diphtheria and typhoid, they may be offered advice, placed under surveillance, asked for laboratory specimens or offered prophylaxis with antibiotics or immunisation. In some circumstances contacts may be excluded from school or work.

Environment

In some circumstances it may be appropriate to investigate the environment of a case of infection. This may involve inspection and laboratory investigation of home or work. Examples are food-borne infections, gastrointestinal infections and Legionnaires' disease. Legal powers may be used to control the environment, including powers to seize, destroy, and prohibit the use of certain objects. This may be necessary in the event of infection caused by a contaminated foodstuff. It may be appropriate to advise on cleaning and disinfection.

Community

The occurrence of cases of infection will have an effect on the wider community. For example, a case of Legionnaires' disease or tuberculosis may generate considerable anxiety in the public, especially for those that might have been exposed to the same source, either an infectious environment (e.g. cooling tower), other human or animals. Some infections, such as meningitis and hepatitis B, will have a similar effect in schools on staff, pupils and parents. Scabies in day-care centres and head lice in schools are other examples. It is helpful to keep all sections of the community informed about certain cases of infection. This can be done by email, letter, leaflets, internet sites or public meetings. In some circumstances it may be appropriate to set up a telephone advice line or website. In addition, it can be helpful to inform local newspapers, radio, television, and politicians. All sections of the community have information needs with respect to the prevention and control of infectious disease. Advice is available from a range of health professionals. This can be reinforced by leaflets, videos and through the media. In community settings such as schools, nursing homes, residential homes and primary care it is helpful to make available written guidelines on infection control in the form of a manual or handbook. These materials can subsequently form the basis for training and audit in infection control.

4.4 Hospital infection control

Healthcare-associated infections (HCAI) are those that occur in patients or healthcare workers either as a direct result of healthcare intervention (such as medical or surgical treatment) or from being in contact with a healthcare setting. HCAI occur in hospital and community healthcare settings (particularly as more vulnerable patients are cared for outside hospital). HCAI includes respiratory tract infections, urinary tract infections and bacteraemias, caused by a variety of pathogenic organisms and most episodes are sporadic but outbreaks and clusters do occur.

Impact of HCAI

Over 4 million people in Europe get a HCAI annually, and around 37 000 die as a direct result of the infection. A 2011/2012 EU survey found that on any given day, 1 in 18 patients in a European hospital has an HCAI. A 2016 survey found an overall prevalence of HCAIs in English hospitals of 6.6% with patients in intensive care medicine having the highest prevalence of 17.6%. The promotion of a culture of patient safety and implementation of high standards of infection prevention and control practice can minimise the risk of HCAI.

Risk factors for HCAI

A number of factors can increase the risk of a HCAI, but hospital patients with underlying disease, particularly the old and young and those with weakened immune systems are at greatest risk. Invasive devices and procedures including surgery, intensive care, previous exposure to antimicrobial agents and previous hospital admission add to the risk.

Surveillance of HCAI

Most European countries have HCAI surveillance programmes. The Healthcare-Associated Infections Surveillance Network (HAI-Net) is a European network for the surveillance of HCAI that is coordinated by the European Centre for Disease Prevention and Control (ECDC). The network undertakes point prevalence surveys and targeted surveillance in a variety of healthcare settings.

EARS-Net is the European Antimicrobial Resistance Surveillance Network, a Europe-wide network of national surveillance systems providing reference data on antimicrobial

resistance for public health purposes. EARS-Net focuses on the surveillance of antimicrobial susceptibility of invasive isolates of specific bacterial pathogens.

In England, mandatory surveillance schemes exists for Meticillin resistant *Staphylococcus aureus* (MRSA) bacteraemia, *Clostridium difficile* infection, Meticillin sensitive *S. aureus* (MSSA) bacteraemia, *Escherichia coli* bacteraemia, *Klebsiella* spp. bacteraemia, *Pseudomonas aeruginosa* bacteraemia and selected surgical site infections. There is now an increasing focus on the prevention and reduction of Gram-negative bacteraemia particularly healthcare associated episodes.

Control of HCAI

The prevention and reduction of HCAIs involves standard infection prevention and control arrangements using evidence-based interventions. These are intended to minimise the risks of infection and ensure the safety of patients/clients, healthcare workers and others who visit the care environment.

HCAI is an indicator of the quality of patient care and a marker of patient safety. The control of infections in healthcare settings is an important aspect of patient safety and should be subject to strict oversight by clinicians and health-service managers. Control measures comprise a range of activities including surveillance (Table 4.4.1) and standard infection control practices (Table 4.4.2). Evidence-based guidelines have been published on handwashing, use of personal protective equipment, handling sharps, care of urinary catheters and vascular access devices. Guidelines, recommendations and summaries of best practice from a wide range of authoritative sources are available on nearly all aspects of the control of HCAI.

Arrangements for the prevention and control of infections in hospitals

Effective management arrangements are vital for the control of HCAI. In the UK, the Department of Health has developed a Code of Practice for health and adult social care on the prevention and control of infections and related guidance. Under the Health and Social Care Act (2008) this code of practice is legally binding on NHS hospitals and private healthcare providers. Overall responsibility rests with the hospital chief executive and hospital board and the Director of Infection Prevention and Control (DIPC). There should be an infection control team (ICT) comprising an infection control doctor (ICD), one or more infection control nurses (ICN) and clerical support. There should also be a multidisciplinary infection control committee (ICC) and antimicrobial stewardship (AMS) committee. Current roles and responsibilities for HCAI in England are summarised in Table 4.4.3 and similar arrangements may exist in other European countries (see also Table 4.4.2).

Outbreaks of infection in hospital

Infectious diseases can spread readily within hospitals amongst staff and patients who may be more susceptible to infection as a result of illness or treatment. Despite high standards of infection control practice, outbreaks of infection or infectious disease incidents may occur.

Recognition of an outbreak

An outbreak is an incident in which two or more people who are thought to have had a common exposure, experience a similar illness or proven infection. Outbreaks in hospital are either detected by existing and sensitive surveillance systems, through the occurrence of sentinel events (e.g. single case of an uncommon infection) or by the laboratory or clinical staff. Suspected clusters and outbreaks should be reported to the ICT.

Action

Consult your organisation's outbreak control plan. Hospitals should have written plans for

Table 4.4.1 Hospital surveillance of HCAI, AMR, and antimicrobial stewardship

Surveillance	Examples
Laboratory-based surveillance of alert organisms detected in clinical specimens. Organisms monitored may be in line with statutory requirements or based on voluntary, local agreements.	• Meticillin-resistant *Staphylococcus aureus* • Meticillin-sensitive *S. aureus* • *Clostridium difficile*
Laboratory based surveillance of antimicrobial resistant organisms, focusing on an agreed list of drug-bug combinations.	• *Escherichia coli* bacteraemia • *Klebsiella* spp. bacteraemia
Surveillance of antimicrobial prescribing and utilisation (there may be a time-limited focus on specific antibiotics of interest)	• *Pseudomonas aeruginosa* bacteraemia • Vancomycin-resistant enterococci • Multi-drug resistant Gram-negative bacteria • Carbapenemase producing enterobacteriaceae • Extended-spectrum beta-lactamases (ESBL) producing enterobacteriaceae • Norovirus and rotavirus
Surveillance data should be collated using a computerised database to allow easy data retrieval and analysis.	Consider using a Microsoft Access or Excel database or other suitable software programs
Weekly, monthly and annual numbers/rates should be reported by clinical setting. Infection rates may be calculated using appropriate denominators (admissions, discharges, occupied bed-days, days of device usage, etc.).	• Antibiotic prescribing rates (by clinical unit, ward or indication) • Count and rate of Gram-negative bacteraemia episodes • Number/rate of MRSA bacteraemia per 10 000 occupied bed days
Surveillance data should be widely circulated and discussed. An annual report should be compiled	Regular reports to the Infection Control Committee and Antimicrobial Stewardship Committee, and the Board Reports of antimicrobial stewardship and IPC audits
Targeted surveillance of defined conditions and in specific clinical units.	• Catheter-associated urinary tract infections (CAUTI) • Central-line associated blood stream infection (CLABSI) • Ventilator-associated pneumonia (VAP) • Surgical site infection surveillance • Bacteraemia surveillance in intensive care (adults and neonatal) and high dependency units • Surveillance in oncology, haematology and transplant units • Fungi infection surveillance in cardiothoracic surgery units • Point prevalence surveys in high risk areas (e.g. intensive care).
Surveillance by ward staff of sentinel events and other alert conditions	• Single case of uncommon infection • Post-surgical sepsis • Diarrhoea (±blood) or vomiting • Influenza-like illness • Tuberculosis • Pyrexia of unknown origin

IPC: Infection prevention and control.

Table 4.4.2 Standard infection control measures in hospitals

General principles	Areas covered	Examples
Promote a patient safety climate	Hand hygiene	• Hand washing, hand decontamination and hand care.
Develop and implement local policies and procedures for IPC, these can be based on national guidelines and other relevant evidence-based guidance	Respiratory hygiene Personal Protective Equipment (PPE)	• Staff immunisation (hepatitis B, seasonal influenza, BCG, MMR, etc.) • Adequate arrangements for handling and disposal of sharps
Policies should be audited, reviewed and updated regularly	Occupational exposure management	• Management of needle stick or sharps injuries • Management of skin and soft tissue infections
Implement systems and arrangements for managing and monitoring IPC including those for reporting and documenting near-misses, serious incidents and never events.	Antimicrobial Stewardship (See Chapter 4.5)	
Antimicrobial stewardship strategy and plans including local antibiotic formulary	Management of care equipment and operating theatres	• Follow guidance and advice from sterile services department (SSD)
Outbreak and incident control plans should be developed, and exercised if not in regular use	Hospital Environmental Hygiene	• Decontamination: cleaning, disinfection and sterilisation of reusable care equipment • Domestic cleaning using appropriate material for decontamination of the environment
Develop and provide regular staff training and education • Induction • Annual update • Other updates depending on job role	Management of linen (used, infected or soiled) and staff uniforms	
	Safe waste management including pest control	
	Detection and effective management of patients at risk of acquiring or transmitting infection	• Active screening cultures (i.e. admission, weekly and on discharge) • Early alert of previously known positive patients
	Outbreaks/Incidents and management of specific communicable diseases	• Cohort nursing, bay/ward closures, contact precautions including the use of isolation facilities and appropriate PPE
	Management of patient movements, transfers and discharge of patients	• Antimicrobial prophylaxis and suppression regimes for colonised patients
	Catering (including food hygiene)	• Air handling systems • Management of hospital water systems
	Mortuary procedures	
	Good buildings design and construction	
Carrying out audits	Environmental cleaning and hygiene Hand hygiene Safe handling and disposal of sharps Antimicrobial prescribing audits	
Communication and expert advice and research	Use of aseptic techniques	

Table 4.4.3 Example of roles and responsibilities for infection prevention and control (England, 2017)

Department of Health and Social Care	• Sets overall national policy • Commission national guidance • Provide expertise and public information
NHS England	• Commissions healthcare services and manages performance of NHS hospitals against agreed quality standards and metrics
Clinical Commissioning Groups (CCGs)	• Ensure that hospitals have arrangements for infection control
NHS Improvement	• Oversees NHS foundation trusts, NHS trusts and independent providers to ensure consistently safe, high quality, compassionate care within local health systems that are financially sustainable
Hospital Trust Chief Executive(NHS Acute Trusts, NHS Foundation Trusts, Community Healthcare Trusts, Mental Health Trust)	• Ensure effective arrangements for infection control • Clinical governance and promotion of patient safety • Appoint DIPC
Director of Infection Prevention and Control (or equivalent role in other EU countries)	• Oversight and assurance of IPC arrangements • Report directly to CEO and the Board • Oversee IPC policy implementation, assess impact of policies and lead the infection control team • Attend relevant IPC and antimicrobial stewardship meetings • Set standards and challenge poor practice • Produce annual report
Infection Control Committee	• Regular review of surveillance information and findings from root-cause analysis (RCA) and local post-infection reviews (PIR)
Antimicrobial Stewardship (AMS) Committee	• Develop, implement and monitor an AMS programme. • Implementation of policy, guidelines, toolkits, etc. • Oversees work of Infection Control Team • Agree annual programme and monitor progress
Infection Control Team (ICT)	• 24-hour advice on control of HCAI • Surveillance of HCAI • Audit and feedback of compliance with policies • Education and training
'Modern Matron' and other clinical champions	• Champion for patient safety and infection control measures like hand hygiene, environmental hygiene, and so on
Public Health England	• Undertake mandatory and voluntary surveillance programmes
Consultants for Communicable Disease Control/Health Protection and team[a] (employed by PHE)	• Monitor and assist in management of nosocomial outbreaks • Liaison and provision of expert advice to CCGs, NHS Trusts and other health and social care organisations
Care Quality Commission (CQC)	• Monitor, inspect and regulate health and social care services • Reviews compliance with infection control arrangements in hospitals against criteria set out in an IPC Code of Practice.

[a] Some of these bodies may be reformed as part of changes to UK health services structure in the future.

responding to infectious disease incidents. These should cover the following:

- Recognition of an outbreak.
- Roles and responsibilities of key individuals/groups (e.g. DIPC, CCDC, etc.)
- Initial investigation by ICD and ICN to determine whether or not an outbreak exists.
- If the outbreak is confined to hospital, whether it can be dealt with by the ICT or if an outbreak control team is needed. A major outbreak is one in which large numbers of people are affected, where the organism involved is particularly pathogenic or where there is potential for spread within the hospital and the community.
- The outbreak to be reported to appropriate authorities (e.g. Public Health England [PHE] and Clinical Commissioning Group [CCG]).
- If the outbreak is not confined to hospital, the CCDC would be involved and the local outbreak plan would be implemented as appropriate
- Outbreaks of limited extent will be dealt with by the ICT along with the relevant clinicians and nurses.
- It would be usual for the CCDC to be informed, although he or she may already know of the outbreak through regular contact with the ICD.
- If the disease involved is statutorily notifiable, the medical staff responsible for the patient(s) must notify the CCDC.
- In any infectious disease incident where food or water is implicated, a local authority environmental health officer should be informed.

Initial investigation of a hospital outbreak

This should consist of the following:

- Collect information on all cases occurring on all wards and units.
- Establish a case definition; request laboratory tests (this may include molecular tests to determine the outbreak strain type(s)).
- Ensure provision of medical and nursing care for affected patients, including appropriate infection control precautions to prevent secondary spread.
- Consider antibiotic prophylaxis or immunisation if appropriate (not usually applicable for gastrointestinal infections).
- Consider catering arrangements, disinfection, handwashing, laundry, food and environmental sampling, and microbiological or serological screening of those at risk.
- If a food-borne or water-borne infection is suspected, the environmental health specialist (EHO) will conduct an environmental investigation, including inspection of kitchen, food handling and storage practices, review of illness amongst staff, requesting faecal samples from members of staff if necessary, review of menus, waste handling and pest-control.
- Implement control measures, for example:
  (a) patient isolation/cohort nursing,
  (b) restriction of transfers and/or discharges,
  (c) staff education in infection control procedures,
  (d) clear instructions and information for ward staff, cleaners, etc.,
  (e) information to patients' relatives and visitors.
- Decide when the outbreak is over.
- Communicate with the CCG, PHE and media as appropriate.

Community outbreak affecting the hospital

Hospitals should have plans for responding to a major community outbreak affecting the hospital. Major outbreaks of infectious disease in the community may place heavy demands on hospital services. Acute outbreaks developing over a few hours are generally toxin-mediated.

Non-acute outbreaks, due for example to influenza or norovirus, develop over days or weeks. The ICT role would include advising on the collection of microbiological samples and any control of infection measures. The hospital may activate its Major Incident Plan and convene an outbreak control team. The hospital response will involve clinical

and managerial staff. Consideration should be given to: admissions policy; appropriate management of patients; opening up additional beds; consequences of staff illness; communications with media, community staff and GPs.

4.5 Antimicrobial stewardship

Antimicrobial resistance (AMR), which is simply defined as the loss of effectiveness of any anti-infective medicine, including antiviral, antifungal, antibacterial, and antiparasitic medicines is one of the most important public health issues of the twenty-first century.

Antimicrobial stewardship programmes (ASP) have emerged largely in response to the growing global problem of antimicrobial resistance. In England, antimicrobial stewardship (AMS) is defined as an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. The primary aim of ASPs is to improve the clinical effectiveness of antimicrobial treatment and limit antimicrobial resistance by reducing the selective pressure for the development of resistance to currently effective antimicrobials, minimise toxicity and other adverse events, and reduce the costs of health care for infections. This should be viewed as the responsibility of all healthcare workers and can be achieved through coordinated interventions designed to measure and improve the appropriate use of antimicrobials (right drug, at the right dose, via the right route, and for the right duration) without compromising the quality and effectiveness of care delivered to patients.

ASP structures vary by country and even within countries, and there is variation by healthcare setting. In some countries, AMS activities are closely linked to infection prevention and control activities as part of regional and national programmes to control healthcare-associated infections and the spread of antimicrobial resistant pathogens. In England, hospitals are legally required to follow antimicrobial stewardship practices in order to maintain their registration with the main healthcare regulator. Additionally, English hospitals are mandated by the Health and Social Care Act of 2008 that provides guidance on compliance for continuing registration and specifies that registered hospitals must have an ongoing antimicrobial stewardship programme. The National Institute for Health and Care Excellence (NICE) guideline also states that commissioning and provider organisations should ensure that antimicrobial stewardship operates across all care settings. Numerous guidelines and toolkits have been published over the past decade to assist organisations in implementing stewardship programmes to improve rational prescribing. These include Start Smart-Then Focus (SSTF) and TARGET (Treat Antimicrobials Responsibly – Guidance and Education Tools) that recommend specific strategies and interventions for AMS in hospital and community settings.

Antimicrobial stewardship programme

When establishing an ASP, organisations should consider including the following components:

- Mechanism for monitoring and evaluating antimicrobial prescribing and how this relates to local resistance patterns,
- Developing systems and processes for monitoring and for providing regular feedback to individual prescribers and prescribing leads in all relevant settings on:
  - individual antimicrobial prescribing benchmarked against local and national antimicrobial prescribing rates and trends,
  - local and national antimicrobial resistance rates and trends,
  - patient-safety incidents related to antimicrobial use, including hospital admissions for potentially avoidable life-threatening infections or *Clostridium difficile* infections,

  - Identifying and reviewing whether hospital admissions are linked to previous prescribing decisions in patients with potentially avoidable infections (for example, *Escherichia coli* bacteraemias, mastoiditis, pyelonephritis, empyema, quinsy or brain abscess).
- Providing education and training to health and social care practitioners about AMS and AMR based on an agreed competency framework (for example, the AMS competency framework in England),
- Integrating audit into existing quality improvement programmes,
- Clearly defined roles, responsibilities and accountabilities for the programme,
- Involving lead health and social care practitioners in establishing processes for developing, reviewing, updating and implementing local antimicrobial guidelines. This may be facilitated by developing local networks across all care settings to communicate information and share learning.

Source: Adapted from NICE Guidance 15: Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. London: NICE, 2015. Available at: www.nice.org.uk/guidance/ng15 *Accessed January 2018.*

Antimicrobial stewardship team

Antimicrobial stewardship teams should ideally be multidisciplinary (either standalone or as part of an existing Infection Prevention and Control Committee). Organisations should identify core members (for example, antimicrobial pharmacist and a medical microbiologist) and opt in additional members depending on the healthcare setting and local context. The team should consider including champions from high-impact areas for stewardship (e.g. critical care, surgery).The potential role of the local health protection team/practitioner is outlined in Box 4.5.1.

Core elements of an antimicrobial stewardship programme

The following core elements of an antimicrobial stewardship program have been proposed by a number of public health institutions:

Leadership Commitment: a formal statement from the board indicating their support for an ASP, identifying dedicated funding for an

Box 4.5.1 The role of the local health protection team/practitioner in an antimicrobial stewardship team

- Support the development and maintenance of antimicrobial prescribing and antimicrobial resistance surveillance systems and facilitate access to good quality surveillance information.
- Provide expert health protection advice as required during the design and operation of the stewardship program.
- Contribute to the work of the infection prevention and control and antimicrobial stewardship committees (for example, in developing, reviewing, updating and implementing local prescribing guidelines).
- Support/lead the investigation and control of clusters/outbreaks of antibiotic resistant infections.
- Support the organisation and delivery of education and training sessions on antimicrobial stewardship.
- Provide system leadership by bringing together health and social care organisations/practitioners across all care settings to work collaboratively to support antimicrobial stewardship.

antibiotic stewardship lead, appointing a board level champion for ASP and receiving regular reports on ASP outcome measures

Structure, expertise and accountability: The ASP should have a designated leader or co-leaders who are accountable to the organisation's leadership for the agreed programme outcomes, goals and performance targets. Within the stewardship team, appoint a pharmacist lead to partner with the ASP lead (if different) to provide the expertise and accountability and to define the priorities and measures of success.

Identify and implement evidence-informed interventions: There are a number of evidence-informed interventions that have been shown to be clinically and cost-effective in improving the rational use of antimicrobials in a variety of settings. The team should consider adopting a multifaceted approach to improve the likelihood that the programme is successfully implemented, sustainable, achieves the desired objectives and leads to meaningful improvements in outcomes at the patient level (e.g. reduction in adverse events, mortality) and societal level (costs and AMR). The ASP should start with a few interventions based on the organisation's needs, available data and extant guidance and modifications to the program should be based on findings from the ongoing evaluation. Potential interventions include (list is not exhaustive):

- Use of antimicrobial cycling, formulary restriction, and pre-authorisation that may include a policy for review of antibiotic orders for specified drugs by a physician or pharmacist based on local needs.
- Require documentation of diagnosis/indication, drug, dose, and duration for all antibiotic orders.
- Establish a process to review antibiotics prescribed after 48–72 hours ('antibiotic time-out' or 'post-prescription review').
- Establish guidance on automatic changes from IV to oral dosing in identified situations.
- Implement time-sensitive automatic stop orders for specified antibiotics (e.g. agents used for surgical prophylaxis or empiric therapy).
- Use real-time, rapid diagnostics such as near patient test for C-reactive protein (CRP) or procalcitonin to improve appropriate antibiotic use.
- Education and training – provide regular antibiotic stewardship education to all relevant staff including updates on existing guidelines and clinical pathways (e.g. TARGET and SSTF).
- Regular review and feedback to prescribing practitioners by the antimicrobial stewardship teams to explore the reasons for increasing, very high or very low volumes of antimicrobial prescribing, or use of antimicrobials not recommended in local (where available) or national guidelines.
- Implement electronic prescribing and clinical decision support systems to facilitate the appropriate prescribing.
- Financial incentives linked to the achievement of agreed quality measures for antimicrobial prescribing and AMR.

Surveillance and information systems: Surveillance systems are needed to monitor antimicrobial prescribing and resistance patterns to support stewardship across all care settings, taking into account available resources. The routine monitoring of prescribing and resistance patterns is critical to support continuous improvement and to assess the impact of improvement efforts.

Identify and report key measurements of improvement: The regular reporting of information on prescribing and resistance to clinicians, hospital leadership, and other stakeholders is an essential component of any ASP. These reports should cover the organisation's and specialty/unit specific resistance patterns for defined drug-bug combinations that have been selected locally or nationally.

Education: The education of clinicians and other stakeholders about the causes and trends in AMR and guidance on approaches to promote optimal prescribing should be adequately funded and promoted as it has the potential to change prescribers' attitudes and support AMS. In England, the competences required to operate an effective ASP is outlined in a competency

framework that consist of five dimensions, namely; infection prevention and control, antimicrobial resistance and antimicrobials; prescribing of antimicrobials, antimicrobial stewardship, and monitoring and learning. The impact of these education/training sessions should be evaluated through audit and feedback.

4.6 Risks to and from healthcare workers

Healthcare workers (HCWs) are at risk of acquiring infection because of exposure at work. They are also a potential source of infection for those they are caring for, particularly those with impaired resistance to infections. Therefore personal and patient protection measures need to be in place at all times.

HCWs are an important sentinel group. Unexplained illness amongst HCWs may be an early sign of an unusual or novel outbreak, as occurred with SARS (Chapter 3.15).

HCWs can be categorised according to the level of probable exposure to infectious disease. Target groups for preventative interventions can then be identified following a risk assessment based upon the likelihood of transmission (e.g. Table 4.6.1 using the concept of exposure-prone procedures [EPPs]) and disease-specific risks identified and controlled (Table 4.6.2).

Lookback studies

Purpose

The purpose of lookback studies is to:

- determine those at risk of acquiring a communicable disease following an exposure, usually related to healthcare,
- inform exposed individuals about the risk to which they have been exposed,
- determine who, amongst those exposed, has been infected,
- prevent further transmission and/or clinical disease,
- provide appropriate interventions (treatment, counselling, etc.) for those exposed, both infected and uninfected, and
- advance understanding about reducing and quantifying exposure risks.

Context

Lookback exercises are usually carried out following exposure, or suspected exposure, to blood-borne viruses (hepatitis B, hepatitis C or HIV) within a healthcare setting (e.g. exposure to a surgeon with hepatitis B, or to contaminated instruments). Similar exercises may be recommended for potential exposures to other infections, such as TB and Creutzfeldt–Jakob disease (CJD). When lookback studies are being undertaken there may well be heightened media interest. Procedures for managing this should be established early to ensure confidence in the service is maintained. Mechanisms for providing reassurance may need to be established, including for the 'worried well'.

Table 4.6.1 Exposure categories for healthcare workers (HCWs)

Category I	Likely to undertake EPPs and work in exposure prone environment (e.g. clinicians working on air ambulances, in medical emergency response teams or critical care practitioners).
Category II	Unlikely to undertake EPPs but likely to work in exposure prone environments (e.g. front line paramedics and technicians).
Category III	Unlikely to undertake EPPs and unlikely to work in exposure prone environment (e.g. emergency care practitioners and others undertaking primary care role).
Category IV	Will not undertake EPPs or work in exposure prone environments as part of defined role but may incidentally render basic first aid (e.g. engineers, gardeners).

See: Public Health England website: Emergency Healthcare Workers, Exposure Prone Procedures

Table 4.6.2 Specific disease risks

Infection	Target group	Rationale	Comments
Diarrhoea	Category I	Personal and patient protection	Staff with diarrhoea should report to occupational health.
Diphtheria	Category I staff caring for patients with diphtheria Category II staff	Personal protection	National immunisation programme should ensure immunity. Category II staff should have immunity checked.
Hepatitis A	Category I staff working in institutions for patients with learning disabilities Category II laboratory staff who may handle the virus Category IV maintenance staff exposed to sewage	Personal protection	Immunisation may be offered following a risk assessment.
Hepatitis B	Category I and II staff with exposure to blood, blood-stained body fluids and tissues	Personal and patient protection	Immunisation may be offered to other groups of staff following a risk assessment.
Hepatitis C	Category I and II staff with exposure to blood, blood-stained body fluids and tissues	Personal and patient protection	See section on lookback exercises.
HIV	Category I and II staff	Personal and patient protection	See section on lookback exercises. Risk assessment to be undertaken, particularly if exposure to TB.
Seasonal Influenza	Category I staff	Personal and possibly patient protection	Annual immunisation should be offered by occupational health service.
Poliomyelitis	All HCWs	Personal protection	National immunisation programme should ensure immunity.
Rabies	Those directly caring for rabid patients	Personal protection	Immunisation
Rubella	Category I HCWs working in maternity departments	For patient protection	National immunisation programme should ensure immunity. HCWs in high-risk areas should have documented immunity.
SARS	Important for all Category I and II staff	Personal and patient protection	Ensure surveillance of HCW in contact with SARS patients is in place.
TB	Important for all Category I and II staff	Personal and patient protection	Staff without a BCG scar or documented BCG immunisation should be tuberculin tested and offered BCG. Staff should report possible TB symptoms promptly.
Tetanus	Category III staff at higher risk of tetanus-prone wounds (e.g. gardeners)	Personal protection	National immunisation programme should ensure immunity.
Varicella	Category I–III HCWs with patient contact, especial attention to those working in high risk clinical areas such as maternity and oncology	Patient protection Varicella-zoster vaccine recommended for all non-immune HCWs with patient contact (i.e. categories I–III)	Varicella-zoster vaccine now licensed in many European countries (including UK). Varicella-zoster antibodies to be checked. Non-immune staff to be excluded from high-risk areas 7–21 days following exposure.

BCG, Bacille Calmette–Guérin; SARS, severe acute respiratory syndrome.

The importance of preserving the confidentiality of the HCW and contacts should be emphasised. In this chapter we are focusing on the guidance on lookback exercises given by the UK Expert Advisory Groups. Similar guidelines are in place in most other European countries.

HIV

Guidance on lookback exercises is given by the UK Expert Advisory Group on AIDS (EAGA). These are summarised in Table 4.6.3.

Table 4.6.3 Lookback exercises for HIV exposure from HCW

When to carry out a lookback	EAGA recommends 'that all patients who have undergone an exposure prone procedure (EPP) where the infected HCW was the sole or main operator should, as far as practicable be notified of this'.		
What is an EPP?	A procedure in which there is a risk that injury to the HCW may result in exposure of the patient's open tissues to the blood of the HCW. This usually involves operations in which the HCWs fingers are not visible whilst exposed to sharp objects.		
	Risk of exposure[a]	**Definition**	**Examples**
	High	Major operations	Vaginal or abdominal hysterectomy, caesarean section, prolapse repair, salpingectomy
	Low	Other procedures, suturing or sharp instruments	Laparoscopy, forceps delivery, episiotomy repair, incision of Bartholin's abscess
	None	Procedures that do not involve suturing or sharp instruments	Manual removal of placenta, dilatation and curettage, cystoscopy, spontaneous vaginal delivery
Methods	Establish incident management team. Ensure overall co-ordination is clear. Establish helplines. Ensure that GPs are kept informed. Define EPP. It may be necessary to define high and low risk procedures in order to concentrate resources on those most at risk. Identify those exposed. This may involve extensive searches through hospital records, operating theatre registers, etc. Contact exposed patients. This may be personally by GPs or their staff, or by letter. The method will need to be sensitive to the risk, and to the need of those contacted for support and counselling. It is important to ensure that helplines/counselling is in place, and that there are clear algorithms for the care of those identified. Ensure close liaison with press office throughout.		
Transmission risk	A number of lookback studies have been carried out following exposure to HIV infected HCWs. Studies of over 30 000 patients (about half of whom have undergone testing) have shown no evidence of transmission of HIV to patients. Three incidents, a Florida dentist who transmitted infection to six patients, a French orthopaedic surgeon who infected one patient and a gynaecologist from Spain have been reported. The risk of transmission from an HIV infected HCW to a patient following an EPP is likely to be low.		
Sources of further advice	EAGA; national specialist CDC/PHE; ECDC; Department of Health and Social care, UK Advisory Panel for Healthcare Workers Infected with Blood-borne Viruses (UKAP)		

CDC, Communicable Disease Control; EAGA, UK Expert Advisory Group on AIDS; ECDC, European Centre for Disease Prevention and Control; EPP, exposure-prone procedure; PHE, Public Health England.

[a] From Communicable Disease and Public Health, 1999, 2:127.

Hepatitis B

HCWs who carry hepatitis B virus (HBV) may infect patients who become exposed to their serum. The UK Health Departments require all HCWs who undertake exposure prone procedures to be vaccinated against HBV, and their subsequent immunity to be documented. Non-responders to vaccination should be investigated for evidence of chronic HBV infection. HCWs who are hepatitis e antigen positive may not undertake EPPs because of the significant risk they pose to patients.

In spite of the recommendations for immunisation and restriction placed upon practice, a number of events have still occurred where patients have been exposed to an infected HCW, or to the risk of transmission in a healthcare setting (Table 4.6.4).

Hepatitis C

HCWs who carry hepatitis C virus may infect patients who become exposed to their serum; however, the risk of transmission is much lower than the risk of transmission for HBV from an e antigen positive surgeon. HCWs are not restricted in carrying out EPPs unless they have been shown to transmit hepatitis C. They should be advised on adherence to precautions for the control of blood-borne infection by the occupational health department (Table 4.6.5).

Table 4.6.4 Lookback exercises for hepatitis B virus (HBV) exposure from HCW

When to carry out a lookback	There is no formal guidance. However, the recommendations given by EAGA for HIV lookback exercises are helpful. Notification exercises should not extend beyond 12 months unless high rates of transmission have been documented.
What is an EPP?	A procedure in which gloved hands may be in contact with sharp instruments, needle tips and sharp tissues (spicules of bone or teeth) inside a patient's open body cavity, wound or confined anatomical space where the hands or fingertips may not be completely visible at all times.
Methods	As above The incubation period for HBV (2–6 months) is such that exposed patients may be identified during the period before seroconversion. Serum should be taken from patients on identification and they should be retested six months after exposure to identify seroconversions. DNA sequencing of fragments of HBV DNA may be useful to establish transmission.
Interventions	Hepatitis B immunoglobulin is effective up to one week after exposure and should be offered to individuals at risk. The value of hepatitis B vaccination is unclear and there is probably little merit in using hepatitis B vaccine more than two weeks after exposure. Systems will need to be put in place for ensuring that those who do not clear the virus are followed up and if appropriate offered treatment for chronic HBV.
Transmission risk	Transmission rates identified in incidents involving surgical staff in the UK have ranged from 0.9 to 20% depending on the procedures and other factors.
Sources of further advice	Expert Advisory Group on Hepatitis; national CDC/PHE: ECDC; Department of Health UK Advisory Panel for Healthcare Workers Infected with Blood-borne Viruses (UKAP).

CDC, Communicable Disease Control; ECDC, European Centre for Disease Prevention and Control; EPP, exposure-prone procedure; PHE, Public Health England.

Table 4.6.5 Lookback exercises for hepatitis C virus (HCV) exposure from HCW

When to carry out a lookback	As for hepatitis B
What is an EPP?	As for hepatitis B
Methods	Serum should be taken from those exposed on identification. Advice should be sought on when repeat testing should be performed. It is recommended that serum is obtained from HCWs exposed to a known positive source at baseline, 6, 12 and 24 weeks and tested for HCV RNA at 6 and 12 weeks and anti-HCV at 12 and 24 weeks. Genotyping may be useful to establish transmission.
Interventions	Although there is some disagreement over the effectiveness of early treatment in preventing progression of disease most experts favour treatment of patients with acute hepatitis C.
Sources of further advice	Expert Advisory Group on Hepatitis; national CDC/PHE: ECDC; Department of Health UK Advisory Panel for Healthcare Workers Infected with Blood-borne Viruses (UKAP). See Appendix for guidance on the risks and management of occupational exposure to hepatitis century

CDC, Communicable Disease Control; ECDC, European Centre for Disease Prevention and Control; EPP, exposure-prone procedure; PHE, Public Health England.

4.7 Co-ordination of immunisation services

Role of the immunisation co-ordinator

The effective delivery of immunisation services requires the co-ordination of the inputs of many different professionals and agencies. Each local health organisation should delegate a particular person (or persons) to take on special responsibility for the commissioning of consistent, resilient, high-quality immunisation programmes within the defined range and the continuous improvement of the programme. The main responsibilities of an immunisation co-ordinator may include (in some national health services, these responsibilities may be combined with those related to the provision of screening services):

- To ensure that an appropriate strategy is devised and implemented, with the aim of ensuring that every person (in the absence of genuine contraindications) has access to high-quality and safe immunisation services;
- To ensure that appropriate resources are in place to support the delivery of the strategy;
- To ensure that appropriate local policies and procedures, based on models of good practice, are in place to support the strategy;
- To provide leadership and co-ordinate the role of all those involved with immunisation in primary care, child health services, hospitals, educational establishments and elsewhere, and to gain their commitment to the strategy;
- To ensure (in collaboration with key stakeholders) that systems and protocols are in place for the identification, response and evaluation of untoward incidents (including outbreaks associated with failure of the immunisation programme);
- To act as a local source of advice and information on immunisation issues for the public and professionals and ensure that expert clinical and public health advice is provided through an appropriate provider;
- To ensure all staff involved in immunisation have access to relevant training courses and meet training requirements both for new immunisers and updates in line with National Minimum Standards in immunisation training;
- To ensure that up-to-date and reliable figures on immunisation uptake rates are available through effective links with

information system commissioners (e.g. Child Health Information System) and to review and interpret performance data at appropriate geographic levels and develop action plans to address variations in performance and oversee their implementation by providers;
- To monitor immunisation uptake and identify inequalities particularly in relation to social class, ethnicity, special need, and develop and implement plans to reduce inequality and ensure that the unregistered and/or unimmunised population have access to high-quality immunisation programmes;
- To ensure that appropriate audit and other quality assurance activities are carried out on the availability, effectiveness and efficiency of local immunisation services.

The separation of functions in some national health services means that some of the above list may be delegated to other individuals. The functions may be split as:
- *Health services commissioning organisation*: assume overall responsibility for delivery of service and meeting national targets, including provision of services, training, public information and collection of vaccine uptake data.
- *Public health specialist service*: provide strategic leadership, co-ordination, expert advice and support to health services in areas in discharging their responsibilities.
- *Paediatric and community health services*: provision of expert clinical advice, supporting clinical services for complex cases and, where appropriate, maintenance of the child health (immunisation) database.

Immunisation oversight groups

The immunisation co-ordinator should be supported by an immunisation oversight group to ensure proper co-ordination of services across relevant geographies, share best practice and support development and service improvement. Membership might include:
- public health service local immunisation lead/co-ordinator (Chair)
- health service commissioning organisation immunisation leads/co-ordinators
- community paediatrician
- information manager (child health/immunisation information systems)
- community services manager
- community services commissioner
- general practitioner
- community nurses, including practice nurse
- pharmacist, and
- health promotion officer

The terms of reference of the immunisation oversight group could be as follows:
- To review and advise on immunisation policies within the geographic area and to develop an integrated, area-wide strategy in order to achieve the maximum immunisation uptake, in line with national guidelines and recommendations from the national technical advisory group (for example: Joint Committee on Vaccination and Immunisation in the UK).
- To implement and monitor the local immunisation programme.
- To ensure accurate information is available via an immunisation information system to support the delivery of the immunisation programme and that this information is appropriately shared with all stakeholders.
- To ensure that the immunisation information system or linked databases can support the delivery of an efficient and effective patient recall system.
- To ensure appropriate training and updating is available on an ongoing basis for all staff involved in the immunisation programme.
- To ensure that clinical management advice concerning the immunisation programme and advice on the appropriate systems for the storage of vaccines is available in the area.
- To co-ordinate health promotion activities within the area on immunisation issues.
- To ensure that arrangements are adequate to report and investigate incidents and serious incidents and where appropriate support serious incidents.

Immunisation information systems

Immunisation information systems (IIS) are confidential, population-based, computerised databases that document all immunisation doses administered by providers to persons residing within a given geographic area. These systems play a key role in monitoring vaccination coverage for use in surveillance and program operations, providing consolidated immunisation histories for use by clinicians in determining the most appropriate vaccinations and in the evaluation of vaccine safety and effectiveness. The IIS in England is called the child health information system (CHIS), and comparable systems exist in other EU/EEA countries. Some important features of an IIS include (not exhaustive):

- Access to complete and accurate denominator population data,
- Unique identifier to support record identification (for example during incident/outbreak investigations),
- Real-time electronic access to IIS to enable complete timely and correct entry of vaccination records,
- Interoperability with other healthcare databases,
- Ability to produce automated outputs to support the work of a range of stakeholders.

Vaccination coverage

The theoretical aim of immunisation services is to achieve herd immunity against those diseases transmitted from person to person (e.g. measles) and to protect everyone against those with other routes of transmission (e.g. tetanus). For an example of a routine immunisation schedule (see Table 4.7.1 for UK schedule). Many countries have set targets for vaccination coverage based on WHO recommendations.

Table 4.7.1 Routine immunisation schedule: UK example[a]

Age	Disease protected against and vaccine given
Neonates	BCG (Infants in areas of the country with TB incidence ≥40 per 100 000; Infants with a parent or grandparent born in a high incidence country) Hepatitis B (Babies born to hepatitis B infected mothers)
2 months	Diphtheria, tetanus, pertussis (whooping cough), polio, *Haemophilus influenzae* type b (Hib) and hepatitis B (DTaP/IPV/Hib/HepB) Pneumococcal (13 serotypes) conjugate vaccine(PCV) Meningococcal group B (MenB) Rotavirus gastroenteritis (Rotavirus)
3 months	Diphtheria, tetanus, pertussis (whooping cough), polio, *Haemophilus influenzae* type b (Hib) and hepatitis B (DTaP/IPV/Hib/HepB) Rotavirus gastroenteritis (Rotavirus)
4 months	Diphtheria, tetanus, pertussis (whooping cough), polio, *Haemophilus influenzae* type b (Hib) and hepatitis B (DTaP/IPV/Hib/HepB) Pneumococcal (13 serotypes) conjugate vaccine (PCV) Meningococcal group B (MenB)
12–14 months	*Haemophilus influenzae* type b (Hib) and Meningococcal group C (MenC) Measles/mumps/rubella (MMR) Meningococcal group B (MenB) booster Pneumococcal (13 serotypes) conjugate vaccine(PCV)
2–8 years old (including children in reception class and school years 1–4)	Seasonal influenza (annual dose) live attenuated influenza vaccine (LAIV)
Three years four months old or soon after	Diphtheria, tetanus, pertussis and polio (DTaP/IPV) Measles, mumps and rubella (MMR)
12–13 years (girls only)	Human papillomavirus (HPV- two doses 6–24 months apart)

Table 4.7.1 (*Continued*)

Age	Disease protected against and vaccine given
14 years	Tetanus, diphtheria and polio (Td/IPV) Meningococcal groups A, C, W and Y disease (MenACWY)
Adult	Boosters for tetanus and polio if less than 5 doses received Vaccines for occupational or lifestyle risks, pregnancy, pre-existing health conditions
65 years	Seasonal influenza (Inactivated influenza vaccine) Pneumococcal (Pneumococcal Polysaccharide Vaccine [PPV] 23 serotypes)
Any age	Seasonal influenza, pneumococcus (medical risk groups) Travel vaccines

(Currently no EU-wide consensus schedule).
[a] Accurate as at September 2017. Available at URL: https://www.gov.uk/government/publications/the-complete-routine-immunisation-schedule

- 95% of children to receive three primary doses of diphtheria, tetanus, polio and pertussis in the first year of life and one dose of MMR by their second birthday;
- 75% uptake of annual seasonal influenza immunisation in recommended groups.

The systematic use of IIS enables geographic areas to monitor vaccination coverage and to manage the performance of the immunisation programme. Many areas fail to achieve coverage targets and these are often those with the highest population density and therefore where a higher than average immunisation uptake is needed to achieve herd immunity. In areas where a significant proportion of their children are vaccinated much later than the target age, this will further increase the pool of susceptibles allowing transmission to continue. An additional example of the consequence of late vaccination is the exposure of infants to pertussis and Hib at an age at which severity of disease is highest.

Contributing reasons for low or late immunisations may be as follows:

- Reduced public confidence in certain vaccines after media scares (e.g. MMR and pertussis). Concern may be highest in certain socio-economic groups such as higher social class parents.
- Confusion among health professionals as to safety and true contraindications of vaccines.
- Factors related to social deprivation, particularly groups with high population mobility such as traveller groups, lone parenthood and large family size.
- Factors relating to religion (particular issue in the Netherlands), lifestyle and ethnicity.
- Immigrant and looked-after children are often not up-to-date with vaccination.
- Problems with the way programmes are organised, delivered and remunerated.

Potential measures to improve uptake rates are given in Box 4.7.1.

Surveillance of vaccine safety

Adverse events following immunisation (AEFI) are events occurring following immunisation, regardless of whether they were or were not caused by the vaccine. The surveillance of AEFI is necessary to provide assurances about vaccine safety. The assessment of vaccine safety needs to be comprehensive, continuous and underpinned by a well-designed reporting scheme. The organisation and delivery of these schemes vary across Europe; however, in most countries there is a requirement to report AEFI to a regulatory agency, particularly for new vaccines (for example Men B). If a cluster of adverse events occurs, the public health department will be involved in the investigation. A single serious event following vaccination is also likely to generate significant workload as anxiety will be high.

Box 4.7.1 NICE recommendations to improve vaccine uptake

Immunisation programmes

- Ensure national guidance and updates are disseminated to professionals and implemented.
- Monitor vaccination coverage.
- Identified professional responsible for each local programme.
- Improve access to immunisation services (for example, providing enough immunisation appointments; ensuring young people and their parents know how to access services, etc.).
- Send tailored invitations for immunisation including tailored reminders and recall invitations to non-attenders and follow up by telephone or text.
- Provide tailored information, advice and support to parents and young people, including in appropriate minority languages.
- Consider home visits for discussion with non-attenders and possible home vaccination.
- Ensure concerns can be discussed with healthcare professional.
- Check immunisation status at all other clinical appointments: discuss and offer any outstanding vaccination.
- Specific co-ordination and process for targeted immunisation programmes (example targeted TB vaccination).

Information systems

- Ensure local health organisation and medical practices have adequate methods for recording, maintaining and transferring accurate data on vaccination status of all persons.
- Encourage and enable private providers to pass on details of all vaccines given.
- Record any factors that may make missed vaccinations more likely.
- Regularly maintain and update immunisation information systems.
- Ensure up-to-date information available to all staff involved in immunisation.
- Use uptake and surveillance data to inform local needs assessment and equity audit.
- Monitor age structure of practice to ensure adequate capacity provided.

Training

- Ensure all staff are trained and can access regular updates. Professional staff to be trained to national minimum standards (example: trained to document vaccinations accurately).

Nurseries, schools and colleges

- Attached healthcare staff should check immunisation status on enrolment/transfer and specific educational stages.
- Attached healthcare staff to discuss with parent or young person and facilitate immunisation.
- Schools should continue to be encouraged to become venues for immunising children.

Targeting groups with low uptake

- Improved access for those with difficulties with transport, language or communication and learning or physical disabilities (e.g. longer appointments, walk-in clinics, extended hours, mobile/outreach services).
- Provide information in variety of formats and translation services.
- Provide information in other settings (e.g. pharmacies, libraries, shops, community venues).
- Check vaccine histories of new migrants, asylum seekers, young offenders and children in care on admission/registration.

Sources: National Institute for Health and Care Excellence (NICE). *NICE Public Health Guidance 21: Immunisations: Reducing differences in uptake in under 19s*. London: NICE, 2009. Available at: www.nice.org.uk/guidance/PH21/chapter/1-Recommendations#recommendation-1-immunisation-programmes. Accessed January 2018, last updated: September 2017

National Institute for Health and Care Excellence (NICE). *NICE Quality Standard 145: Vaccine uptake in under 19s*. London: NICE, 2017. Available at: www.nice.org.uk/guidance/qs145/chapter/Quality-statement-2-Offering-outstanding-vaccinations. Accessed January 2018, last updated: March 2017

Clusters of AEFI should be investigated in line with extant national guidance to determine whether they are programme-related (e.g. due to faulty administration technique or failure of vaccine cold chain), vaccine related (e.g. due to a contaminated batch) or co-incidental. Control measures for a programme-related cluster could involve re-education of staff giving vaccines and recall of patients for revaccination. If a defective vaccine is suspected, this should be reported to the national regulatory agency, including details of the vaccine name, manufacturer, batch number, expiry date and nature of defect. The decision to undertake a vaccine recall or quarantine and patient notification should only be made in consultation with the national regulatory agency.

Vaccine failures may be programme-related (e.g. inadequate cold chain or poor vaccine administration), vaccine-related (e.g. failures in vaccine attenuation) or host related (e.g. inadequate host immunity or nutritional status). Suspected vaccine failures should be investigated to ensure laboratory confirmation of infection and reported to the national public health institute, who should be involved in the investigation. Control measures will depend on the cause, and may include education of providers on handling, storage and administration, use of different vaccine products/doses in different age groups, and review of vaccination schedules.

4.8 Co-ordination of sexual health services

According the WHO sexual health is a state of physical, mental and social well-being in relation to sexuality. It requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence. It is an important part of physical and mental health and a key human right. In sexual health there is an *individual* level (e.g. prevention and care) and a *societal* level (e.g. communities free of sexual violence, acceptance of different sexualities).

To maintain and improve sexual health and avoid the risks of unintended pregnancy, disease and violence, the population requires access to accurate information and high-quality sexual health services. STI diagnosis, treatment and prevention is included, but services for contraception and reproductive health, psychosexual problems and sexual assault are equally important aspects of sexual health services. Healthcare-commissioning organisations are responsible for ensuring that there is a full range of screening, treatment, care and prevention services (these responsibilities may be split between organisations in some countries). Services can be delivered by a range of providers including specialist hospital-based infectious disease services, genitourinary medicine (GUM) clinics, GPs, community-based sexual health services, health promotion services, social services departments and voluntary organisations. It is advisable to appoint a sexual health co-ordinator to oversee this work, as is for instance done is most regions of the UK. Investment in services should be based on sound evidence and epidemiological data, which may be available from relevant national organisations. Nationally, countries should formulate a National Strategy for Sexual Health and HIV and an Action Plan to promote its implementation.

As so many stakeholders are involved, it is useful to set-up an Independent Advisory Group for Sexual Health and HIV to monitor and report on the progress towards implementation of the Action Plan. For monitoring progress, important indicators are not only STI incidence rates, and microbiological resistance patterns, but also teenage pregnancy rates, access to state-funded abortions, quality of GUM services, access to testing and treatment including participation in *Chlamydia* screening. In overseeing the efforts to achieve optimal care the HIV care continuum is used ('cascade of care'): the estimated total number of infections (100%), known infections (e.g. 80%), people in care

(e.g. 60%), people on continuous treatment (40%), people with viral suppression (30%). In most European countries emphasis is now on uncovering the hidden, silent, undetected HIV-infections, and *Chlamydia*-infections.

Despite the acceptance of a holistic view of sexual health and integrated care based on patient need, the wider determinants of sexual health such as social exclusion, poverty, stigma and substance abuse demand continuous attention. Action to improve sexual health can be grouped into five priority areas (Table 4.8.1). Further details on specific measures to reduce the burden of HIV (many also relevant to all aspects of sexual health) can be found in Chapter 3.37.

Table 4.8.1 Priorities for sexual health improvement

Priority area	Details
Leadership at local, regional and national levels	Appoint designated local sexual health champions and co-ordinators Carry out comprehensive sexual health needs assessments Promote joined-up provision to allow seamless patient journeys across sexual health services Monitoring of performance, including monitoring of outcomes Multi-agency outbreak control plans
Building strategic partnerships	Joint planning between health services, local government services and voluntary agencies
Commissioning for improved sexual health	Develop commissioning skills Adopt a holistic service commissioning model Strengthen the public voice in commissioning Base commissioning on best evidence and best practice
Investing in prevention	Ensure effective sexual health promotion Ensure prevention is an integral part of sexual health service provision Intensify efforts to tackle stigma Provide evidence-based advice and information to public and promote their ability to make healthy choices. Improve dissemination of evidence about effective interventions in relation to African communities, men who have sex with men and young people Embed sexual and relationships education in school curriculum
Deliver modern sexual health services	Ensure sexual health and HIV services are included in primary care centres/polyclinics Increase quality of and access to services, including confidential, open-access services Supervise quality of home based testing Link workforce planning and training to changing models of care Ensure access to the full range of contraceptive methods Improve access to early medical and surgical abortion Improve STI and HIV incidence data Increase HIV testing in a range of existing and new settings Ensure availability of and access to anti-HIV treatment Facilitate prompt testing and treatment for STIs Ensure adequate and complete partner notification Improve health and social care for people living with HIV

4.9 Prevention of blood-borne viral infections

Human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) are the main blood-borne viruses (BBV) of public health importance. Other important and emerging BBVs are hepatitis D virus (HDV) and hepatitis E virus (HEV). These viruses persist in the blood and body fluids of affected people and can be transmitted to others through various routes, often in an occupational setting (Box 4.9.1). Although immunisation and post-exposure prophylaxis may be available, the key to minimising the public health impact of these infections is prevention of exposure through careful management of contact with blood, body fluids and tissues (Box 4.9.2).

Box 4.9.1 Routes of transmission of BBVs

Common	Less common
1 Sexual intercourse	**1** Open wound contaminated with blood of infected person during sporting activities
2 Sharing injecting equipment and drug paraphernalia/accessories	**2** Skin lesions (e.g. eczema) contaminated with blood of infected person
3 Skin puncture with sharp objects contaminated with blood of infected person (example: through contaminated tattooing equipment)	**3** Splashes of the mucous membranes of eye, nose or mouth with blood of infected person
4 Vertical transmission from mother to infant before or during birth or by breast-feeding	**4** Human bites (which break skin) by infected person
5 Transfusion of infected blood or blood products when screening for BBVs has not been undertaken	

Box 4.9.2 Minimising exposure to BBV

Prevention of exposure and use of personal protective equipment (PPE)	Avoid contact with blood or body fluids. Cover cuts and abrasions with waterproof dressings. Control environmental contamination by blood and body fluids.
	Protect skin, eyes, mouth and nose from blood splashes by using PPE including gloves, plastic aprons, impermeable gowns, rubber boots or overshoes, protective eye wear and masks.
Avoid sharps injury, stay 'sharp safe'	Avoid using needles and sharp instruments if possible. Where available use innovative products that reduce the risk of sharps injuries such as retractable needle syringes.
	Dispose of sharps into a suitable container (ISO Standard 23907 and British Standard 7320) immediately after use and at the point of use. Do not re-sheath. Do not overfill the container.
Dispose of waste safely	Health care staff have a duty to dispose of waste properly. In the UK the safe disposal of waste is regulated by the 2005 Hazardous Waste regulations made under the Environmental Protection Act. Guidance on implementing these regulations is available: *Management and disposal of healthcare waste*. https://www.gov.uk/government/publications/guidance-on-the-safe-management-of-healthcare-waste (accessed August 2018)

(*Continued*)

Box 4.9.2 (*Continued*)

	Health care waste is classified as infectious clinical waste, medicinal waste or offensive/hygiene waste. Waste should be classified and segregated in colour coded and labelled receptacles before collection, transport and disposal. BBV contaminated waste will usually be classified as infectious clinical waste and will require incineration.
Managing blood and body fluids: spillages	Spills of blood and body fluids are a potential source of infection for others and should therefore be made safe as soon as possible. Local procedures should be followed which may specify use of spill kits and disinfectants.
Collection and transport of specimens	Only staff that have been trained should collect and handle specimens. Local procedures should be followed. Guidance on *Transport of Infectious Substances* is available at: www.hse.gov.uk/biosafety/blood-borne-viruses/transportation-of-infectious-substances.htm
Decontamination	HIV, HBV and HCV can all survive outside the human body for several weeks and so blood contaminated surfaces, equipment and clothing that have not been decontaminated may lead to transmission. Decontamination is a combination of processes that removes contamination so that BBVs cannot reach a susceptible individual in sufficient quantities to produce infection. Decontamination may include cleaning, disinfection and sterilisation. Wherever possible single-use disposable devices should be used. Re-usable medical devices should be decontaminated by a sterile services department (SSD). Best practice advice on decontamination of medical equipment is available on the Medicines and Healthcare Products Regulatory Agency (MHRA) website www.mhra.gov.uk and the decontamination section of the NHS website: https://www.gov.uk/government/collections/decontamination-and-infection-control (accessed August 2018). Household bleach is usually supplied at a strength of 100 000 parts per million (ppm) of chlorine. Adding one part bleach to nine parts cold water gives a solution for disinfecting blood and body fluids (10 000 ppm). For general use, such as disinfecting work surfaces, a 1000 ppm solution of bleach is adequate (i.e. 1 in 100 dilution of household bleach). Undiluted Milton is equivalent to a strength of 10 000 ppm. All dilutions become ineffective with time and should be freshly made up every day.
Linen	Blood-stained linen should not be sorted but should be placed in a water soluble primary bag. This in turn should be placed within a secondary bag for storage and transport. The washing programme should include a disinfection cycle. Guidelines are available at: http://www.hse.gov.uk/biosafety/blood-borne-viruses/laundry-treatments.htm

Management of blood exposure incidents

Following a needle-stick or other sharps injury (from an infected patient) the risk of HIV infection is <0.3%, the risk of HCV is <2% and the risk of HBV is around 30% (depending on the presence of hepatitis e antigen). The risk of acquiring HIV infection from a mucous membrane exposure is less than 0.1% while the risk of HCV from a single mucous membrane exposure is negligible.

There should be a written policy detailing the local arrangements for risk assessment, advice, provision of post-exposure prophylaxis, and follow-up. The policy should designate one or more doctors to whom exposed persons may be referred urgently for advice and should ensure that adequate 24-hour cover is available. Primary responsibility usually rests with the occupational health service, with out-of-hours cover provided by accident and emergency departments. These arrangements should be included in the programme of mandatory staff training.

Following an exposure, the wound should be washed liberally with soap and water and free bleeding should be encouraged. Exposed mucous membranes including conjunctivae should be irrigated and contact lenses should be removed. The injury should be reported promptly.

The designated doctor should assess the risk of transmission of HIV, HBV and HCV and the need for post-exposure management. The risk assessment is based on the type of body fluid involved and the route and severity of the exposure.

As a routine, the designated doctor or member of the clinical team (not the exposed worker) should approach the source patient (if known) and obtain informed consent, after pre-test discussion, to test for anti-HIV, HBsAg, anti-HCV and HCV RNA. Testing of the source patients should be completed within 8–24 hours.

If there is an HIV risk, post-exposure prophylaxis (PEP) should be started within one hour. Subsequently PEP may be discontinued if it is established that the source patient is HIV negative. Various PEP regimens have been recommended. In the UK, on the basis of acceptability and shelf life, the following PEP starter packs are used:

One Truvada tablet (245 mg tenofovir disoproxil [as fumarate] and 200 mg emtricitabine [FTC]) once a day

plus

One Raltegravir tablet (400 mg) twice a day

PEP should be started within hours and certainly within 48–72 hours of exposure and continued for at least 28 days. The exposed person should be followed up weekly during the period of PEP, to monitor treatment side effects and ensure compliance.

The HBV immunity status of the exposed person should be assessed and if necessary blood should be taken for urgent anti-HBs testing. An accelerated course of vaccine, a booster dose of vaccine and/or HBIG may be given.

For HCV, no immunisation or prophylaxis is available. A baseline blood sample should be obtained from the exposed person and stored for two years. If the source is HIV infected, the exposed person should be tested for anti-HIV at least 12 weeks after the exposure or after HIV PEP was stopped whichever is the later. Testing for anti-HIV at six weeks and six months is no longer recommended. If the source is HCV infected, the exposed person should be tested for HCV RNA at 6 and 12 weeks and for anti-HCV at 12 and 24 weeks.

In the absence of seroconversion, modification of working practices is not necessary but infection control measures, safe sex practices, and avoiding blood donation should be observed during the follow-up period. Generally management of workers exposed to a potential BBV source whose status is unknown or a source that is unavailable for testing will depend upon a risk assessment and a discussion of the benefits of intervention.

Healthcare providers should follow local policies on reporting occupational exposures. In the UK exposures should be reported to Public Health England. Some types of occupational exposure are required to be reported under the Reporting of Injuries, Diseases and Dangerous Occurrences (RIDDOR) legislation.

Employment policies

In the UK guidelines for healthcare workers with blood-borne viral infections who carry out *exposure prone procedures* (EPP) have been published: *New healthcare workers: clearance for hepatitis B and C, TB, HIV*. London: Department of Health. https://www.gov.uk/government/publications/new-healthcare-workers-clearance-for-hepatitis-b-and-c-tb-hiv (accessed December 2017).

EPPs are those in which there is a risk that injury to the healthcare worker could result in exposure of the patient's open tissues to the blood of the healthcare worker. Such procedures occur mainly in surgery, obstetrics and gynaecology, dentistry and midwifery. Healthcare workers who will perform EPPs should be HIV antibody negative, hepatitis B surface antigen negative (or, if positive, e-antigen negative with a viral load of 10^3 genome equivalents ml^{-1} or less) and hepatitis C antibody negative (or, if positive, negative for hepatitis C RNA).

In the UK, employers are required by the Control of Substances Hazardous to Health Regulations (COSHH) to assess the risk to their staff from exposure to BBVs and implement necessary protective measures. There are no vaccines available against HCV or HIV, but routine pre-exposure HBV immunisation is recommended for healthcare workers, laboratory staff, staff of residential, long-term care facilities and other accommodation for those with learning difficulties, morticians and embalmers and prison service staff. Other occupational groups such as police and fire and rescue services, tattooists and needle exchange service staff may also be at risk and for these groups of staff an assessment of the frequency of likely BBV exposure should be carried out prior to immunisation. Generally those who receive HBV immunisation because they are at occupational risk should have their immunity confirmed by post-immunisation testing for anti-HBs.

Advice for people living with blood-borne viral infections

All persons found to be infected with a blood-borne virus should be considered potentially infectious and should be counselled concerning infectivity. The following advice should be given:

- Keep cuts or grazes covered with a waterproof plaster until the skin has healed.
- Avoid sharing your razor or toothbrush (or anything which might cut the skin or damage the gums and cause bleeding). Use your own towel and face cloth.
- If you cut yourself, wipe up any blood with paper tissues and flush these down the toilet. Wipe any surfaces where blood has been spilt with household bleach diluted in cold water (1 part bleach to 10 parts water). Do not use this on your skin or on any fabrics. In these circumstances wash thoroughly with soap and water.
- Tell any carers that you are a carrier of a blood-borne virus and that blood precautions should be taken. If available they should wear plastic gloves. Otherwise they can use a towel or cloth to prevent them from getting blood on to their skin.
- If your clothing is soiled with blood or other body fluids, wash them using a prewash and hot washing machine cycle.
- Dispose of used tampons straight away by flushing down the toilet. Dispose of sanitary towels in your rubbish after first sealing inside a plastic bag.
- If you go for medical or dental treatment, tell your doctor or dentist you have a blood-borne viral infection.
- Do not donate blood or carry an organ donor card.
- Do not have acupuncture, tattooing, ear piercing, electrolysis or fish pedicure.
- If you are an injecting drug user do not share your injecting equipment or paraphernalia and dispose of used needles and syringes safely by putting them in a rigid container with a lid. If possible use a local needle exchange scheme. Return used injecting equipment to the scheme in the special plastic sharps bin.
- If you have HCV infection you should limit weekly alcohol consumption to less than 14 units per week for both men and women.
- Blood-borne viral infections are not infectious under normal school or work conditions and there is no need to stay away from school or work.
- Sexual intercourse, pregnancy and birth advice is given in Box 4.9.3.

Box 4.9.3 Sexual intercourse, pregnancy and birth: advice to patients

	HCV	HBV	HIV	HEV
Sexual intercourse	If you are in a stable relationship with one partner you may not feel the need to start using condoms; however it is advisable to avoid sexual intercourse during a menstrual period. Otherwise condom use should be encouraged and safe-sex should continue to be promoted for the prevention of HIV and other sexually transmitted infections.	Condom use recommended until sexual partners are immunised against HBV and have had immunity confirmed.	Condom use recommended.	There is a theoretical risk of person-to-person transmission through oral-anal intercourse.
Pregnancy and birth	The risk of transmission from mother to child appears to be very low. At the present time there is no need to advice against pregnancy based on HCV status alone. Mothers who are viraemic should not breast feed.	All babies of HBsAg positive mothers should receive hepatitis B vaccine. Babies whose mothers are e-antigen positive, HBsAg positive without e-markers (or where e-marker status has not been determined) or had acute hepatitis during pregnancy also require hepatitis B immunoglobulin G (HBIG).	The risk of transmission from mother to child can be reduced by anti-viral treatment during pregnancy, caesarean section (not usually done if adequate antiviral treatment taken), and avoiding breast feeding.	Transmission from mother to child can occur, particularly in the third trimester of pregnancy. Transplacental transmission is associated with prematurity, low birthweight, hepatic dysfunction, and an increased risk of perinatal mortality. HEV infection in neonates is self-limiting.

4.10 Co-ordination of services for tuberculosis control

TB remains an important public health issue in Europe with an estimated 323 000 cases occurring in the WHO European Region in 2015, of which 32 000 are estimated to have died. There is significant variation by country, with 18 high-priority countries having been identified, including 5 in the EU: Romania, Lithuania, Latvia, Bulgaria, and Estonia.

The WHO European Region TB Action Plan 2016–2020 identifies the following key areas of intervention:

Integrated patient-centred care and prevention

- Systematic screening of contacts and high-risk groups.
- Early diagnosis of all forms of tuberculosis and universal access to drug-susceptibility testing, including the use of rapid tests.
- Equitable access to quality treatment and continuum of care for all people with tuberculosis, including drug-resistant tuberculosis, and patient support to facilitate treatment adherence.
- Collaborative tuberculosis/HIV activities and management of comorbidities.
- Management of latent tuberculosis infection and preventive treatment of persons at high risk, and vaccination against tuberculosis.

Bold policies and supportive systems

- Political commitment with adequate resources, including universal health coverage policy.
- Health systems strengthening in all functions, including well-aligned financing mechanisms for tuberculosis and human resources.
- Regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines, and pharmacovigilance.
- Air-borne infection control, including regulated administrative, engineering and personal protection measures in all relevant healthcare facilities and congregate settings.
- Community systems and civil society engagement.
- Social protection, poverty alleviation and actions on other determinants of tuberculosis, such as migration and prisons.

Intensified research and innovation

- Discovery, development and rapid uptake of new tools, interventions and strategies.
- Research to optimise implementation and impact, and promote innovations.

The *Collaborative Tuberculosis Strategy for England 2015 to 2020* is an example of a national level plan to improve the prevention and control of TB. This promotes multiagency planning and working to achieve the following 10 aims:

- Improve access to services and ensure early diagnosis.
- Provide universal access to high quality diagnostics.
- Improve treatment and care services.
- Ensure comprehensive contact tracing.
- Improve BCG vaccination uptake.
- Reduce drug-resistant TB.
- Tackle TB in under-served populations.
- Systematically implement new entrant latent TB screening.
- Strengthen surveillance and monitoring.
- Ensure an appropriate workforce to deliver TB control.

A key aspect of the strategy is the creation of formal local TB Control Boards to strengthen the co-ordination and oversight of all aspects of TB control, including developing multiagency strategies and plans, and reviewing and improving the effectiveness of services. Nine regional level Boards have been set up and include representative from health service commissioners (CCGs) and providers (acute, community and primary care), local authority departments (e.g. public health, social services, housing), specialist health protection organisation (PHE) and voluntary organisations.

The regional TB Control boards are supported by local TB clinical networks. With an accountable lead for both clinical and public health aspects of TB control and a mixture of

units to support simple and more complex TB cases, including those with the facility and expertise to manage MDR-TB. Local TB clinical networks should also ensure appropriate staffing and facilities to address case mix and complexity with:

- all TB cases assigned to a TB specialist and named TB case manager.
- use of enhanced case management (ECM) as appropriate.
- adequate provision of staff (nurses/administrators/lay outreach workers), outreach and venues for directly observed therapy (DOT).
- more local, and flexible, access points for routine treatment by using community DOT workers, pharmacists and other providers of treatment, home-based contact tracing and DOT.
- paediatic cases managed by a paediatric TB specialist (or access to such specialist advice available).
- TB/HIV co-infected cases managed by physician with joint HIV/TB expertise.
- adequate provision of negative pressure facilities.
- fast-track referrals and support to necessary social care.
- service users involved in service design.

A key function of TB Control Boards is monitoring and improvement of local TB services and outcomes. Potential indicators for this task are given in Box 4.10.1. Good quality

Box 4.10.1 Potential TB indicators for use at national, regional or local level

Some indicators will not be suitable for local calculation, because of small numbers. Others cannot be assessed from national data and require local compilation.

Incidence

- TB incidence per 100 000 population.
- TB incidence per 100 000 population by country of birth.
- TB incidence per 100 000 population in UK-born children aged less than 15 years.

Diagnosis

- Number and proportion of pulmonary TB cases starting treatment within two months of symptom onset.
- Number and proportion of pulmonary TB cases starting treatment within four months of symptom onset.
- Number and proportion of pulmonary TB cases that were culture confirmed.
- Number and proportion of culture-confirmed TB cases with drug susceptibility testing reported for the four first line agents.

Treatment

- Number and proportion of drug sensitive TB cases who had completed a full course of treatment by 12 months.
- Number and proportion of drug sensitive TB cases that were lost to follow-up at last reported outcome.
- Number and proportion of drug sensitive TB cases that had died at last reported outcome.
- Number and proportion of drug resistant TB cases who had completed treatment at 24 months.
- Number and proportion of drug resistant TB cases who were lost to follow-up at last reported outcome.
- Number and proportion of drug resistant TB cases who had died at last reported outcome.
- Number and proportion of TB cases offered a HIV test.
- Number and proportion of drug sensitive TB cases with at least one social risk factor who completed treatment within 12 months.
- Number and proportion of culture confirmed TB cases with any first line drug resistance.
- Annual number and proportion of culture confirmed TB cases with MDR-TB.

(*Continued*)

Box 4.10.1 (*Continued*)

Possible additional local indicators

- Proportion of TB patients with social risk factors recorded who received enhanced case management.
- Proportion of pulmonary TB cases who had close contacts identified.
- Proportion of identified close contacts of pulmonary TB cases that were evaluated.
- The number of local authorities that have a systematic new entrant LTBI (latent infection) screening initiative in place.
- Proportion of eligible new entrants covered by screening programmes who accept LTBI screening.
- Proportion of individuals who complete LTBI treatment amongst those who start treatment.
- Proportion of babies in areas with a universal BCG programme who received BCG vaccine.

data from enhanced TB surveillance is necessary for this, but it can also be complemented by regular local 'cohort reviews', which are the multidisciplinary, systematic, quarterly appraisal of the case management and contact investigation of every case of TB.

Further detail of specific prevention and control activities can be found in Chapter 3.78.

4.11 Travel health

Globally there are over 1200 million international tourist arrivals each year with an increasing trend, at least 60 million to developing countries; half of those travelling to the less-developed world for one month will have a health problem associated with the trip. These are mostly minor and less than 1% require hospitalisation.

Individuals carry their epidemiological risk with them; hence cardiovascular disease is the most common causes of death in travellers from Europe. Injury and accidents (particularly motor vehicle) are the next most common cause of serious morbidity and mortality. Infection contributes substantially to this morbidity in travellers, particularly diarrhoeal disease, but only to about 3% of deaths.

Infectious disease complications of travel depend on pre-existing disease, destination and risk behaviour. Ever more exotic locations and activities increases contact with, and susceptibility to, organisms one would not routinely meet.

Prevention of ill health in travellers

Travel health providers can, through providing up-to-date advice on risk and risk reduction, prevent ill health by simple precautions and interventions. Travel clinics must have access to up-to-date information and recommendations as the epidemiology of travel-related infection risk changes rapidly and continuously. Giving appropriate advice to those with complex itineraries and/or pre-existing conditions may be a difficult task. Opportunities should be taken to ensure that those who travel at short notice have their vaccination status reviewed regularly.

Advice should cover the following:

- Basic food, water and personal hygiene.
- Avoiding insect vectors (advice about bed nets, avoiding tick bites).
- Safe sex and avoidance of potential blood-borne virus exposure.
- Malaria prophylaxis.
- Vaccination against specific diseases as appropriate.
- Avoiding dog bites and other potential rabies exposures (other types of exposure e.g. scratches, being licked and other animal bites).

Travellers' diarrhoea

Diarrhoea, usually short-lived and self-limiting, is a major cause of illness in travellers; 20% of cases are confined to bed. The main risk factor is the destination; incidence rates vary from less than 10% per two-week stay in industrialised countries to over 50% in parts of Africa, Central and South America and South-East Asia. Infants and young adults are at particularly high risk.

The likelihood of diarrhoea is related to dietary indiscretions. The risk of travellers' diarrhoea and other faeco-orally transmitted disease (e.g. hepatitis A and typhoid) in those who travel to developing countries can be reduced by the following measures:

- Washing hands after toilet and before preparing or eating food.
- Using only sterilised or bottled water for drinking, cleaning teeth, making ice and washing food (e.g. salads).
- Avoiding uncooked food (unless you can peel it or shell it yourself), untreated milk or milk products (e.g. ice cream), uncooked shellfish, food that may have been exposed to flies and any other potentially contaminated food.
- It is usually safe to eat freshly cooked food that is thoroughly cooked and still hot; hot tea and coffee; commercially produced alcoholic and soft drinks.
- Antibiotic chemoprophylaxis is not recommended for most travellers.

Mosquito-borne infections

Over 6000 cases of malaria are imported in the EU annually, with a low case fatality rate (<1%) (see Chapter 3.45). The risk varies by season and place; it is highest (1:50–1:1000) in sub-Saharan Africa and Oceania (excepting Australasia).

Compliance with antimalarial chemoprophylaxis regimens and use of personal protection measures are key to the prevention of malaria. However, fewer than 50% of travellers at risk adhere to basic recommendations for malaria prevention.

In 2014, around 1800 Dengue cases were reported in Europe (see Chapter 3.19). It is endemic throughout the tropics and subtropics and a dramatic increase in the incidence has been seen worldwide. In 2013 the island of Madeira experienced an outbreak of Dengue. A Dengue vaccine is now available but not yet recommended in travellers; however there is advice for travellers on avoidance of mosquito bites.

Other mosquito-borne infections, such as Zika (Chapter 3.88), Chikungunya (Chapter 3.8) and Yellow fever (Chapter 3.86), are also a risk to travellers to some destinations.

Measures to reduce the risk of mosquito bites include the following:

- Sleep in screened rooms, use knockdown insecticide in the evening and use an electrical pyrethroid vaporiser overnight.
- If the room cannot be made safe, use impregnated bed nets.
- Wear long-sleeve shirts and long trousers in the evening. Use insect repellent.

Advice on chemoprophylaxis has been made more difficult by the increase in chloroquine and multidrug-resistant falciparum malaria, and primaquine and chloroquine-resistant strains of *Plasmodium vivax*. The recommended regimen will depend upon the proposed itinerary: most situations will be covered by the latest published guidance (https://www.gov.uk/government/publications/malaria-prevention-guidelines-for-travellers-from-the-uk).

Travellers to endemic countries should be aware of the symptoms of malaria and the need to seek urgent medical attention. Those who will be out of reach of medical services can be given stand-by therapy.

Immunisation and travel

Many countries and the WHO produce recommendations for vaccination of travellers (see Appendix); these should be consulted.

Diphtheria, tetanus and polio

Foreign travel is an ideal opportunity to have these immunisations updated. Diphtheria is

a problem worldwide, with large outbreaks in the early 1990s in the Russian Federation and more recently in Haiti. There are low levels of tetanus antitoxin and immunity to polio serogroups in many adults. Polio outbreaks have occurred in Tajikistan and Angola and polio is still endemic in parts of India, Nigeria, Afghanistan and Pakistan.

Hepatitis A

Hepatitis A is a common vaccine-preventable infection in travellers. It is endemic in many parts of the world, including Southern Europe. The risk is especially high for those who leave the usual tourist routes. Immunisation is recommended for travellers to countries in Africa, Asia, Central and South America and the Caribbean, where hygiene and sanitation may be poor, and for some countries in Eastern Europe, although it may be less important for short stays in good accommodation.

Hepatitis B

Immunisation against hepatitis B virus should be given to all those who may come into contact with body fluids (e.g. those planning to work as healthcare workers). The incidence also appears raised in other long-stay overseas workers, perhaps as a result of medical and dental procedures received abroad or sexual transmission. Immunisation is not necessary for short-term business or tourist travellers, unless their sexual behaviour or other at-risk behaviours (e.g. getting a tattoo) puts them at risk.

Typhoid

The risk of typhoid is especially high for those leaving the usual tourist routes, or visiting relatives or friends in developing countries. According to WHO in 2014 a total of 21 million cases with 222 000 typhoid related death occurred worldwide annually. Typhoid vaccine is available. Vaccination against paratyphoid is not recommended.

Cholera

The risk of cholera is extremely low; cholera vaccine is not indicated for travellers. No country requires proof of cholera vaccination as a condition for entry.

Yellow fever

A yellow fever vaccination certificate is required for entry into most countries of sub-Saharan Africa and South America in which the infection exists. Many countries require a certificate from travellers arriving from or who have been in transit through infected areas. Some countries require a certificate from all entering travellers.

As the areas of yellow fever virus circulation exceed the officially reported zones, vaccination is strongly recommended for travel to all countries in the endemic zone (particularly if visiting rural areas), even if these countries have not officially reported the disease and do not require a vaccination certificate.

The vaccination has almost 100% efficacy (see Chapter 3.86). In recent years, fatal cases of yellow fever have occurred in unvaccinated tourists visiting rural areas within the yellow fever endemic zone.

Rabies

Rabies vaccination should be considered in those who are likely to come into contact with animals where the disease is present (e.g. veterinarians), and those undertaking long journeys in remote areas.

Japanese B encephalitis

Immunisation should be considered in those staying for a month or longer in rural areas of endemic countries and those whose itineraries take them to rural areas of wetland (marsh, rice fields) in the transmission season.

Meningococcal disease

Immunisation should be considered in those going to areas of the world where the incidence

is high (e.g. the 'meningitis belt' of sub-Saharan Africa, and areas in the north of the Indian subcontinent). Pilgrims travelling to Saudi Arabia for the Hajj must have proof of vaccination.

Tick-borne encephalitis

Vaccination is recommended for those who are to walk, camp or work in late spring and summer in warm, heavily forested parts of Central and Eastern Europe and Scandinavia. They should also cover arms, legs and ankles and use insect repellent.

Pregnancy, infection and travel

Pregnant travellers should be helped to balance the benefits and risks of travel during pregnancy. Dehydration resulting from diarrhoea can reduce placental blood flow, therefore pregnant travellers must be careful about their food and drink intake; infections such as toxoplasmosis and listeriosis have potentially serious sequelae in pregnancy. Women should be encouraged to breastfeed if travelling with a neonate. A nursing mother with travellers' diarrhoea should not stop breast-feeding but should increase her fluid intake.

Malaria during pregnancy carries a significant risk of morbidity and death. Pregnant women should be advised of this increased risk if intending travelling to endemic areas. If travel is essential, then chemoprophylaxis and avoidance of bites are essential (take specialist advice).

Zika is especially of relevance for pregnant women. According to WHO it is recommended that to prevent the onward transmission of Zika and adverse pregnancy and fetal outcomes, all returning travellers should practice safer sex, including through the correct and consistent use of condoms, or consider abstaining from sex for at least six months.

The Immunocompromised Traveller

The immunocompromised traveller may be at risk of serious infection. Those with AIDS, $CD4^+$ counts of less than $200\,mm^{-3}$ and those who are symptomatic should seek specialist advice, particularly before going to the developing world. Those with a $CD4^+$ cell count above 500 probably have a risk similar to a person without HIV infection.

The HIV-infected traveller needs to be particularly careful about the foods and beverage consumed. Travellers' diarrhoea occurs more frequently, is more severe, protracted and more difficult to treat when in association with HIV infection. Infections are also more likely to be accompanied by bacteraemia. Organisms particularly associated with severe chronic diarrhoea in HIV positive travellers include *Cryptosporidium* and *Isospora belli*.

All of the HIV-infected traveller's routine immunisations should be up-to-date. In general, live attenuated vaccines are contraindicated for persons with immune dysfunction. Live oral polio vaccine should not be given to HIV-infected patients or members of their households. Inactivated polio vaccine (IPV) should be used. Live yellow fever vaccine should not normally be given to HIV infected travellers; however, if travel in an endemic area is absolutely necessary, vaccination may be considered after a risk assessment and consideration of the CD4 count. Bacille Calmette–Guérin (BCG) should not be given because of disseminated infection in HIV infected persons.

4.12 Migrant and refugee health

Migrant populations and the refugee crisis in europe

A substantial proportion of people living in Europe have their roots in other countries. On 1 January 2015, there were 34.3 million people living in an EU Member State born outside the Union (representing 6.7% of the EU population), and 18.5 million people who had been born in a different EU Member State from the one where they were resident.

At the same time, Europe is facing an unprecedented influx of refugees. In 2015, more than one million refugees, displaced persons and other migrants, many of whom were children, entered the EU and the flow of refugees continues. Many of these people arrive in the EU after perilous journeys over land or sea, and are in immediate need of emergency shelter, clean water and health care.

Available information indicates that migrants as a group are often comparatively healthy, a phenomenon sometimes referred to as the 'healthy migrant effect'. At the same time migrants are not a homogeneous group and, especially newly arrived displaced people, are more vulnerable to specific infectious diseases. Factors associated with a higher vulnerability to infectious diseases among these persons include the endemic situation of infectious diseases in their country of origin, specific conditions during the journey before entering the EU, access to health care in the country of origin, during the travel and upon arrival to the EU, high-risk behaviours, and crowded living conditions in reception centres. The biggest risk of transmission of infectious diseases after arrival is within the migrant population itself, and the risks to the general European population is very low.

After entering Europe, the migrants, and especially children, are at risk of contracting the same infectious diseases as the general population in the country. In addition some specific health risks remain for groups of migrants for many years after arrival to the EU, related to belonging to a group with higher prevalence of certain chronic infectious diseases. Furthermore, many other risk factors are associated with vulnerability among migrant populations residing in Europe, including poverty, crowded living conditions, unemployment, isolation and discrimination. Language barriers, religious beliefs, gender roles and, especially for irregular migrants, lack of entitlement to healthcare, may also influence access and utilisation of health services. Many migrants also regularly return to their countries of origin to visit relatives and friends.

It is, therefore, important that migrants benefit from the same access to health care, including access to vaccinations, as the native population. Health care staff working with newly arrived migrants should also be aware of specific risks of infectious diseases linked to their country of origin and countries visited during the journey to Europe. This is to ensure that infections are readily diagnosed and treated and relevant immunisations offered. In addition to diseases normally encountered in the general population, other more unusual differential diagnoses should be considered when migrant patients are presenting with fever (typhoid fever, malaria, louse-borne diseases, visceral leishmaniasis, amoebic abscess, arboviruses), respiratory symptoms (tuberculosis), gastrointestinal symptoms (cholera, typhoid fever, shigellosis, amoebic colitis and helminthiasis such as ascaris, whipworm and hookworm).

Diseases in overcrowded settings

During times of a sudden, large influx of displaced persons, many new arrivals are placed in overcrowded reception and detention centres. In these settings, poor hygiene, sharing of dormitories, insufficient early case detection and lack of health care may contribute to outbreaks of meningococcal meningitis, gastrointestinal infections, measles, varicella and influenza. Spreading of lice, fleas and mites may also cause scabies and infections such as relapsing fever due to *Borrelia recurrentis*, trench fever due to *Bartonella quintana*, epidemic typhus due to *Rickettsia prowazekii* and murine typhus.

ECDC has published a Preparedness Checklist tool to strengthen preparedness against communicable disease outbreaks at migrant reception/detention centres and a Handbook on implementing syndromic surveillance in migrant reception/detention centres and other refugee settings, available at: www.ecdc.europa.eu

Chronic infectious diseases

For many of the chronic infectious diseases such as HIV/AIDS, hepatitis B and C and tuberculosis, the prevalence among refugees reflects the situation in their country of origin although voluntary migrants are often healthier than the general population in these countries. In their new countries migrants often constitute epidemiological subpopulations where transmission is mainly seen within the migrant group itself. In countries that are generally low endemic for these diseases but with high influx of migrants, for example in north-western Europe, the contribution of the migrants to the national prevalence is substantial, calling for extra efforts for prevention and control, including testing, counselling and providing access to treatment, with specific attention to women's health. As late diagnosis is more common among migrants and with the cultural and language barriers, innovative ways of outreach and community engagement is necessary.

Review of immunisation status

The immunisation status of newly arrived migrants should be assessed as early as possible upon arrival and supplementary vaccines offered according to the national immunisation programme of the hosting country. People with no or uncertain documentation of previous immunisations should be considered as unvaccinated.

Priority vaccines protecting against easily transmitted and/or serious infections, such as measles, rubella, diphtheria, tetanus, pertussis, polio, Hib and hepatitis B, should be given within the first two weeks after arrival (Table 4.12.1), while other immunisations could be scheduled at the place of long-term residence. In crowded settings, these priority vaccines could be complemented with vaccines for protection against invasive meningococcal disease, varicella, invasive pneumococcal disease and influenza.

Social stigma

As George Rosen wrote in his History of Public Health (1958): 'Throughout known history, man living in communities have had to take account in one way or the other of health problems that derive from the biological needs and attributes of their fellows'. This has led to series of social and cultural habits (a set of basic hygienic precautions) integrated in daily life that originated from the desire *not* to get an infectious disease from others and to prevent transmission *to* others. For instance, out of this intention not to harm others most people with even a minor disease (common cold) will not visit a new born family member. This measure of contact restriction is a form of intentional social stigma that is valuable and beneficial for the group as a whole and always attached to an infectious disease. However, the fear of transmission can lead to overreaction, overprotection and totally unrealistic measures. This was known since Biblical times for patients with leprosy, a disfiguring disease with limited or no infectiousness, but the fear of transmission victimised patients to total societal exclusion. Even today, unjustified exclusion is imposed on patients, HIV-positive individuals, but also carriers of MRSA experience stigmatisation in health care and among their friends.

Social stigmas can originate from many different qualities other than infectious diseases; most common are culture, gender, race and mental illness. Migrants are inherently 'other' than the original population and are therefore easily subject to social stigma. In those situations the fear of transmission of infectious diseases can augment the stigma. It is important that public health authorities inform the public about the real risks of infectious disease transmission in general, and those that might be transmitted by migrants specifically.

Table 4.12.1 Vaccinations to be offered in the absence of documented evidence of prior vaccination

Disease/age group	Children and adolescents (<18 years)	Adults (>18 years)
Priority vaccinations		
Measles, mumps, rubella	Administer to individuals ≥9 months of age. Two doses of MMR[a] should be administered at least 1 month apart but preferably longer according to national guidelines. Measles vaccine provided before 12 months of age does not induce protection in all and should be repeated after 12 months of age.	Administer one or two doses of MMR to all individuals, according to national guidelines[a]
Diphtheria, tetanus, pertussis, polio, Hib	Administer to individuals ≥2 months, three doses of DTaP-IPV-Hib (Hib-component only for children <6 years unless other country-specific recommendations) containing vaccines at least 1 month apart, followed by a booster dose according to national guidelines. Pentavalent- and hexavalent combination vaccines are authorised up to 6 years of age.	Administer to all adults, three doses of TdaP-IPV-[b] containing vaccines according to national guidelines.
To be considered		
Hepatitis B	Administer to individuals ≥2 months, three doses according to national guidelines[c] Administer to new-born infants of HBsAg-positive mothers within 24 hours of birth, according to national guidelines.	Administer to all adults, with or without previous screening, according to national guidelines.
Meningococcal disease	National guidelines for meningococcal vaccines against serogroups A, B, C, W135 and Y should be followed, unless the epidemiological situation suggests otherwise.	
Pneumococcal disease	Administer to individuals ≥2 months with 1–3 doses of conjugate vaccine at least 1 month apart, according to national guidelines.	Administer to individuals ≥65 years, according to national guidelines.
Varicella	National guidelines should be followed unless the epidemiological situation suggests otherwise. If used, administer to individuals ≥11 months of age, two doses of varicella at least 1 month apart, but preferably longer.	National guidelines should be followed unless the epidemiological situation suggests otherwise. Consider vaccinating non-immune non-pregnant women of childbearing age.
Influenza	National guidelines should be followed unless the epidemiological situation suggests otherwise. Consider vaccinating risk groups over 6 months of age ahead of and during influenza season.	National guidelines should be followed unless the epidemiological situation suggests otherwise. Consider vaccinating risk groups, including pregnant women, ahead of and during influenza season.
Tuberculosis	Administer BCG according to national guidelines. Re-vaccination with BCG is not recommended.	BCG is generally not recommended for adults, unless specific reasons suggest otherwise.

(source: ECDC, 2015).

[a] MMR vaccine is contra-indicated in immunocompromised individuals and during pregnancy. Pregnancy should be avoided for one month after MMR vaccination.

[b] If there is a vaccine shortage, administer at least one dose of vaccine containing acellular pertussis-component.

[c] Testing for hepatitis B virus infection (HBsAg) could be done before the vaccine is administered.

4.13 Emergency preparedness planning and response

Events during the past 15 years, starting with the wide-spread outbreaks of H5N1 highly pathogenic avian influenza, followed by severe acute respiratory syndrome (SARS) in 2003, the 2009 H1N1 influenza pandemic and later the West Africa Ebola and the Middle-East respiratory syndrome (MERS) corona virus outbreaks have put the issue of emergency preparedness planning in the forefront of global health security. Large international outbreaks often come with substantial costs that go well beyond the healthcare sector. It has been estimated that the total world economy costs related to the 2003 SARS outbreak amounted to a staggering US$40 billion and the West Africa regional economic losses for 2014–2017 are estimated at an average of US$3.6 billion per year. Ebola has also led to an increased risk of poverty, heightened food security challenges, the disruption of national childhood vaccination campaigns, and negative impacts on the overall social fabric in the affected countries. Conversely, the United Nations Development Programme's (UNDP) 'Act Now, Save Later' campaign calculates that each dollar spent in preparedness saves seven dollars in emergency response. Preparedness is thus not only a humanitarian and health priority, but also a financially sound investment.

Preparedness has been defined by the United Nations Office for Disaster Risk Reduction (UNISDR) as 'the *knowledge* and *capacities* developed by governments, professional response and recovery organisations, communities and individuals to effectively *anticipate*, *respond to*, and *recover from*, the impacts of likely, imminent or current hazard events or conditions'. In this definition the 'capacities' concerns volumes, having enough staff, hospital beds, ambulances, vaccine doses, and so on while the 'knowledge' relates both to staff involved in preparedness having the right skills (competencies) and the necessary routines and processes to apply them in an appropriate setting (capabilities). The definition also indicates that preparedness is not a one-off effort but an iterative cycle of quality improvements, optimising the anticipation of, response to, and recovery from various health threats. While preparedness was long focused on influenza pandemics, the recent trend is moving towards generic preparedness with an all-hazard approach. This has been emphasised in the present EU legislation in the field, Decision 1082/2013/EU on serious cross-border threats to health, as well as in the International Health Regulations (IHR).

Anticipation phase

The anticipation (planning) phase is about identifying, understanding and prioritising the risks. In a planning perspective, this includes assessing possible risks (diseases) and their determinants and drivers, which could include climate change, migration, deforestation, intensified trade and agriculture, an ageing population and socio-economic factors. Such assessments could be informed by innovative methods such as epidemic modelling, forecasting and using Geographic Information Systems (GIS) to combine and analyse different datasets (epidemiological, environmental, physical, infrastructure, populations). One such example is the mapping of competent vectors for important diseases (e.g. West Nile fever, malaria and tuberculosis) as a consequence of climate change. During the anticipation phase, the (global) epidemiological situation is constantly monitored through epidemic intelligence to rapidly identify new risks at the horizon. The European Centre for Disease Prevention and Control (ECDC) is performing 24/7 epidemic intelligence activities, and report on the active threats in a weekly bulletin for epidemiologists and public health professionals, the ECDC Communicable Disease Threats Report (CDTR). These reports are publically available on the ECDC website. More confidential information is shared between the responsible national health authorities within

the closed Early Warning and Response System (EWRS). Threats that may pose a risk to Europe are further analysed by ECDC and national experts and published as Rapid Risks Assessments on the ECDC website.

Preparedness planners need to take into account a multitude of risks, some with a low probability but high potential consequences and others occurring more frequently but with less societal impact. Prioritisation of risks is therefore essential in the anticipation phase. ECDC has developed a methodology of 'risk ranking' based on a multi-criteria decision analysis to solicit multidisciplinary opinion. Using this or similar methodologies should make decision making better informed and bring relevant actors across disciplines together; this is also valuable in the subsequent planning phase following the risk prioritisation, where a multidisciplinary and multi-sectoral approach looking at various vulnerabilities and societal factors is useful, given the often complex setting of an epidemic. The planning should always start with a deeper understanding of the threat, which would necessitate further more-detailed assessments. Elaborating different scenarios is a useful exercise, giving a richer background for the design of various preparedness options. In all preparedness planning there are some parts that are generic for any event, 'all-hazard approach', some parts that may be specific for any communicable disease, and some parts more specifically related to the type of disease or mode of transmission, forexample mosquito-borne diseases, water-borne diseases or respiratory diseases. In a hospital setting it is necessary to consider the consequences of some severe diseases being air-borne.

Preparedness planning also needs to take into account the specific national or local circumstances. In a large health crisis, a multitude of sectors will be involved, including transportation, energy, water treatment, environment, and civil protection, and the lead national crisis manager would often reside outside the health sector. While planning templates are useful as a starting point, they would in the detailed design phase always need to be adapted to fit the specific context. A broad ownership, including political, is essential. When looking at long-term planning, knowledge of the demographic profile of the workforce is important, taking into account that it may take many years to build the necessary competencies across those assigned to respond to a crisis. An essential part of building strong preparedness plans are testing them and subsequently adjusting them based on the outcome. Ahead of a crisis, this can only be done through simulation exercises. Well prepared and implemented, such exercises will expose the gaps in the plans (capacities, competencies and capabilities). Such exercises need to involve all actors across sectors to be involved in a real crisis, and provide a good learning opportunity for those involved, and a deeper understanding of the competencies and roles of other sectors.

Response phase

Once the crisis is imminent, the preparedness plans and strategies are implemented in the response phase. This is the time when resources are mobilised and the plan tested in real life. As in war, no plan will survive longer than the first battle. However well-rehearsed and exercised, each crisis has its own dynamics that could not be foreseen, but at best mitigated during the planning process. There is, therefore, a need to have processes in place to adapt and update the plan and its assumptions during a prolonged crisis. Many public health events also call for a parallel planning and response phase. The recent West-African Ebola outbreak is a good example of response on site while initiating or further developing a disease-specific preparedness planning in all other countries. It has been increasingly recognised that no major health crises could be handled as a strict national matter. Response actions taken in one country (e.g. border controls, contact-tracing and trade restrictions) may affect other countries. The way the risks are communicated in one country may also become viral and affect the discourse in a neighbouring country.

Some inconsistences in risk communication are inevitable as both the response strategies and capacities (e.g. access to vaccines and antivirals) may differ between countries. However, well-coordinated emergency risk communication across borders and sectors is a potent tool in the risk-management arsenal. Decision 1082/2013/EU provides an integrated European framework for throughout the different preparedness phases and aims to ensure a consistent European response across multiple types of hazards (biological, chemical, environmental). Already at the very start of the response, a future full evaluation of the crisis should be anticipated, and any organisation involved in the crisis should have a monitoring mechanism in place, and someone with the responsibility to neutrally observe all the events, without being personally involved in the response activities.

Recovery phase

In the recovery phase, the attention and resources are diverted back to routine activities. This is the time to analyse and reflect on the effectiveness of the response in order to learn for the future. This could be formalised in a 'critical incident review', which is a systematic review of all aspects of the response leading to concrete recommendations for the future. A good monitoring system during the crisis with appointed observers now shows its added value. Such an incident review should not only focus on specific aspects as the crisis organisation or the various intervention, but be seen as an opportunity to review the performance of the whole health system and beyond. Focus of the evaluation should also go beyond structures and process to evaluate to what extent the preparedness activities had actually contributed to an effective response. Following the evaluation review, all lessons learned should be evaluated and if pertinent included in an updated preparedness plan. Some of the experiences could also be implemented in the daily practice between the crises. The more the experiences are implemented in the routine public health activities, the likelier it will be that they will function well during the next crisis.

4.14 Non-infectious environmental hazards

Environmental health comprises aspects of human health and quality of life that are determined by physical, biological and social factors in the environment. Some physical and chemical factors in particular have the potential to affect health adversely and are described as environmental hazards (Table 4.14.1). However, there are other equally important environmental determinants of health, including transport policy, energy policy, housing and planning policy, social inclusion and sustainable development, and industrial accidents and occupational health and safety. Other determinants are natural disasters such as flooding, adverse weather and climate change. Environmental health practice is concerned with assessing, controlling and preventing environment factors that can adversely affect health now or in the future. Of relevance to the work of the local health protection team are: surveillance of diseases and their environmental determinants to identify unusual or novel patterns; detection and investigation of spatio-temporal clusters of disease (acute) or a longer-term increase in the incidence of a disease (chronic) that may be associated with a point or continuing source exposure to an environmental hazard; and the response to an acute incident or other accident.

Investigating the health effects of environmental hazards

Communities living near potential sources of environmental hazards such as industrial sites and contaminated land are often concerned about possible effects on health. They may link locally observed increases in

Table 4.14.1 Environmental hazards and sources

Hazard	Notes
Factories and industrial processes	These may cause nuisance as a result of soiling of the environment, noise, odour or road traffic. Potential health effects may arise from chemical releases, fumes and particulates. In the UK, Environmental Permits regulate the environmental impact of industrial activities including emissions. Such regulation requires that there is local and open consultation. Public health professionals should be involved in this consultation process as they are can offer the Regulator independent advice on both the impact of emissions on the environment and the health of the local population. In the UK, local government authorities and Public Health England (PHE) are consulted on the potential health effects of industrial activities. A similar process of consultation on infrastructure developments that may have an effect on health is required by the Planning Act 2008.
Hazardous industrial sites	Factories and other industrial establishments in the European Union where dangerous substances are used or stored in large quantities are potentially at risk of a major accident that could threaten public health. The regulation of these sites falls under the Seveso-III (Directive 2012/18/EU) which aims to mitigate the risk of major accidents. In the UK, this Directive is implemented through the Control of Major Accident Hazards Regulations 2015 (COMAH) and through planning legislation.
Chemicals (see also Chapter 4.15 for acute chemical incidents)	Chemicals either exist naturally in the environment or will have been manufactured. There are over 133 million known chemicals with several thousand entering the market each year. Chemicals may have beneficial, harmful or no effect on health. Most chemicals have had little or no toxicological assessment. Large scale industrial releases with serious effects are rare but smaller scale events do occur including leaks and fires. It is helpful to identify local sites that may represent sources of major chemical hazard. This will allow action to be taken in the event of an accidental release. The Control of Substances Hazardous to Health Regulations 2002 (COSHH) are made under the Health and Safety at Work, etc. Act 1974. They require employers to assess the risks from hazardous substances and take necessary precautions to control exposure in order to prevent ill health. Increasingly people are adopting a precautionary approach and limiting unnecessary exposure to chemicals that may be found in commercial products sold for home or workplace use.
Outdoor air quality	Air pollution is considered to be the world's largest single environmental health risk. Every year 3.7 million deaths occur from exposure to outdoor air pollution. Across Europe, emissions of air pollutants have decreased over the decades but air pollutant concentrations are still too high and are known or suspected to cause harmful health effects. These pollutants are mostly the products of combustion of fossil fuels for electricity generation, transportation and space heating, agriculture or waste treatment and their concentrations vary from region to region and from day to day. Both short-term and long-term increases in the concentrations of air pollutants can have measureable health effects. Short-term increases in certain pollutants can increase hospital admissions and mortality from cardiovascular and respiratory diseases. Long-term exposure is associated with increases in cardiovascular disease and some cancers. For some pollutants, there is no threshold of effect and any concentration should be assumed to be associated with some effect on health.

Table 4.14.1 (*Continued*)

Hazard	Notes
	In the EU, the National Emission Ceilings (NEC) Directive (2016/2284/EU) restricts emissions for five key air pollutants: nitrogen oxides (NOx), non-methane volatile organic compounds (NMVOCs), sulphur dioxide (SO_2), ammonia (NH_3) and fine particulate matter ($PM_{2.5}$). The UK maintains an extensive network of air quality monitoring stations that provide real-time and retrospective data that can be accessed online, via the UK Air Information Resource website (UK-AIR), at http://uk-air.defra.gov.uk. In the UK, a 'Daily Air Quality Index' is published that covers five pollutants that are most likely to acutely affect the health of susceptible members of the population, leading to premature mortality and hospital admissions in those with pre-existing respiratory disease. These pollutants are ozone (O_3), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), particulate matter (as PM_{10}), and fine particulate matter (as $PM_{2.5}$). The Daily Air Quality Index uses a scale of 1–10 to describe air pollution, divided into four colour coded bands that correspond to 'Low', 'Moderate', 'High' and 'Very High' air pollution levels. Each band comes with recommended actions and health advice for 'at risk' individuals – adults and children with heart or lung problems are at greater risk of symptoms – and the general population.
Indoor air quality	The WHO estimates that 4.3 million deaths are attributable to indoor air pollution each year. Exposure to high concentrations of pollutants like allergens, tobacco smoke, VOCs, oxides of nitrogen and formaldehyde in indoor spaces such as homes, schools and workplaces are known or suspected to be linked to increasing rates of respiratory diseases like asthma and chronic obstructive airway disease, ischaemic heart disease, strokes and allergic conditions.
Drinking water	In Europe, about 50% of drinking water is taken from groundwater, about 40% from surface water, and 10% from other sources, like artificial groundwater recharge or bank filtration water. Drinking water in the UK is also derived from multiple sources, including underground aquifers, rivers and upland storage reservoirs Over 99% of the population in the UK receives mains water supplies; the quality of these supplies is very high and all are safe to drink. The basic unit of water supply is the water supply zone, which is designated by the water company, normally by reference to a source of water, and which covers a population that must not exceed 100 000 people. Strict standards for the quality of the UK public water supply are laid down in national regulations derived from the EU Drinking Water Directive which is based on the WHO Guidelines for Drinking Water Quality. The maintenance of these standards from source to tap is supported by a multi-agency Water Safety Plan (WSP). The standards include microbiological, chemical, physical and aesthetic parameters. In 2014, only 0.04% of tests on drinking water samples failed to meet one or more of the required standards, this a significant improvement on the figure of 1.5% reported in the early 1990s. Raised levels of lead ($\geq 10\,\mu g\,l^{-1}$) and nitrate ($>50\,mg\,l^{-1}$) continue to be common reasons for non-compliance with the standards but these are mostly attributable to lead pipes in older homes built before 1970 and inadequate management of nitrate levels in private water supplies. Of the population in England and Wales, 1% use private water supplies. These are regulated by local authorities that have a number of statutory duties under the Private Water Supplies Regulations 2016 to conduct a risk assessment of each private water supply and undertake periodic monitoring to determine compliance with extant standards.

(*Continued*)

Table 4.14.1 (*Continued*)

Hazard	Notes
Sewerage systems	To reduce pollutants discharged into the environment with wastewater, the EU implemented legislation on urban wastewater treatment (Directive 1991/271/EC). In northern and western European countries most households are connected to wastewater treatment plants that efficiently remove nitrogen, phosphorus and organic matter. In central European countries more than three-quarters of the wastewater is treated in this way, apart from Croatia, Slovenia, Serbia, and Romania where the figures are lower. In Southern and EU candidate countries only around half of the population is connected to wastewater treatment plants.
Water resources management	Under the Water Resources Act 1991 in England and Wales, the Environment Agency regulates any discharges to water to improve the quality of bathing waters.
Solid waste	Between 2004 and 2010, the EU-28, Iceland and Norway reduced the amount of total waste (excluding mineral, combustion, animal and vegetable wastes) deposited in landfills by 23%; from 205 billion tonnes(t) to 157 billion tonnes. The decrease in landfilling is partly attributed to increased recycling and incineration of waste. In the EU, use of materials averages 15–16 t per capita per year (Italy 12, Finland 38) and results in 4–5 t of waste per capita each year. Waste is sent to landfill (45%), recycled or composted (37%), or incinerated with energy recovery (18%). There are EU regulations governing the management of solid waste, its storage, carriage, treatment and disposal and health and safety aspects.
Contaminated land	In the UK, a long industrial history has resulted in a substantial legacy of land contamination. In the UK, the legal definition of contaminated land explicitly links land with the potential to cause significant harm. Contaminated land is defined in Part 2A of the Environmental Protection Act 1990 as land where by virtue of contamination there is a *significant possibility of significant harm* or where there may be water pollution. The local authority takes the lead on most issues to do with contaminated land and they may be assisted by PHE's local health protection team and the Centre for Radiation, Chemical and Environmental Hazards (CRCE) with interpreting human health risk assessments and communicating the results to the community. The UK Environment Agency has useful technical guidance on the management of contaminated land including how to investigate, assess and manage the risks (https://www.gov.uk/government/collections/land-contamination-technical-guidance)
Ionising and non-ionising radiation (see also Chapter 4.16)	Radioactivity occurs naturally and various medical, scientific, commercial and educational activities involve the use of radioactive material and result in radioactive waste. In recent years there have been incidents involving the accidental and deliberate release of radioactive materials in the environment. Expert services exist to protect public health from the harmful effects of radiation through surveillance, monitoring, advice and intervention. A key international organisation that advises on standards of protection against ionising radiation is the International Commission on Radiological Protection (ICRP). In the UK, the Radiation Protection Services of PHE fulfils these functions and there are regulations that govern workplace exposure.

Table 4.14.1 (*Continued*)

Hazard	Notes
	Exposure to man-made radiation gives rise to great public concern, although natural sources, such as radon, have greater health effects. A national survey of exposure to radon in homes has shown that while radon exposure in most homes is low, there are some in which it can pose a risk to health. Monitoring should identify homes above the radon action level (see http://www.ukradon.org) so that appropriate remedial action can be taken. Other sources of ionising radiation include planned exposure from medical devices such as x-rays.
Noise	Noise is one of the most important risk factors after air pollution contributing to the environmental burden of disease in Europe. In the EU, more than 120 million people suffer from noise levels that are considered to have a negative effect on health. Road traffic noise is the most widespread form of noise disturbance, but people also frequently object to neighbour noise. Annoyance is probably the most widespread adverse effect of noise but it is important to note that there is a wide variation in individual sensitivity to noise. Populations exposed to high noise levels can exhibit stress reactions and sleep-stage changes that interfere with daily activities at school, at work, at home and during leisure time. It can also lead to conditions like hypertension and cardiovascular disease, reduce performance, and provoke annoyance responses and changes in social behaviour. All of these health effects can contribute to premature mortality and it is estimated that noise is associated with the loss of 1.6 million healthy life years per year in the EU. The World Health Organization (WHO) reports an onset of adverse health effects in humans exposed to noise levels at night (Lnight) above 40 dB (dB). In the EU, it is estimated that around 40% of the population are exposed to road traffic noise at levels exceeding 55 dB(A); 20% are exposed to levels exceeding 65 dB(A) during the daytime; and more than 30% are exposed to levels exceeding 55 dB(A) at night.

specific health conditions with exposure at these sites. These clusters are defined as an unusual or unexpected aggregation, real or perceived, of health conditions that are grouped together in time and space and that are reported to a health agency. Most types of diseases may cluster, but cancer clusters receive the most attention and greater significance is attached to a cluster when a site of industrial pollution is suspected. The local health protection team may be asked to investigate suspected clusters and other health problems associated with environmental hazards. The methodology is similar to that used for the investigation of infectious disease clusters but, as a general rule, site-specific epidemiological studies are not recommended because they often have insufficient statistical power to confirm or refute hypotheses. Similarly small area level data in the context of single sites or events can be difficult to interpret. When investigating health problems that may be associated with environmental hazards a systematic approach should be adopted (Table 4.14.2).

Dealing with the concerns of the public and media is fundamental to investigating these clusters. Risk communication, risk perception and skills in handling enquiries from the public and the media are all important. From a public health perspective addressing the community's perception of a cluster and the risk from any environmental hazard may be more important than epidemiological or statistical arguments.

Table 4.14.2 Key stages in the investigation of clusters of non-infectious disease

1 *Screening stage*	
Initial report and follow up with the informant(s)	Use a standard form to record preliminary information provided by the person(s) making the initial report in order to determine whether the cases could represent a real cluster. Collect information on the person(s) reporting the suspected cluster (you will have to contact them again). What disease/health event/syndromes or symptoms are being reported? Where is the affected area/population? How many people are suspected to be affected (index cases) and what are their socio-demographic characteristics including length of time in residence in the affected area? Over what time period did the cases occur? What are the suspected exposures and likely period of exposure (if any)?
Review findings and decide	Current knowledge may indicate that the disease is common, affected persons may only recently have moved to the area, or there is no plausible environmental hazard identified. The investigation may be resolved at this stage and as a minimum, the informant should be told the decision and rationale. If appropriate, a written report should be prepared and disseminated. Further investigation may be indicated if there is an apparently higher than expected number of cases for the area, indication of a biologically plausible exposure(s) or there is ongoing community concern.
2 *Epidemiological Assessment stage*	
Confirm diagnosis	Involve informant(s), clinicians and other sources like medical records, registries and surveillance systems to verify the diagnoses. Consent of the index case(s) may be needed.
Develop a case definition that describes the disease, geographic area and time period of interest[a]	Agree a case definition (CD) – the sensitivity and specificity may vary over time as more information becomes available.
Intensive case finding	Based on the agreed CD, use existing data, such as surveillance databases, death certificates, birth certificates, hospital case notes, cancer and birth defect registries, occupational health records and GP records to identify further cases. Collect a minimum dataset on each case: name, date of birth, ethnic group, sex, age at diagnosis, residence and length of residence at diagnosis, past residence, diagnosis, family history, exposures, confounding factors such as smoking, occupational history.
Analyse the data	Use appropriate statistical methods to produce summary measures of disease frequency, central tendency, variation, precision and other estimates. Determine whether observed case numbers are greater than expected (i.e. calculate the excess number of cases) using an appropriate reference population. Determine appropriate numerator and population denominator (i.e. person-time) data and compare observed with expected rates using appropriate statistical methods like direct and indirect standardisation and tests of statistical significance. *Note:* statistically significant estimates may not be of aetiological/public health importance and may be chance findings and should not be used as proof of causation. Mapping the data may be helpful; a geographical information system (GIS) can be used to map cases spatially and also to examine the spatial relationship between cases, purported source(s) and other factors like wind patterns.

Table 4.14.2 (*Continued*)

Literature review	Undertake a detailed review of the literature to identify previously reported clusters of the disease, identify reported associations with environmental exposure(s) and any other epidemiological and toxicological information on biological plausibility of any initial hypotheses.
Review findings and decide	The cases may not be verified or may have different diagnoses. Also there may not be an excess number of cases, or the apparent excess may be due to inward migration to an area or a chance occurrence. The cluster may be explained because it involves a common disease or because of the characteristics of the local population. **(a)** Findings indicate that no further action is required: a written report should be produced and disseminated to key stakeholders. **(b)** Findings indicate further action required: undertake detailed analyses of the cluster dataset using analytical epidemiology. If a statistical excess is confirmed and the assessment suggests a biologically plausible relationship of public health importance between a putative exposure(s) and the condition of interest, then undertake an environmental health assessment.
3 *Environmental Health Assessment – Hazard assessment and exposure assessment*	
Hazard identification	Hazards identification – identify potential exposure to a range of hazards using a variety of data sources. Company records, aerial photographs, maps, records of water, soil and air quality monitoring, meteorological data and planning records about previous industrial sites and property uses may be used.
Assess exposure(s)	Exposure to putative hazards via personal contact, food, water or drug consumption can be assessed by questionnaire. Exposure via water, air, soil, or dust is more difficult to assess. The assistance of an environmental health specialist or an occupational hygienist may be needed but measurement of exposure is usually not necessary. Plume dispersion modelling may be helpful. Determine whether the putative hazard(s) identified is linked to the condition of interest. The findings from the literature review may be helpful in determining whether there is a plausible pathway between exposure to the putative hazard(s) and the cases.
Review and decide	If there has been a recent increase in cases or if the cases are concentrated around suspected environmental hazards or in particular occupational groups then further investigation may be necessary. If there is a plausible pathway between exposure to the putative hazard(s) and the cases, then further investigation is necessary. As a minimum, if no further action in recommended then a report should be written and the results disseminated.
4 *Further investigation: Analytical epidemiology and surveillance*	
Feasibility assessment	Undertake an assessment of the feasibility and potential utility of undertaking an analytical epidemiological study to examine the association between the condition of interest and reported exposure to a putative hazard(s). The assessment may also explore the feasibility of establishing a health register or surveillance system. Such an assessment may need to consider the public health importance of the condition, the available resources (i.e. manpower and funding), viable research options, and key political, economic, legal and community factors.

(*Continued*)

Table 4.14.1 (*Continued*)

Review and decide	If the assessment shows that an analytical study or bespoke surveillance system is unwarranted then a report should be written and the results disseminated. Undertake an analytical study if the assessment indicates that it is feasible and likely to be useful.
Analytical epidemiological study, targeted surveillance or health register	An analytical study using a case–control, cohort or cross-sectional study design may be undertaken to investigate a biologically plausible hypothesis of an exposure–disease relationship. These studies may involve the collection of new data and should consider potential confounding factors such as smoking and socio-economic status. The findings of the study are expected to contribute to the evidence base and inform public health prevention and control measures. A surveillance programme over several years will allow the epidemiology to be more clearly described. A health register or reporting system may have to be established Ethical approval may be required
Review	Review and share findings from different investigative streams.

[a] Beware of the Texas sharp-shooter fallacy when selecting a geographic area of interest. This arises when a time period or geographic area is selected to match a pre-specified hypothesis adduced by the reporting individual(s) or investigator.

Investigation of clusters of non-infectious diseases

Spatio-temporal clusters of similar cancers, chronic diseases, congenital anomalies or of unusual illnesses may be reported from healthcare professionals and individuals to a health agency. These reports are often associated with concerns of an association between the observed cluster and exposure to an environmental hazard. The cluster investigation is usually conducted in stages and at the end of each stage, a decision is made on whether and how to proceed to the next stage and who to share the findings with. The investigations are resource intensive and should adopt a systematic and integrated approach that may involve experts in epidemiology/statistics; environmental health, psychology, risk assessment/management and communications. In England, the Director of Public Health for the area usually plays a key co-ordinating role when responding to reports of suspected clusters and the roles and responsibilities of other key stakeholders should be clearly defined.

4.15 Managing acute chemical incidents

An acute chemical incident is defined as an unforeseen, uncontrolled release of a chemical from its containment leading to:

- two or more individuals suffering from a similar illness which might be due to exposure to toxic substances;
- a potential threat to health from toxic substances.

Potentially harmful chemicals may be released into the environment as a result of leakage, spillage, explosion, fire or inappropriate disposal. Deliberate release (see Chapter 4.17) may be part of a criminal or terrorist activity. Exposure by swallowing, inhalation or contact with skin and mucous membranes may be direct or indirect, via contaminated air, food, water or soil. Chemicals can be dispersed from the site of an accident as gas, vapour or particulate cloud; by water; and on clothing, equipment, livestock or vehicles (including on human casualties, emergency service personnel

and equipment). Exposure to a harmful chemical may result either in acute injury or poisoning, or in longer-term health effects. Following a chemical incident, public health interventions include shelter, evacuation, decontamination, supportive treatment, specific treatment with antidotes; short-term and long-term follow up of those affected with clinical and biological monitoring if necessary, population studies and establishments of health registers. Various agencies are involved in the management of an acute chemical incident (Table 4.15.1). In the UK, the Consultant in Communicable Disease Control (CCDC) on behalf of the National Health Service (NHS) has particular responsibilities for the health aspects of the response to chemical incidents: Table 4.15.2 gives a useful checklist for local

Table 4.15.1 Responsibilities of agencies and groups involved in the planning for, and response to an acute chemical incident (UK example)

Police	Co-ordinate response of emergency services Save lives, protect and preserve the scene Advice to the public on sheltering, evacuation Investigation of the incident Casualty information Media enquiries
Fire and Rescue services	Control and prevent fires Urban search and rescue Save lives Manage hazardous materials Safety of first responders Minimise effect of incident on environment On-site decontamination of casualties and exposed persons Clean up spillage Arrange with contractor to remove substance, etc.
The ambulance service	Co-ordinate all health service activities on site Immediate care and treatment of casualties Transport to hospital Assist with casualty decontamination (with fire service)
Local authority Public Health and/or Environmental Health departments supported by local health protection teams	Planning for chemical incidents Support the emergency services Open emergency rest centres if necessary Co-ordinate response of other organisations including voluntary agencies Lead and co-ordinate health-service response Assessing health risk Health advice to the public Environmental sampling Establish health registers to monitor and follow up of affected persons Mobilise resources to ensure provision of health care (resuscitation, decontamination, treatment with antidotes, intensive care, supportive care, community response) Restore environment Lead the long-term recovery process
Specialist chemicals advice services (PHE Centre for Radiation, Chemicals and Environmental Hazards in UK)	24-hour advice and support to public health and other health professionals on managing chemical incidents, toxicology, personal protective equipment, decontamination and evacuation, health effects, industrial processes, antidotes and medical treatment, chemical incident surveillance, emergency planning, training, research

(*Continued*)

Table 4.15.1 (*Continued*)

Hospitals (including Toxicology laboratories)	Support the Ambulance Service In-hospital decontamination Treatment and care of casualties Undertake tests to identify the toxic substance(s)
Health and safety agency (Health and Safety Executive in UK)	At sites at which chemicals are manufactured or used: Inspect workplaces Investigate accidents and cases of ill-health Enforce good standards and legislation
Environment Agency	Advise on environmental impact and disposal of contaminated water and other materials
Local water company	Advise on disposal of contaminated water via sewers and impact on water sources
Food Standards Agency	Advise on chemical contamination of the food-chain
Meteorological Office	Forecast behaviour of chemical plume according to prevailing weather conditions
National Poisons Information Service (NPIS)	Advice on diagnosis, treatment and management of patients who have been poisoned. In the UK, NPIS provides clinical toxicology services for healthcare professionals from four UK centres. Online TOXBASE database at http://www.toxbase.org

Table 4.15.2 Check-list for local public health officer in acute chemical incidents. These questions and actions will assist the public health officer identify the source, pathway and receptor in order to guide actions needed to reduce the impact of the incident on public health

Action	Notes
Details of incident (what is known NOW?)	
What type of incident?	Initial report may come from PHE CRCE, Emergency Services, public, media
Where and when?	
What medium is affected?	
Source of contamination	
What chemical(s) are involved/ Chemical Abstract Service (CAS) number if available/composition/concentration/quantity?	
Have any immediate control measures been taken?	
Has on-the-scene monitoring started?	
Has there been a request for modelling (for example: CHEMET)?	
Weather conditions	
Could this be a deliberate release?	
Adverse health effects or complaints	
How many people are exposed?	Seek information from ambulance service, GPs, emergency department, water company, telehealth (e.g. NHS 111)
How many are affected?	
What symptoms?	
How serious?	
How many have been transferred to hospital?	
Are similar symptoms being reported in the surrounding area/ wider community?	
Initial response	
What agencies are involved?	Consider implementing the local public health authorities chemical incident plan, convening response team and setting up an incident room
What are the command and control arrangements?	
Should other agencies be called?	
Is the site secure?	
Has sheltering or evacuation been advised?	
Decontamination	
Antidotes, first aid	
What has been said to media?	

Table 4.15.2 (*Continued*)

Action	Notes
Assessing risk to health	
• Review health effects and exposure pathways to inform a dynamic risk assessment	Obtain toxicological advice from specialist agencies.
• Define affected population	Plume modelling, e.g. using CHEMET and GIS.
• Define population at risk including sensitive receptors in the area (for example: hospitals, nursing/care homes.)	Consider biological sampling of sentinel cases, other exposed persons, animals and environment.
• Is an Air Quality Cell (AQC) required?	Collect dataset on those affected by the incident or exposed to the chemical(s).Consider using syndromic surveillance systems to monitor the health effects of the incident
• Establish register of exposed/symptomatic persons	
Communications	
Partner agencies (local and national)	Set up telephone helpline, consider using existing telephone health advice line (e.g. NHS 111)
Professionals	
Media	
Public (public health messages)	
Post acute-phase response	
• Site clean-up	Seek advice on environmental sampling, site remediation and monitoring.
• Environmental effects	
• Epidemiological study	As a minimum there should be a descriptive study, but there may be an opportunity for an analytical study to determine the strength of any association between the chemical exposure and its health effects.
• Long-term surveillance including health register	Those affected may require examination, testing, advice, treatment or follow-up, normally carried out by local clinicians.
	Counselling may be considered to avoid stress-related illness.
Post incident	Incident documented, report prepared and circulated.
Written report	
Incident debrief and evaluation of response	

Note: See Table 4.17.1 for details of health effects and public health interventions following exposure to specific chemical hazards.

public health staff involved in the response to acute chemical incidents.

Surveillance of chemical incidents

The public health effects of chemical incidents include chemical-related morbidity and mortality, stress and anxiety, and societal/economic costs. In the EU/EEA area, catastrophic chemical incidents are rare. In England, data on chemical incidents is collected by Public Health England (PHE) via the Centre for Radiation, Chemical and Environmental Hazards (CRCE). Almost 9000 incidents were notified in England between 2007 and 2016, an average of 890 incidents per year. The most commonly identified chemicals were products of combustion,

while the most commonly reported setting for these incidents were residential, followed by industrial and commercial locations. The most common incident type was fire, followed by leaks/spills and release of chemicals.

4.16 Managing acute radiation incidents

Major radiation incidents are defined as events that have led to significant consequences to people, the environment or the facility, such as accidents involving nuclear reactors, military operations, and nuclear-powered satellites crashing to earth. Such major incidents are uncommon; however, because of the widespread use of radioactive materials in medicine, science and industry, small-scale incidents following transportation accidents, leaks and the loss or theft of sources do occur. In a radiation incident, radioactive material may be released into the atmosphere as a gas or particles. This forms a windborne plume, which is dispersed and diluted. Some material will fall to the ground, particularly if there is rain. People may be exposed by direct radiation from the plume, by inhalation, by contamination of the environment leading to direct radiation, or by consumption of contaminated food or drink. In the UK, health services do not normally take the lead in responding to releases of radioactive materials, but they do have a role in dealing with their health effects and allaying public anxiety (Box 4.16.1 and Table 4.16.1). They must have a written plan to cover this and a named person to take overall responsibility who, in the UK, is usually the local Director of Public Health (DPH). The DPH can ask for advice and practical assistance from Public Health England (PHE), which has a specialist Radiation Protection Service.

Box 4.16.1 Check-list for CCDC in acute radiation incidents

Enquire about:
- nature and scale of the incident
- whether anyone has been exposed to radiation as a result of the incident
- whether they can be traced
- the likely clinical effect of exposure to the source of radiation
- the extent and nature of any environmental contamination
- the wider population that might have been exposed
- Carry out an initial risk assessment.
- Consult with local, regional or national sources of expert advice (keep up-to-date contact details in written plan).
- Agree countermeasures, public information, follow-up

Countermeasures

Intervention after a radiation incident is based on countermeasures that aim to do more good than harm. Countermeasures include sheltering, evacuation, iodine prophylaxis and banning contaminated foodstuffs. In an incident involving radioactive iodine-131, 60–70% of uptake can be blocked if potassium iodate tablets are given within three hours and 50% at approximately five hours. The protective effect of a single dose lasts approximately 24 hours, so repeat administration may be indicated if exposure is ongoing. In the UK, potassium iodate tablets are part of the UK National Reserve Stock for Major Incidents. However local accident and emergency departments are advised to maintain stocks for small scale local incidents. Criteria for countermeasures during emergencies are based on agreed Reference Levels (RL). These RLs are levels of residual dose or risk above which it is generally judged to be inappropriate to allow exposures to occur. They are expressed in millisieverts (mSv) ranges and the higher range (20–100 mSv) represents an emergency situation with uncertain consequences (see Box 4.16.2) that always requires urgent

Table 4.16.1 Radiation incidents: responsibilities in the UK

Office for Nuclear Regulation (ONR)	ONR is responsible for the regulation of nuclear safety and security across the UK. It regulates 36 licensed nuclear sites by undertaking site permission and compliance inspections and enforcing extant regulations. The Radioactive Material (Road Transport) Regulations 2002 is legislation that aims to facilitate the safe transportation of civil radioactive material and minimise the risk of accidents. This requires transport operators to prepare an emergency plan and some operators subscribe to the RADSAFE scheme to ensure mutual assistance if needed.
Health and Safety Executive	Health and Safety at Work etc. Act 1974 places duties on all employers, including those in the nuclear industry, to look after the health and safety of both their employees and the public.
Local authorities	The Radiation (Emergency Preparedness and Public Information) Regulations 2001 (REPPIR) require site operators, local authorities and fire services to prepare and provide information for the public living near nuclear installations on the action to be taken should a radiation emergency[a] arise and also provide information if an emergency occurs. Site operators must consult with local authorities and other agencies to draw up these emergency plans including plans to deal with off-site emergencies. REPPIR have been developed alongside other pieces of legislation such as the Control of Major Hazards Regulations 2015 (COMAH) (to implement Council Directive 2012/18/EU on the control of major accident hazards involving dangerous substances, known as the Seveso III Directive).
Ministry of Defence	Maintains a Nuclear Accident Response Organisation (NARO) to respond to an accident or incident at defence nuclear installations, transport accidents involving nuclear materials including one arising through terrorist acts.
Department of Environment, Food and Rural affairs (DEFRA)	Plays a key role during the recovery operation following a nuclear incident by ensuring that government provides all the necessary on-going support to the agencies involved in environmental restoration and to the affected individuals and communities. This includes incidents at nuclear installations overseas.
Meteorological Office (Met Office)	The Met Office, working in partnership with DEFRA & DECC, operates the UK Radioactive Incident Monitoring Network (RIMNET). As at 2017, this consisted of 96 fixed radiation (gamma dose) monitoring sites that support the UK response to any radiological event. RIMNET automatically measures, analyses and provides hourly updates on background radiation levels 24/7 to detect any abnormal increases in radiation levels. All measurement and reference data is stored in the UK National Nuclear Database.
The Department of Energy and Climate Change (DECC)	

(*Continued*)

Table 4.16.1 (*Continued*)

PHE Centre for Radiation, Chemical and Environmental Hazards (CRCE) – Radiation Protection Service	Advice to government, other agencies and the public on all aspects of protection from radiological hazards. The National Arrangements for Incidents Involving Radioactivity (NAIR) was set up to protect the public from hazards arising from the use and transport of radioactive materials and in situations where no formal contingency plans exist. NAIR is usually activated by the Police and other emergency services and is co-ordinated by PHE CRCE. Assistance is provided in two stages and is drawn from expertise in hospitals, the nuclear industry and government departments. Stage 1 assistance comes from a local radiation expert who with the aid of simple monitoring equipment will aim to determine the existence of a hazard and provide appropriate advice. Stage 2 assistance comes from a small team of radiation experts using readily available transport, monitoring and decontamination equipment and special clothing
Health services including public health, ambulance service and hospitals	Prepare emergency plans. Reception, treatment and decontamination of casualties at designated hospitals, monitoring people and their personal belongings following exposure by local medical physics departments, distribution of potassium iodate tablets, information to the public and the media on health aspects of the accident, collating advice from expert sources, telephone advice line, long-term follow-up of exposed persons for clinical or epidemiological purposes.
Food Standards Agency Environment Agency Water companies	Monitor that radioactivity in food, environment and water from authorised releases and discharges does not affect people's health or the environment.
Home Office	Nuclear-powered satellite accidents. Terrorism

[a] A 'radiation emergency' is an event that is likely to result in a member of the public receiving an effective dose of 5 mSv during the year immediately following the emergency.

Box 4.16.2 Ionising radiation

Ionising radiation is a type of energy released when an unstable element or radionuclide decays. It is either electromagnetic radiation (X-rays and gamma-rays) or fast-moving particles (alpha particles, beta particles). Ionising radiation releases energy as it passes through biological tissues, resulting in damage. The amount of radioactivity is measured in Bequerel (Bq), the physical quantity of energy deposited by radiation is measured in Greys (Gy) and the effective dose of the radiation which is a measure of radiation-induced biological effect is measured in sieverts or millisieverts (mSv). The average annual exposure in the UK is 2.6 mSv (0.0026 Gy). Of this 85% comes from natural background radiation (radon, cosmic rays), 14% comes from medical X-rays, 0.1% from nuclear discharges and 0.4% from fallout. The maximum permitted radiation from artificial sources is 1 mSv per year. A person will be exposed to ionising radiation by being in close proximity to a radioactive source in their surroundings. Prolonged exposure will follow contamination of skin, clothing and wounds and ingestion. Cells that divide frequently are most sensitive to the effects of ionising radiation.

The effects of rapid whole body radiation exposure (Acute Radiation Syndrome [ARS]) are summarised in Table 4.16.2. ARS has four stages namely; the prodromal, latent, manifest illness, and recovery or death.

Table 4.16.2 Effects of rapid whole body radiation exposure (Acute radiation syndrome)[a]

Absorbed dose in Grey (mSv)	Clinical features
>0.5 and <1 Gy (<1000 mSv)	Usually asymptomatic Mild GI symptoms in first 48 hours in 1–10%
Whole body doses less than 0.5 Gy are unlikely to cause acute symptoms	Low white blood cell count at 2–4 weeks No foetal effects if effective dose less than 100 mSv Counselling needed if pregnant and effective dose more than 100 mSv
1–6 Gy (1000–6000 mSv)	*Haematopoietic syndrome* GI symptoms occur within 1–4 hours to 2 days after exposure After 2 days to 4 weeks: bone marrow depression, bleeding, and bruising Hair loss at 2–3 weeks LD50/60[b] is around 3.5–4 Gy without treatment
6–20 Gy (6000–20 000 mSv)	*Gastrointestinal syndrome* Early GI symptoms (within hours) In first week severe gastrointestinal symptoms LD100[c] is about 10 Gy, death usually within 2 weeks
More than 20 Gy (>20 000 mSv)	*Neurovascular syndrome (cardiovascular and central nervous system)* Immediate (within minutes) and severe GI symptoms Persistent and severe nausea and vomiting Convulsions, coma, hypotension, shock No recovery is expected and death occurs within 2–3 days Stage may last for hours but can be less

[a] Grey (Gy) values indicate the whole body absorbed dose. One sievert (1000 millisieverts) is the amount of radiation necessary to produce the same effect on living tissue as one grey of high-penetration x-rays.
[b] LD50/60 is the dose necessary to cause death in 50% of irradiated population in 60 days
[c] LD100 is the dose necessary to cause death in 100% of the irradiated population.

countermeasures, such as sheltering and evacuation to minimise the impacts of possible radiation exposures (Table 4.16.2). The lower range (1–20 mSv) represents situations where the implementation of countermeasures should be considered, but is not essential.

4.17 Deliberate release of biological, chemical or radiological hazards

Deliberate release (DR) of biological, chemical or radiological agents may be overt or covert.

An overt release may be preceded by a warning, there may be an obvious release in a public place or a number of individuals may present with contamination by an unknown substance. Those exposed may or may not be acutely ill and a sample of the agent may be available for analysis. The health service may be alerted by the police. Should those exposed develop symptoms within the first few minutes or hours the most likely cause is a chemical agent, followed by a biological toxin or hysteria. A slightly longer period between exposure and developing disease suggests that an infectious or radiological hazard may be responsible. Many incidents will turn out to be a hoax or a misinterpretation of a normal event, for example the use of powdered silica in packaging triggering a 'white powder' incident. The principles of dealing with these incidents build on those followed when managing accidental releases.

Box 4.17.1 When to consider possibility of a deliberate release

- Number of ill people with similar disease or syndrome presenting around the same time.
- Number of cases of unexplained disease, syndrome or death.
- Single case of disease caused by uncommon agent.
- Recognised illness occurring in an unusual setting or key sector within a community.
- Failure of a common disease to respond to usual therapy.
- Disease with unusual geographic or seasonal variation.
- Multiple atypical presentations of disease agents.
- Similar typing of agents isolated from temporally or spatially distinct sources.
- Unusual, atypical, genetically engineered or antiquated strain of agents.
- Simultaneous outbreaks of similar illness in non-contiguous areas.
- No local cause for unexpected acute event with syndrome of confusion, nausea, vomiting, respiratory, eye and skin irritation, collapse, difficulty seeing, fright and possible delayed effects. May be smell or plume without explained cause.
- Deaths or illnesses among animals that precede or accompany illness or death in humans.
- Suspected or known deliberate release in other countries.

A covert incident, for example a substance introduced into the food or water supply, may only become apparent when ill patients present to health services. This may be some time after exposure, depending on the nature of the agent. Cases may not occur in an obvious geographic area or in people with an obvious common exposure. Potential indicators of a covert release are given in Box 4.17.1. It is likely that the health services will be the first agency to discover a covert release and will have to inform other agencies of their suspicions. The principles of investigating such incidents build on those used in controlling outbreaks or other longer-term incidents (see Chapter 4.2).

Advance preparedness is the key to success in organising a response and consists of

- Multiagency contingency plans.
- Ensuring access to personal protective equipment (PPE), decontamination facilities and therapeutic counter measures.
- Training of staff and multi-agency exercises.

Organisational response to acute/overt incidents

Co-ordination, command and control of acute deliberate release incidents follow the same principles as those adopted for the emergency response to any incident (e.g. explosion, plane crash or flooding) and comprise three levels:

- Bronze (operational), usually located at the scene and operating at 'activity' level (e.g. individual patient care).
- Silver (tactical), usually located near the scene and operating at function or range of activities level.
- Gold (strategic), which is usually off-site at a headquarters office and is responsible for multiagency strategic co-ordination.

In the case of suspected deliberate release incidents, an overall lead agency is required to co-ordinate the response. In the UK, this is the police. The multi-agency strategic (gold) group will be supported by a team to provide health advice (called a 'Scientific and Technical Advice Cell' [STAC] in the UK) which:

- takes advice on the health aspects of the incident from a wide range of sources.
- provides advice to the Gold Commander and/or Strategic Co-ordinating Group (SCG, Gold Command) on the health consequences of the incident, including the consequences of any evacuation or containment policies.
- provides information on the available evidence base underlying the advice.
- agrees the advice to be given to the public on health aspects of the incident with the Gold Commander.

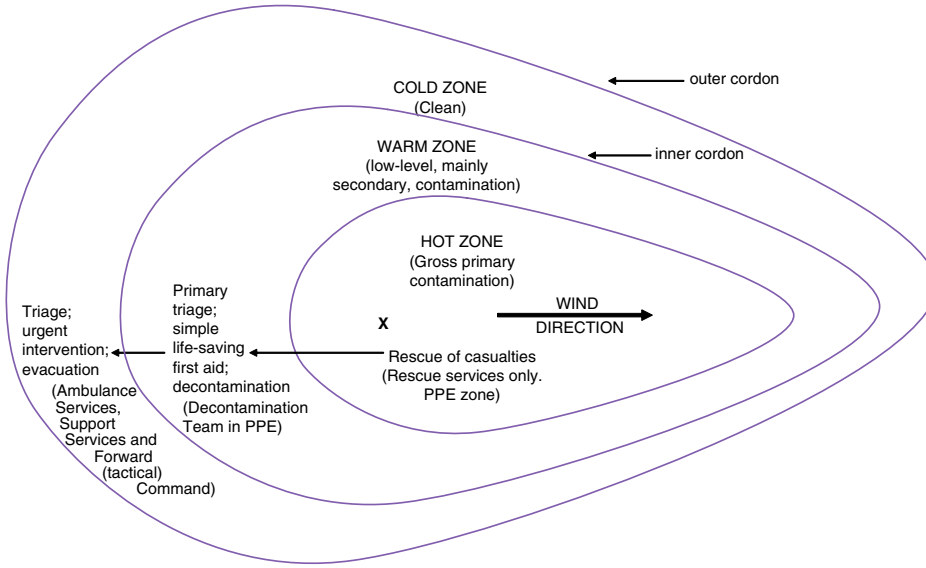

Fig. 4.17.1 Organisation of on-scene response.

- liaises with the national Department of Health and other national and local health agencies.
- formulates advice to health professionals in hospitals, ambulance services and primary care.
- formulates advice on strategic management of the health service response (but does not actually do the strategic management).
- provides clarification on advice provided to the SCG, to a single, nominated, point of contact within a multiagency Tactical Co-ordination Group (Silver Command).

The STAC is chaired by the local Director of Public Health or a health protection consultant (both subject to having received appropriate training) and has multiagency membership similar to that for an accidental incident or outbreak, plus national experts made available via national arrangements.

Technical aspects of response

In chemical and biological incidents, the actions in order of priority are containment, decontamination, resuscitation, primary treatment, definitive care and follow up. A schematic illustration of how this might be organised at the scene is given in Figure 4.17.1. In general, only simple, life-saving treatment can be carried out in the 'warm zone' before decontamination. This comprises simple airway opening manoeuvres, bag-valve-mask ventilation, and pressure on 'bleeding wounds'.

Specialist advice should be taken on decontamination, but in general:

- Remove exposed person from scene of contamination.
- Remove all clothing (80% reduction in contamination).
- General decontamination: the decontaminant of choice for most chemicals is water and detergent using the 'rinse-wipe-rinse' method (water or saline only for eyes and mucus membranes).
- Liquid chemical contamination must be removed as soon as possible.
- Water and hypochlorite are preferred for biological contamination of small numbers of casualties.
- Biological contamination of large numbers can usually wait for mass decontamination facilities to be set up.

- Contaminated clothing, equipment and effluent, where possible, to be stored in safe area, awaiting disposal (or evidence collection).
- For radiation, external decontamination is similar to that for non-radioactive chemicals, but extra care is taken with clothes etc.
- Decontamination team must wear Personal Protective Equipment (PPE).
- Ensure that decontaminated persons are kept separate from those awaiting decontamination (and moved away from contamination).

Following decontamination, triage will separate those exposed into priority groups for treatment and evacuation. Advanced life support procedures and other generic interventions can then be deployed.

It may be possible, based on the symptom profile of those who become ill or the results of screening of samples from the environment and patients, to identify the causal agent. This will allow specific countermeasures or antidotes to be deployed (see Table 4.17.1 for potential symptoms and possible antidotes of main chemical and biological toxin threats: please check for up to date national guidelines). Exposure to chemicals and toxins may be via ingestion (e.g. through food or water), inhalation (e.g. from indoor or outdoor aerosols) or direct contact (e.g. from contaminated environment): the symptoms are likely to vary according to the route of exposure.

Suspicious packages or materials

A package may be considered suspicious because of:

- suspicious or threatening messages written on it,
- envelope is distorted, bulky, rigid, discoloured, has an oily stain, has an obvious odour or feels like it has powder inside,
- unexpected envelope, particularly from a foreign country,
- no postage stamp, no franking, or cancelling of stamp,
- incorrect spelling of common names, places, or titles,
- handwritten envelope from unknown source, particularly if addressed to individual and marked personal or addressee only,
- on opening, suspicious powder, or material found,

The immediate response should be:

- do not open package,
- call police immediately for advice,

If package opened or suspect material found, then in addition:

- shut windows and doors to room and switch off any room air-conditioning,
- room occupants to move to unoccupied adjacent room away from hazard,
- seek medical advice for anyone showing symptoms,
- notify building manager to switch off air-conditioning, close fire doors and close all windows in rest of building,
- do not touch or attempt to clean up any suspect material.

The police should then perform a risk assessment, to decide whether threat is credible. Figure 4.17.2 gives an example of action to be taken in response to their assessment (check up-to-date national guidelines). A number of agencies will need to be involved if a credible threat is declared and specialist advice should be taken.

Investigation of incidents of unusual illness

A cluster of an unusual or unknown illness, a single occurrence of an unexpected illness for that community or illness that fails to behave as expected should be investigated according to standard epidemiological and public health practices (see Chapter 4.2). However, there may be some features that should raise the suspicion of a deliberate release (see Box 4.17.1). Infectious agents that are considered to have bioterrorist potential are given in Table 4.17.2 (Please check for up-to-date national guidelines or advice): of note is that in deliberate release scenarios, the presentation may be more sudden, more severe and involve larger numbers than in natural

Table 4.17.1 Potential chemical and biological toxin terrorism agents

Chemical/toxin	Clinical effects	Speed of action	Antidotes and treatment (*Expert advice should be sought*)
Nerve agents (Organophosphates and related agents e.g. Sarin, VX, Novichok agents)	Mild: headache, nausea, small pupils, visual difficulties, painful eyes, running nose, excess salivation, mild weakness and agitation Moderate: dizziness, disorientation, confusion, sneezing, coughing, wheezing, drooling, excess phlegm, vomiting, diarrhoea, marked weakness, difficulty breathing Severe: respiratory difficulty, convulsions, arrhythmias.	Unconsciousness and convulsions within seconds; death in minutes	Atropine Oximes (e.g. pralidoxime chloride) – give within a few hours. Diazepam if seizures.
Mustard	Early: nausea, vomiting, retching, eye irritation, erythema Hours: nausea, fatigue, headache, painful eyes, lacrimation, blepharospasm, photophobia, runny nose, erythema, sore throat, hoarseness, tachycardia, tachypnoea, oedema Days: inflammation, blistering, pus, necrosis, coughing	½–2 hours 2–6 hours 13–72 hours	Decontaminate asap No specific antidote Symptomatic and supportive care only. May need ITU facilities
Chlorine	Inhalation: irritation of eyes, nose and throat, followed by coughing, wheezing, dyspnoea, sputum, bronchospasm, chest pain. Metabolic complications from mild alkalosis to severe acidosis and hypoxaemia. Cardiorespiratory arrest due to hypoxia may occur. Dermal: skin irritation with burns at high concentration.	Irritation occurs rapidly. Chemical pneumonitis and pulmonary oedema can take 12–24 hours.	Removal from contaminated area. No specific antidote. Symptomatic and supportive care only. May need ITU facilities.
Hydrogen Cyanide	Low dose: dyspnoea, headache, dizziness, anxiety, tachycardia, nausea, drowsiness, possibly metallic taste. High dose: hyperventilation, unconsciousness, convulsions, fixed dilated pupils, cyanosis, death.	Unconsciousness and convulsions in seconds. Death in minutes	Removal from contaminated area and resuscitation. Dicobalt edetate, sodium nitrite, amyl nitrate, sodium thiosulphate.
Phosgene	Initial phase: eye irritation, lacrimation, nausea, vomiting, chest tightness, retrosternal discomfort, bronchoconstriction, hypertension, brady or tachycardia. Severe exposure can lead to haemolysis and rapid death. Latent phase: may appear well, symptoms precipitated by exercise. Oedema phase: pulmonary oedema, dyspnoea, bronchospasm, frothy sputum, hypotension, tachycardia, hypoxia, ARDS, death (severity of initial phase not related to severity of oedema).	Major effects usually take hours, but may be immediate pain at exposed sites.	Decontaminate asap Symptomatic and supportive. No specific antidote. May need ITU facilities.

(*Continued*)

Table 4.17.1 (*Continued*)

Chemical/toxin	Clinical effects	Speed of action	Antidotes and treatment (*Expert advice should be sought*)
Lewisite (arsenical compound)	Very irritating, pain on contact. Similar to mustard. Damage to eyes, skin, airways (depending on exposure route). High dose may result in shock.	Seconds to minutes	Decontaminate asap. British-Anti-Lewisite.
Ricin	Fever common. Ingestion causes irritation of oropharynx and oesophagus plus gastroenteritis. Bloody diarrhoea, vomiting, abdominal pain, conjunctivitis, miosis, mydriasis, pulmonary oedema, pneumonia, ARDS, seizures, CNS depression, multiorgan failure, death. Abnormal LFTs, haematuria, proteinuria, high creatinine.	Delayed	Symptomatic and supportive. No specific antidote.
Saxitoxin	Paralytic shellfish poisoning (Chapter 3.89.8). May be confused with nerve agents.	10–120 minutes	Induce vomiting. May need ITU. Avoid Atropine!
Tricothecene mycotoxins ('Yellow rain')	Burning skin, redness, tenderness, blistering, necrosis Dyspnoea, wheezing, coughing, weakness, prostration, dizziness, ataxia. Tachycardia, hypothermia, hypotension.	Minutes	Decontamination of skin. No specific antidote.
Abrin	Depends on route of exposure and dose. Ingestion: Dysphagia, vomiting, diarrhoea, GI bleed. Systemic symptoms, shock, organ failure. Inhalation: Dyspnoea, fever, cough, nausea, chest tightness. Pulmonary oedema, respiratory failure. May also be eye irritation.	Few hours to several days	Decontamination, including administering charcoal if ingested. Symptomatic and supportive. No specific antidote.

See Table 4.17.2 for botulinum toxin and staphylococcal enterotoxin B.
Further detail on these and other agents is available at: https://www.cdc.gov/niosh/ershdb/AgentListCategory.html#Biotoxins

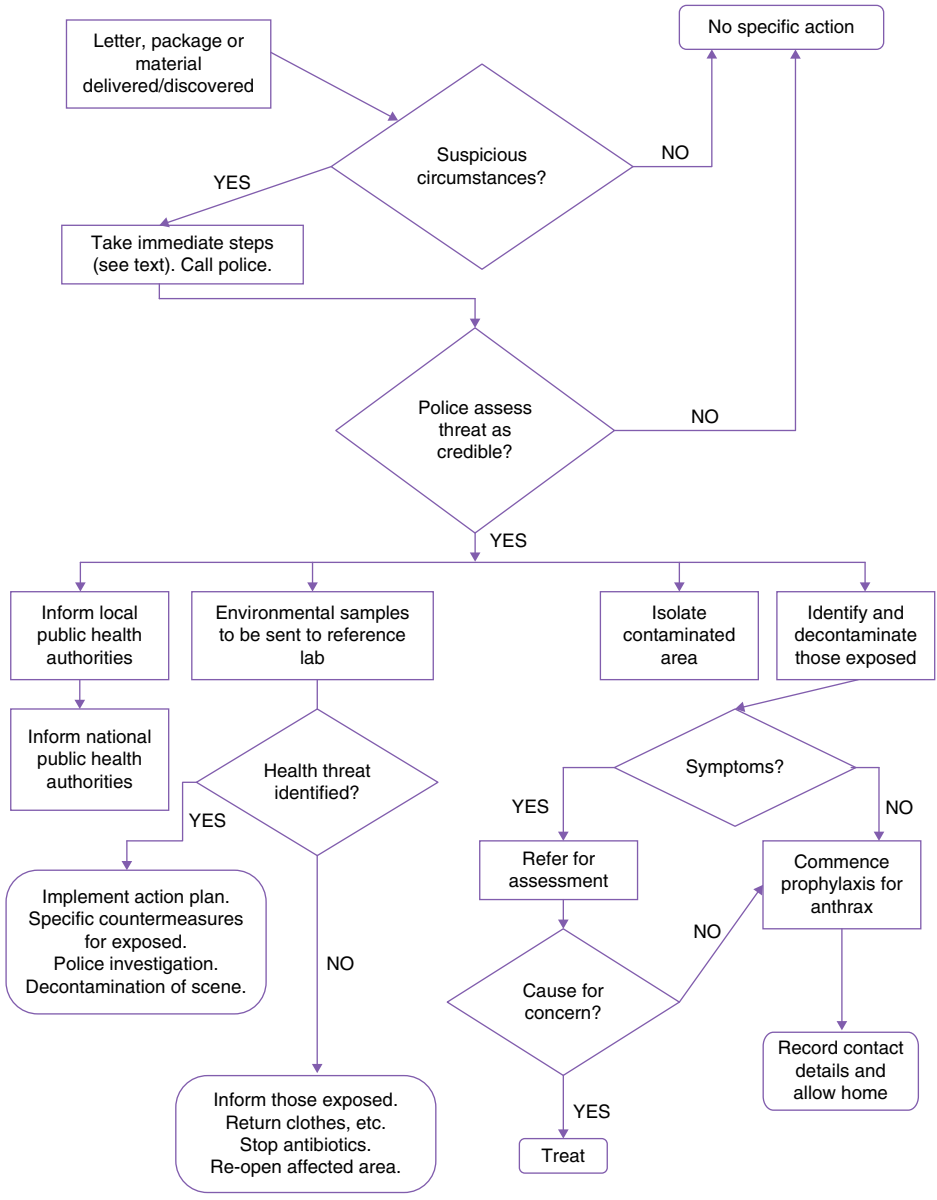

Fig. 4.17.2 Response to suspicious package or material.

outbreaks, particularly if aerosol dispersion has been used. Fortunately most such agents do not spread onwards from person to person, although smallpox and pneumonic plague are important exceptions. Symptoms suggestive of a covert release of a radioactive substance are given in Box 4.16.3 and further detail on radiological hazards can be found in Chapter 4.16.

In addition to notifying local, regional and national public health authorities, a suspected deliberate release must also be

Table 4.17.2 Potential bioterrorism organisms and toxins

Agent (Disease)	Potential route of dissemination	Risk of contracting disease	Incubation period	Ability to spread from person to person	Possible chemoprophylaxis *(to be discussed with national health protection organisation)*	Further details
Bacillus anthracis (Anthrax)	Aerosol (spores)	Moderate	1–6 days	None	1. Ciprofloxacin 2. Doxycycline 3. Amoxycillin	Chapter 3.2
Brucella sp. (Brucellosis)	1. Aerosol 2. Food	High	Days to months	None	1. Ciprofloxacin 2. Doxycycline	Chapter 3.5
Burkholderia mallei (glanders)	Aerosol	High	Days to weeks	Low	1. Doxycycline 2. Ciprofloxacin	Chapter 3.89.1
Burkholderia pseudomallei (Melioidosis)	Aerosol	High	1–7 days	Negligible	1. Ciprofloxacin 2. Doxycycline	Chapter 3.89.1
Chlamydia psittaci (Psittacosis)	Aerosol	Moderate	Range from 4 to 28 days to (usual 5–15 days)	Negligible	Doxycycline	Chapter 3.57
Clostridium botulinum toxin (Botulism)	1. Food/water 2. Aerosol	High	Ranges from a few hours to 8 days (usually 12 hours–3 days)	None	None. Antitoxin available.	Chapter 3.4
Coccidioides immitis (Coccidioidomycosis)	Aerosol	High	1–2 weeks	None	Fluconazole	Stable agent of low lethality. Chapter 3.89.6
Coxiella burnetii (Q Fever)	1. Aerosol 2. Food supply	High	7–32 days (median 19)	Negligible	1. Doxycycline 2. Erythromycin	Chapter 3.58
Ebola/Lassa/CCHF (Viral Haemorrhagic Fevers)	Aerosol	High	3–15 days	Moderate (body fluids)	None available	Chapter 3.82
Francisella tularensis (Tularaemia)	Aerosol	High	2–10 days	None	1. Ciprofloxacin 2. Doxycycline	Chapter 3.79
Hantavirus	Aerosol	High	4–42 days	None	None available	Chapter 3.27
Histoplasma. capsulatum (Histoplasmosis)	Aerosol	High	1–2 weeks	None	Fluconazole	Can persist in soil, but low lethality. Chapter 3.89.6
Influenza virus	Aerosol	High	7–67 hours	High (respiratory)	1. Oseltamivir 2. Zanamivir	Chapter 3.38

Junin Virus	Aerosol	Moderate	7–16 days	Low	None (ribavirin if fever)	Chapter 3.89.2
Machupo virus	Aerosol	Moderate	7–14 days	Low	None (ribavirin if fever)	Chapter 3.89.2
Rickettsia prowazekii (Typhus)	1. Aerosol 2. Infected vectors	High	6–16 days	None	Doxycycline	Chapter 3.89.3
Rickettsia rickettsii (Rocky Mountain Spotted Fever)	1. Aerosol 2. Infected vectors	High	3–10 days	None	Doxycycline	Not very stable but high lethality. Chapter 3.89.2
Rickettsia tsutsugamushi (Scrub Typhus)	1. Aerosol 2. Infected vectors	High	4–15 days	None	Doxycycline	Not very stable and low lethality. Chapter 3.89.2
Rift Valley Fever virus	Aerosol	Moderate	2–12 days	None	None (ribavirin if fever)	Would also cause disease in sheep and cattle. Chapter 3.89.3
Salmonella sp. (Gastroenteritis)	1. Food 2. Water	Low	4 hours–5 days (usually 12–48 hours)	Moderate (faeco-oral)	Ciprofloxacin	Chapter 3.65
Salmonella Typhi (Typhoid fever)	1 Food/water 2. Aerosol	Moderate	3–40 days (median 14)	Low (faeco-oral)	1. Ciprofloxacin 2. Ceftriaxone	Chapter 3.80
Shigella sp. (Dysentery)	1. Food 2. Water	High	12 hours–4 days (usually 1–3 days)	High (faeco-oral)	Ciprofloxacin	Chapter 3.68
Smallpox virus	Aerosol	High	10–17 days	High (aerosol)	None available. Vaccine for contacts.	Chapter 3.70
Staphylococcal enterotoxin B	1. Sabotage 2. Aerosol		1–6 hours	None	None	Stable toxin of low lethality.
Venezuelan Equine Encephalitis virus	Aerosol	High	1–6 days	None	None	Chapter 3.89.3
Vibrio cholerae (Cholera)	1. Food/water 2. Aerosol	Low	1–5 days	Negligible	1. Ciprofloxacin 2. Doxycycline	Chapter 3.11
STEC (Haemorrhagic Gastroenteritis)	1. Food 2. Water	High	6 hours–10 days (usually 2–4 days)	High (faeco-oral)	None	Chapter 3.69
Yellow fever virus	Aerosol	Moderate	3–6 days	None	None	Chapter 3.86
Yersinia pestis (Plague)	1. Aerosol 2. Vectors	High	2–3 days	High (pneumonic)	1. Ciprofloxacin 2. Doxycycline	Chapter 3.54

reported to the police, who will have their own investigative needs. As always, meticulous record keeping is essential.

In addition to standard outbreak/incident investigation steps (case-definitions; case finding; data collection and recording; laboratory investigations; descriptive epidemiology; hypothesis generation and testing), particular issues for management include:

- defining those 'exposed but not ill' and collecting data on them,
- guidance on investigation and best treatment of rare illnesses or variant organisms,
- risk to contacts, including health care staff,
- information for the public,
- communications arrangements,
- environmental contamination.

4.18 Clinical governance and audit

Clinical governance provides a framework in which organisations involved in public health protection are accountable for continuously improving the quality of their services and safeguarding public health by creating an environment in which high standards of service are assured and excellence in health protection practice will flourish. An appropriate system of clinical governance and audit is mandatory in some countries (e.g. the UK, on which the examples used in this chapter are based) and should be considered for all.

The main components for clinical governance can be defined as:

- clear lines of responsibility and accountability for the overall quality of the service provided,
- a comprehensive programme of quality improvement activities,
- clear policies aimed at managing risk, and
- procedures to identify and remedy poor performance.

Responsibility

Clinical governance in the UK emphasises that the organisational responsibility for quality lies at board level, which has a responsibility for encouraging an environment in which quality can flourish. The Board of the organisation needs to set clear objectives for the service. It must also take a particular interest in the organisations 'strategic capacity' to deliver a quality service and assess and control the risk to that capacity. This includes:

- workforce capacity and competence
- leadership
- culture or organisational behaviour
- accountability for key elements of service
- the system of service assessment and improvement
- team working
- adequate finance
- information management and technology
- partnerships
- facilities and equipment, and
- policies and procedures.

The health commissioning organisation is also responsible for ensuring that other health services involved in communicable disease control and health protection (CDC/HP) which may not be under the direct management of the health authority (e.g. laboratories, TB clinics and STI clinics in the UK) have adequate clinical governance arrangements to ensure the quality of their contribution to CDC/HP.

In practice, the executive lead for surveillance, prevention and control of communicable diseases (and other related functions) in many countries locally lies with the local health protection team (HPT) or equivalent, whose Director should therefore take the lead in assuring the quality of the local CDC/HP function. The HPT Director is also responsible for ensuring that support staff provide a quality service by encouraging training, openness, teamwork, the seeking of advice where appropriate, and performance review.

Quality improvement

CDC/HP teams should complete a baseline self-assessment of their strengths and weaknesses. This could cover the following areas:

- Service structure, personnel and skills.
- Arrangements for on-call and for covering leave.
- Access to operational support and infrastructure within healthcare and health protection organisations, e.g. administrative, IT, statistical expertise, communications, public relations.
- Access to specialist advice from internal and external expertise in CDC/HP and complementary disciplines.
- Access to library services, internal quality/evidence base resources and relevant internet sites.
- Arrangements for multiagency working, particularly with Environmental Health Departments and hospital Infection Control Teams. Should include relevant operational support from other health organisations (e.g. healthcare commissioning and provider organisations) for activities such as surveillance, contact tracing and incident control.
- Clarity of roles and responsibilities of different organisations and individuals.
- How well the unit functions as a team.
- Adequacy of surveillance: data access (timeliness, quality), analysis and dissemination.
- Completeness and updating of policies and plans.
- Use of evidence-based practice and mechanisms for disseminating good practice.
- Support to prevention and control in community settings.
- Mechanisms to maintain patient confidentiality.
- Multiagency fora and committees (e.g. district control of infection, immunisation) for agreeing policies and procedures.
- Patient, service user, carer and public involvement.
- Audit and evaluation (see later).

Departments may also wish to invite an external peer reviewer to comment on how their services compare with standard/best practice elsewhere.

The HPT Director should formulate a risk register in the light of the baseline assessment, with a prioritised action plan with clearly assigned responsibilities and timescales. This should then be discussed with the appropriate clinical governance lead for the organisation. Progress on the action plan needs to be regularly reviewed.

One important element of quality improvement will be continuing professional development (CPD) for CDC/HP staff. Each staff member should have a personal development plan, which should be discussed with their line manager. This could include training and updating in:

- Epidemiology and control of communicable diseases.
- Epidemiological methods and statistics for surveillance, outbreaks and research.
- Information technology.
- Infection control and environmental health.
- Management methods such as leadership, organisation, supervisory skills, team working, time management, presentation and media skills.
- New governmental, organisational or professional priorities.
- Non-communicable risks to health (where relevant to team).
- Clinical governance issues such as information governance (particularly patient confidentiality), adverse incident reporting (including near misses) and safeguarding (e.g. for vulnerable patients).

Departmental CPD should include training and updating in on-call issues for all staff on the out of hours rota. Those whose routine work does not include a large component of CDC/HP would benefit from regular refresher/update training (see Box 1.5.1). In the UK, the introduction of a system of professional revalidation means that doctors and some other health professionals need to

be able to demonstrate regularly that they are keeping themselves up to date and remain fit to practise in their chosen field.

Policies for managing risk

Such policies should include:

- Policies and procedures (e.g. standard operating protocols or SOPs) for dealing with common or serious diseases.
- Incident response plans for
  - community outbreaks;
  - hospital outbreaks;
  - water-borne diseases;
  - instances requiring patient tracing, notification and helplines;
  - chemical incidents;
  - radiation incidents;
  - major emergencies;
  - deliberate release.

  These plans need regular revision. If used in an incident, a written report should be produced. If not recently used, consideration should be given to a simulation exercise.
- A regularly updated on-call pack, which includes relevant policies and contact details for staff and other organisations.
- Good documentation of incidents and requests for advice.
- A system for reporting and learning lessons from complaints, problems encountered in delivering service, or poor outcomes. The system should include a mechanism for ensuring that action is taken in response to lessons learned.
- Service standards, based on good practice, to provide a guide for all staff/managers to know what is expected of them, to promote quality and act as a basis for audit. An example of standards that could be set for the acute response function is given in Box 4.18.1.

Rectifying poor performance

In CDC/HP, this primarily revolves around clinical audit and CPD (there is obvious overlap with quality improvement processes) together with identifying and responding to adverse incidents and complaints.

- Clinical audit involves:
  - setting standards,
  - comparing actual performance to standards,
  - rectifying identified deficiencies.
- Audit should involve an element of peer-review: one useful mechanism is to involve staff in neighbouring teams, perhaps as part of a regional audit group. Where national standards do not exist, this group can devise regional ones on which to base audit. Peer-review visits from other teams may also be helpful.
- Suitable topics for audit might be:
  - adequacy of contingency plans,
  - adequacy of district surveillance systems for spotting outbreaks and analysing trends,
  - response of on-call staff (including partner organisations),
  - review of management of an actual outbreak,
  - review of response to (randomly selected) cases of key infections/hazards,
  - immunisation uptake rates and methods used to improve them,
  - appropriateness of local HIV prevention strategy.
- A report should be written on all significant outbreaks and incidents detailing the lessons learnt. More minor episodes (e.g. sporadic case of typhoid) can be discussed informally, for example at weekly departmental surveillance and information meetings.
- Discussion and monitoring of formal and informal complaints from the public or health professionals. Staff members should also contribute to identifying adverse incidents and 'near misses'.
- It is important in all cases to ensure that someone is responsible for ensuring that identified deficiencies in the service are rectified. This should include identifying corrective action to rectify the immediate problem, preventative action to prevent a recurrence, and sharing any lessons learned with others.

Box 4.18.1 Example of potential case-management standards for the acute response team

Reporting of cases outbreaks and incidents

Each HPT has a standard documented and audited system for:

- Recording incoming notifications, phone calls, e-mails or other requests/referrals.
- Alerting others within the HPT to new reports.
- Alerting other HPTs, specialist teams and external partners as appropriate.
- Providing real time access to all information about cases/incidents for all relevant HPT staff.
- Checking whether a newly reported case may be linked to others previously reported.

Clinical response

- Each HPT should have Standard Operating Procedures (SOPs) for the investigation and public health management of individual cases of specific infections, in line with current best practice.
- Each HPT should have agreed multiagency plans for investigating and managing outbreaks and incidents.
- All staff should receive induction training and updating on SOPs and plans.
- Cases, outbreaks and incidents are regularly audited against SOPs.

Clinical supervision and leadership

- Responsibility for every case or incident is held by a named consultant[1] (although action within SOPs and/or individual competence may be delegated to other members of the acute team or to an appropriately qualified Case Worker/Manager (e.g. a health protection nurse).
- There is a named accountable Duty Consultant (see note 1) every day, who will be responsible for all new cases and incidents until any formal handover to another Consultant (see note 1).
- There is a clinical review of all new or active issues each day by the Duty Consultant (see note 1).
- Management of significant outbreaks clusters and incidents are discussed with appropriate specialists and/or experienced colleague(s).
- A regular (e.g. weekly) team meeting to review of all open cases and incidents is held.

Record keeping

The following are fully documented:

- Initial and updated risk assessments and reasoning.
- Decisions taken.
- Advice given and rationale.
- Actions taken.
- Any outstanding actions and timescale.
- Communications (inform, alert, advise, requests) with other individuals or agencies.
- Outcomes or subsequent problems.
- Closing of case/incident and lessons learned.

Handover of responsibility

- Formal handover should occur where responsibility passes from one individual to another, for example:
  - Where responsibility passes from an in-hours team to out-of-hours and vice-versa
  - Where responsibility passes from one in-hours team to another
  - Where responsibility passes from the duty (acute response) team to another team and vice-versa, (and from an individual case worker to another individual case worker in the case of leave/absence)
- Handover should involve a full update and be documented.
- Each HPT must have a robust system for scheduling actions for future dates.
- Each HPT should have a process in place for review and reallocation of the workload and for outstanding actions of an unexpectedly absent colleague (e.g. due to sick leave).

Source: Adapted from list created by Dr. Amal Rushdy and other HPA staff

[1] or other appropriately qualified senior person

It is clear that the quality of CDC/HP work and the ability to carry out clinical governance and audit are both dependent upon the level of resources available to the CDC/HP department and the overall culture of the organisation. Nonetheless, the individual practitioner can use his/her leadership, management and professional skills to maximise the resources available and to prioritise their use: clinical governance is a tool that can be used to further those objectives.

4.19 Global health security

The World Health Organization (WHO) defines global health security (GHS) as the 'activities required … to reduce the vulnerability of people around the world to new, acute, or rapidly spreading risk to health, particularly those that threaten to cross international borders'. A number of international initiatives have been taken to strengthen preparedness and response as part of GHS. While communicable diseases are at its core, GHS deals more broadly with all kinds of global threats related to biological, chemical, radiological and nuclear threats (CBRN). These threats may be intentional (e.g. the Sarin attack on the Japanese subway or the 2001 US anthrax attacks), accidentally (e.g. the Bhopal gas tragedy) or naturally occurring (e.g. pandemic influenza or Ebola virus disease). A number of international initiatives are supporting GHS, all building on a broad all-hazard approach.

International health regulations

A corner stone in GHS is the international disease reporting and capacity building requirements under the International Health Regulations (IHR) (see Chapter 5.1). The new WHO health emergencies reform, based on the experience from the West Africa Ebola outbreak, was initiated to strengthen the operational and co-ordinating capacities of the WHO to respond to major international health threats. The priorities of the new WHO Health Emergencies Programme include:

- Increasing core capacities in priority countries in Africa, the Middle East and Asia;
- Optimising delivery at country level through standardised strategies and service packages for emergency response;
- Expanding partnership arrangements including the Global Outbreak, Alert and Response Network (GOARN) and emergency medical teams and finalising standard operating procedures for significant outbreaks in co-ordination; and
- Supporting country preparedness through an all hazards approach, for example through joint assessments of country capacities to implement the IHR using the Joint External Evaluation tool.

Sendai framework

Another UN initiative supporting GHS, but having an even broader scope, is the Sendai Framework for Disaster Risk Reduction 2015–2030 under the United Nations Office for Disaster Risk Reduction (UNISDR) (http://www.unisdr.org/we/coordinate/sendai-framework). The Sendai Framework emphasises the responsibilities of each State to prevent and reduce disaster risk, including through international co-operation. The four priority areas under the framework include:

- Understanding disaster risk,
- Strengthening disaster risk governance to manage disaster risk,
- Investing in disaster risk reduction for resilience, and
- Enhancing disaster preparedness for effective response and to 'Build Back Better' in recovery, rehabilitation and reconstruction.

EU initiatives

The EU Decision 1082/2013/EU on serious cross-border threats to health (see Chapter 5.2) has incorporated the IHR reporting into an EU legislative context with regular mandatory

reporting by the Member States on their state of preparedness, but also having provisions for threat detection (surveillance), early warning (EWRS), a closer coordination of health threats response under the EU Health Security Committee and otherwise supporting country capacities, for example through a joint procurement mechanism. In the broader global CBRN context, the EU is working in partnership with 54 countries to encourage local ownership of CBRN action plans, policies and project proposals. This is done under the umbrella of an EU CBRN Risk Mitigation Centres of Excellence Initiative (EU CBRN CoE) (http://www.cbrn-coe.eu). The EU CBRN CoE aims to 'strengthen regional security by increasing local ownership, local expertise and by ensuring long-term sustainability through this dynamic network that continues to evolve'. A large number of projects are funded under this mechanism with focus on networking, training, facilitating co-operation and developing methodology and guidance.

Global health security initiative

The Global Health Security Initiative (GHSI) (www.ghsi.ca) was launched in November 2001, following the 9/11 events and the US anthrax attacks, by Canada, the EU, France, Germany, Italy, Japan, Mexico, the UK and the USA, with the WHO as an expert advisor. The GHSI was envisaged from the start as an informal platform to support GHS, through close co-operation and sharing of experiences and information around issues related to procurement of vaccines, development of rapid testing, vaccine research, global disease surveillance, emergency preparedness planning, improved linkages between laboratories and preparedness and response to CBRN threats. Later pandemic influenza preparedness was added to the scope. The GHSI operates through annual ministerial meetings and between the meetings via a Global Health Security Action Group (GHSAG) of senior officials.

Global health security agenda

A more recent initiative is the Global Health Security Agenda (GHSA), which is a US-funded framework, including 31 countries, to improve global response to disease outbreaks and close gaps in surveillance and response. The GHSA builds upon other existing programmes and initiatives to improve health and supports the full implementation of the 2005 IHR and the World Organization for Animal Health (OIE) Performance of Veterinary Services (PVS) Pathway. The GHSA aims to stimulate investments and actions to *prevent* avoidable epidemics, *detect* threats early and *respond* rapidly. GHSA has developed targets related to national legislation, antimicrobial resistance, zoonotic diseases, food safety, biosafety and biosecurity, immunisation, national laboratory systems, real-time surveillance, reporting, workforce development, preparedness, emergency operation centres (EOCs), linking public health and security authorities, medical countermeasures and personnel deployment, and risk communication. An external assessment tool has been developed and reports are available for a number of countries, including three from the EU (Finland, Portugal and the UK).

Section 5
Communicable disease control in Europe

5.1 WHO and International Health Regulations

World Health Organization

The World Health Organization (WHO) is a United Nations organisation with a strong mandate in global public health. It is organised in a central headquarters in Geneva, with six regional offices. The Regional Office for Europe, located in Copenhagen, serves 53 countries in Europe and Central Asia, including all the EU countries.

Core functions for WHO include provision of technical support and capacity building, knowledge dissemination, health monitoring, shaping research agendas and establishment, promotion and monitoring of norms. The organisation works closely with international and national partners for joint actions, and relies on voluntary contributions for more than 70% of its budget.

In the area of communicable diseases, WHO mainly works on global health control programmes such as HIV, hepatitis, tuberculosis and malaria. Following the successful global eradication of smallpox in 1979, WHO is also working to eradicate polio, and eliminate measles and rubella through promotion of the expanded programme on immunisation, and provide global leadership on influenza surveillance and control.

The 2014 Ebola outbreak in West Africa exposed several weaknesses in the ability of the WHO to respond effectively to a major health emergency. This was the starting point for the ongoing reform of the WHO's work in health emergency management and the setup of a new Health Emergencies Programme, designed to 'bring speed and predictability to WHO's emergency work, using an all hazards approach, promoting collective action, and encompassing preparedness, readiness, response and early recovery activities'. With increased resources, supplies and training in countries, the programme will develop standardised strategies and services for emergency response, expand partnership arrangements and support country preparedness. The Global Outbreak Alert and Response Network (GOARN), a technical collaboration of institutions and networks with the capacity to combat the international spread of outbreaks through technical assistance in affected outbreak areas, will work under the new programme.

International Health Regulations

In today's globalised world, many infectious diseases have the potential to spread from one part of the world to another in a very short time. Recent examples are the 2009 H1N1 pandemic, the West Africa Ebola outbreak and the global spread of Zika virus infection. To respond effectively to infectious disease outbreaks and other public health risks (e.g. chemical and nuclear accidents) with the potential to affect many countries, the new International Health Regulations (IHR) (http://www.who.int/ihr/en) have been set up as an international legal instrument that is binding on 194 countries, including all the WHO Member States.

The new IHR, which entered into force in June 2007, aim to prevent the spread of disease and public health risks while at the same time limiting unnecessary interference with international travel and trade. The IHR provide a framework for the international co-ordination of information sharing, assessment and public health response to events that may constitute a 'public health emergency of international concern' (PHEIC).

Under the IHR, designated National IHR Focal Points in each country are obliged to report potential PHEICs to the WHO within

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

24 hours of assessment and to continuously provide the organisation with updated information. The WHO then forwards information, in confidence, to other states' parties that may need this information for public health actions. Within the EU, the National IHR Focal Points are normally identical with the EU Early Warning and Response (EWRS) Focal Points (see Chapter 5.2), and the two systems are to a large degree harmonised.

The Director General of the WHO also has the right to issue temporary recommendations, including health measures to be implemented in response to a PHEIC. The recommendations may include measures related to individuals (mainly travellers) and transportation of goods. The recommendations on individuals, which should respect travellers' dignity, human rights and fundamental freedom, may include the following:

- review travel history in affected areas,
- review proof of medical examination and any relevant laboratory analysis,
- require medical examinations,
- review proof of vaccination or other prophylaxis,
- require vaccination or other prophylaxis;
- place suspect persons under public health observation,
- implement quarantine or other health measures for suspect persons,
- implement isolation and treatment, where necessary, of affected persons,
- implement tracing of contacts of suspect or affected persons,
- refuse entry of suspect and affected persons,
- refuse entry of unaffected persons to affected areas, and
- implement exit screening and/or restrictions on persons from affected areas.

Core capacities

The IHR requires countries to have the capacity to detect, assess, notify and respond to PHEIC and other public health risks. This requires every country to fulfil certain minimum core capacities throughout their territories. Eight core capacities are defined and relate to:

1 National legislation, policy and financing
2 Coordination and national focal points communications
3 Surveillance
4 Response
5 Preparedness
6 Risk communication
7 Human resources and
8 Laboratory capacity.

To have IHR fully implemented thus requires substantial capacity building in many countries. Since 2015, there has been a move from 'exclusive self-evaluation' to more transparent external evaluations based on a joint external evaluation tool.

Point of entry

Also regulated under the IHR is the responsibility for countries to designate specific airports, ports and ground crossings with capacity at all times:

- to provide access to appropriate medical services, staff, equipment and premises for prompt assessment and care of ill travellers;
- to provide access to equipment and personnel for the transport of ill travellers to an appropriate medical facility;
- to provide trained personnel for the inspection of conveyances;
- to ensure a safe environment for travellers using point of entry facilities, including potable water supplies, eating establishments, flight catering facilities, public washrooms, appropriate solid and liquid waste disposal services and other potential risk areas; and
- to provide as far as practicable a programme and trained personnel for the control of vectors and reservoirs in and near points of entry.

For responding to events that may constitute a PHEIC the entry points should also have capacity to:

- provide appropriate public health emergency response by establishing and maintaining a public health emergency contingency

plan, including the nomination of a co-ordinator and contact points for relevant point of entry, public health and other agencies and services;
- provide assessment of and care for affected travellers or animals by establishing arrangements with local medical and veterinary facilities for their isolation, treatment and other support services that may be required;
- provide appropriate space, separate from other travellers, to interview suspect or affected persons;
- provide for the assessment and, if required, quarantine of suspect travellers, preferably in facilities away from the point of entry;
- apply recommended measures to disinsect, derat, disinfect, decontaminate or otherwise to treat baggage, cargo, containers, conveyances, goods or postal parcels including, when appropriate, at locations specially designated and equipped for this purpose;
- apply entry or exit controls for arriving and departing travellers; and
- provide access to specially designated equipment, and to trained personnel with appropriate personal protection, for the transfer of travellers who may carry infection or contamination.

Other requirements under the IHR

The IHR also include a number of other requirements all aimed at diminishing the risk of transmission of communicable diseases and other public health risks across borders.

Technical requirements pertaining to conveyances and conveyance operators

Conveyance operators shall facilitate:
- inspections of cargo, containers and conveyance;
- medical examinations of persons on board;
- application of other IHR health measures; and
- provision of relevant public health information requested by the country.

Conveyance operators shall provide valid sanitation and health certificates to the national authorities.

Specific measures for vector-borne diseases

Disinfection and other vector-control measures shall be recommended for conveyances arriving from certain risk areas. The WHO shall on a regular basis publish lists of such areas, and also issue recommendations how such measures should be carried out. To prevent autochthonous spread of infections via imported vectors, countries shall establish vector control programmes for the near vicinity (minimum 400 m) from point of entry facilities involving passengers or goods from risk areas.

Requirements concerning vaccination or prophylaxis for certain diseases

In addition to vaccinations normally recommended for travel, the IHR can specifically list diseases for which proof of vaccination or prophylaxis may be required for entry to a country. Countries are obliged to offer vaccines or prophylaxis of suitable quality for these diseases and issue international certificate of vaccination or prophylaxis.

Currently, this list includes yellow fever. Yellow fever vaccination may also be required for leaving areas with yellow fever transmission (as determined by the WHO). Countries have the right to quarantine persons arriving from areas with yellow fever up until the day the vaccination certificate becomes valid (10 days post-vaccination) or the full incubation period (6 days), whichever occurs first. India, which is particularly concerned by the possible introduction of yellow fever on its territory, has made a specific reservation regarding yellow fever, including the right to continue all health measures stipulated in previous IHR from 1969.

5.2 Collaboration within the European Union

In 2010, the population of the (then) 27 EU Member States surpassed half a billion people. An unwanted side effect of the free movement of people, goods, services and money within the EU is free movement of microbes. This requires effective, coordinated measures at the EU level for the control of cross-border health threats due to communicable diseases. Although mainly the responsibility of the Member States, public health has been covered by EU actions since the Maastricht Treaty of 1992. The three EEA/EFTA countries (Norway, Iceland and Liechtenstein) contribute to the EU public health budget and are included in all EU activities in this field.

The European Commission is responsible for strategy and policy making at EU level in the area of health. It has a part in the decision-making process, notably by introducing new legislation and overseeing the correct implementation of the Treaties and European Law. The main instrument of the Commission for implementing EU health strategies is the third EU Health Programme (2014–2020), with an overall budget of €450M over the period, through which actions and programmes can be funded. The programme is administered by the Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) (http://ec.europa.eu/chafea). Communicable disease control is under the responsibility of the Directorate-General for Health and Food Safety (DG SANTE) (https://ec.europa.eu/info/departments/health-and-food-safety_en). Important policy areas include preparedness and response, antimicrobial resistance, patient safety and vaccine issues. DG SANTE also coordinates all issues related to risk management at the EU level.

Legal framework

The legal framework for EU collaboration in the area of communicable disease is formalised in Decision 1082/2013/EU of the European Parliament and of the Council (1998) on serious cross-border threats to health. The Decision lays down rules on epidemiological surveillance, monitoring, early warning of, and combating serious cross-border threats to health, including preparedness and response planning related to those activities, in order to co-ordinate and complement national policies.

Decision 1082 requires of the Member States to regularly report their state of national preparedness in order to facilitate interoperability of these plans. This reporting includes the information reported by the countries under the International Health Regulations (IHR), which is now part of the EU legislation. Preparedness focus is no longer on specific diseases but takes an all-hazard approach with an intersectoral dimension.

The Early Warning and Response System (EWRS) is an important risk management tool, which enables the European Commission and the public health authorities in the Member States to exchange information and co-ordinate measures against major outbreaks and other health threats of importance to more than one country. The EWRS system is operated by the European Centre for Disease Prevention and Control (ECDC) on the behalf of the Commission, and most messages are also accessible to the WHO. The system is extensively used during major public health events.

The legislation provides the legal basis for the EU-level epidemiological surveillance system operated by the ECDC, including a common list of diseases under surveillance, case definitions and laboratory methods. Other articles of Decision 1082 cover joint procurement of medical countermeasures (e.g. pandemic vaccines and personal protective equipment), public health risk assessments, co-ordination of response and recognition of emergency situations.

European Centre for Disease Prevention and Control

ECDC is an independent expert agency of the EU, set up in 2005 following the global SARS epidemic in 2003. Its role is to provide

independent scientific and technical advice and support to the Member States on all issues related to communicable disease control. The agency has some 300 staff members and in-house consultants and operates on an annual budget of approximately €60 M. As public health action (risk management) is the responsibility of the countries and the Commission, ECDC has only a supporting role in this field. With its limited staff and budget, the strength of ECDC is its ability to co-ordinate and draw from the extensive resources in the countries. The main public health functions of ECDC include the following:

- *Epidemiological surveillance and networking of laboratories*: ECDC operates the European Surveillance System (TESSy), collecting case data on some 50 notifiable diseases. As ECDC does not have any laboratories, the centre works with a network of national European reference laboratories.
- *Preparedness and response*: on a 24/7 basis, the ECDC Emergency Operation Centre (EOC) detects and assesses threats, and provides support for response to Member States and the Commission.
- *Scientific advice*: public health decisions have to be based on independent scientific evidence. Scientific issues arising in the area of communicable diseases vary widely, ranging from questions of clinical medicine and epidemiology through to standardisation of laboratory procedures. ECDC brings together scientific expertise in specific fields through its various EU-wide networks and via ad hoc scientific panels and expert groups.
- *Training*: ECDC organises a two-year fellowship programme for young professionals to support European surveillance and response capacities. The programme has one path for intervention epidemiology (EPIET) and one for public health microbiology (EUPHEM). ECDC also supports lifelong learning for mid-career and senior professionals through its Continuous Professional development Programme.
- *Health communication*: ECDC provides independent information to experts, policy makers and the general public, and promotes coherence in risk communication messages at EU level. ECDC also co-operates with the countries on public health campaigns (e.g. by co-ordinating the annual European Antibiotic Awareness Day, 18 November). The journal *Eurosurveillance* has been published by the ECDC since 2007 with full editorial independence. It is published electronically every Thursday and with a very short publishing time for rapid communications it provides very timely information on ongoing outbreaks.
- *Country support and capacity building*: ECDC provides technical support and capacity building on all issues within its mandate, including preparedness. This is done not only through training activities, but also through country visits by invitation, in which ECDC experts as well as experts from other countries review present systems and suggest improvements. ECDC mainly works with the EU/EEA countries via a mechanism with a Co-ordinating Competent Body in each country, whose experts constitute the networks in various fields. Increasingly ECDC also has a role in integrating the candidate and potential countries and otherwise work on the global public health arena through various Commission mechanisms.
- The work on *specific diseases* is organised in seven disease programmes; the Antimicrobial resistance and healthcare-associated infections programme, the Emerging and vector-borne diseases programme, the Food- and water-borne diseases and zoonoses programme, the Influenza and other respiratory viruses programme, the HIV, sexually transmitted infections and viral hepatitis programme, the Tuberculosis programme and the Vaccine preventable diseases programme.

Other agencies and institutions

Other EU agencies with a public health mandate with the EU family include the European Food Safety Agency (EFSA)

in Parma (http://www.efsa.europa.eu), the European Medicines Agency (EMA) in London (Amsterdam from 2019) (http://www.ema.europa.eu), the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in Lisbon (http://www.emcdda.europa.eu) and the European Environment Agency (EEA) in Copenhagen (https://www.eea.europa.eu). All these agencies work in close collaboration and partnership with other actors in the field, notably the national institutes of public health in Europe and beyond, the WHO and other EU agencies in related fields.

EFSA was set up in 2002 following a number of European food crises in the late 1990s, notably the epidemic of bovine spongiform encephalopathy (BSE) in the UK and other countries, with the subsequent emergence of the new variant Creutzfeldt-Jakob's disease (nvCJD). Like ECDC, EFSA operates with an independent risk assessment mandate, while risk management and policy lies with the Commission and the Member States.

EFSA produces scientific opinions and advice on food and feed safety, nutrition, animal health and welfare, plant protection and plant health, informing policies and legislation in the field. Most of EFSA's work is responding to requests from the EU institutions and the Member States.

5.3 Detailed national example: organisational arrangements for health protection, England, 2017

(For other EU/EEA countries, intruding other parts of the UK, see Chapters 5.4–5.34.)

Health protection describes the subset of public health activities aimed at protecting individuals, groups and populations from infectious diseases and environmental hazards such as chemical contamination and radiation. A major re-organisation of health protection services in England took place in 2013, including the merger of the Health Protection Agency into a new agency called Public Health England (PHE) and the transfer of some public health responsibilities from the NHS to Local Authorities (LAs), including the post of the local Director of Public Health (DPH).

Public Health England

PHE provides support and leadership on public health, including health protection. PHE advises government on health protection policies and programmes, it provides authoritative information and advice to professionals and the public, and it responds to emerging threats to public health and health emergencies, including outbreaks and deliberate release incidents. PHE also has a key role in health emergency planning as a 'Category 1 Responder' under the Civil Contingencies Act 2004. PHE has national, regional and local tiers.

The local tier of the PHE in England comprises nine local Centres, each of which contains one or more Health Protection Teams (HPTs), together with other local public health staff involved in population health improvement and healthcare service improvement, and outposted specialist teams from national directorates. Each HPT is staffed by Consultants in Communicable Disease Control (CCDCs, now sometimes called Consultants in Health Protection [CHP]), health protection practitioners (often from a nursing background) and other support staff. The HPT undertakes local surveillance, investigation and management of cases, incidents and outbreaks and the delivery of local and national action plans in collaboration with Local Authorities, NHS Clinical Commissioning Groups (CCGs), hospital trusts and others (see Table 5.3.1).

PHE also has a number of national Directorates that work on national priorities and provide support to local centres and other stakeholders. National Directorates include:

- the new National Infection Service (NIS), which employs specialist teams of

Table 5.3.1 Core activities of local health protection teams

1 The surveillance of infectious diseases (working with NIS), and tracking health protection incidents and exposures, to inform local action.
2 Alerting partners to emerging infectious and environmental threats to health.
3 Responding to cases of communicable disease and exposure to infectious and environmental hazards.
4 The timely investigation and management of local incidents, outbreaks and trends and clusters of disease (supported by NIS) and contributing to the investigation of national incidents.
5 The provision of evidence-based specialist health protection advice for action across the full range of health protection hazards to local stakeholders.
6 Preparing for and taking action to manage and control health protection incidents and emergencies.
7 Working with stakeholders to identify training and planning needs and providing specialist input to the design and delivery of training.
8 Working with stakeholders to the develop strategies and plans to protect health.
9 Supporting NHS and LA partners in their statutory responsibilities.
10 Leading or contributing to prevention and control programmes and other actions to protect health.

epidemiologists, microbiologists and others: these include a Field Services department which includes outposted specialists in field epidemiology, public health microbiology and food, water and environment (FWE) microbiology at each local Centre. It is planned that there will be five other specialist national departments to cover healthcare associated infections and antimicrobial resistance (HCAI and AMR); immunisation and countermeasures; blood safety, hepatitis, sexually transmitted infections and HIV; tuberculosis, acute respiratory, gastrointestinal, emerging/zoonotic, and travel/migrant health (TARGET); and a time-limited whole genome sequencing development and implementation service. Cross-cutting NIS services include NIS laboratories, which includes the operation of PHE's national reference laboratories and regional public health laboratories.

- the Health Protection Directorate, which includes the Centre for Radiation and Chemical Hazards (CRCE, which provides advice, research and services to protect the public from hazards resulting from exposure to chemicals and poisons, ionising and non-ionising radiation, ultrasound and infrasound and some aspects of noise from staff based in its national centre in Chilton and in various PHE Centre locations); the Emergency Response Department (ERD, which works with partners to ensure that healthcare professionals are able to respond to emergencies, including the deliberate or accidental release of chemical, biological, radiological or nuclear substances); PHE's Antimicrobial Resistance Programme; the Healthcare Public Health team; and PHE Medical Director functions. PHE also has a Global Public Health team.
- the Health Improvement Directorate, which has teams that cover alcohol, drugs and tobacco; diet and obesity; health equity and mental health; healthy people; screening and quality assurance; knowledge and intelligence; national disease registration; and research, translation and innovation.

Department of Health and Social Care

The overall aim of the Government's Department of Health and Social Care (DHSC) is to improve the health and wellbeing of the population by supporting activity to protect, promote and improve health and securing the provision of high quality health- and social-care services.

Local government Authorities

Local government (LAs) in England and Wales is based on elected councils, which are accountable to the residents that they serve. In most

areas there are two levels: a county council and a district council, although some areas (usually cities and large towns) have single 'unitary' authorities. County councils provide most public services, including schools, social services (which includes residential accommodation for those who are in need of care, because of age, illness or disability), waste disposal, civil defence, highways, consumer protection and planning and public transportation. Each county has several district councils that provide local services, including environmental health, housing, planning, refuse collection, cemeteries and crematoria, markets and fairs, licensing activities and leisure and recreation. Police and fire services are organised at county level but under separate organisational structures. Councils consist of elected members (councillors) and exercise their powers through committees, subcommittees or delegation to salaried officers. Officers acting on behalf of a council must ensure that the powers and responsibilities they exercise have been lawfully delegated to them by the elected members. Often legislation requires that the council exercises its power through a specific officer, usually referred to as the proper officer. For some public health legislation the proper officer would be the CCDC.

Since 2013, LAs have been responsible for improving the health of their local population and for some public health services including most sexual health services and services aimed at reducing drug and alcohol misuse. LAs also have a duty to promote the preparation for and participation in health protection arrangements. These responsibilities are overseen by Health and Wellbeing Boards (HWBs), which are statutory committees of all upper-tier (and unitary) LAs and are intended to: improve the health and wellbeing of the people in their area; reduce health inequalities; and, promote the integration of services. LAs and HWBs are supported in these functions by a Director of Public Health (DPH), a local post that transferred from the NHS to upper tier LAs, along with support staff in 2013. Key indicators for LAs have been set out by DHSC in the Public Health Outcomes Framework.

The responsibilities of *environmental health departments* include food safety, air quality, noise, waste, health and safety, water quality, port health controls at air and sea ports, refuse collection and pest control. Environmental health officers (EHOs) investigate outbreaks of food- and water-borne infections, advise on and enforce food safety legislation, inspect food premises and investigate complaints and provide food hygiene training. EHOs liaise with a wide range of other professionals including the CCDC, general practitioners, teachers, microbiologists and veterinarians. Other agencies with a role in communicable disease control are summarised in Table 5.3.2 and some of the key individuals in Table 5.3.3.

National Health Service

The UK National Health Service (NHS) was set up in 1948 and provides a comprehensive range of health services, usually free of charge, for people ordinarily resident in the UK. NHS services are commissioned by a national body, NHS England, and by local Clinical Commissioning Groups (CCGs) and are provided mostly by NHS Trusts and General Practitioners, but also, increasingly, by private companies. CCGs are responsible for commissioning healthcare services to meet the reasonable needs of patients registered with their member practices, together with any unregistered patients living in their area, except for those services that NHS England or LAs are responsible for commissioning. This includes CCG responsibility for treatment of infectious diseases. Some public health services, including national immunisation and screening services, are commissioned by the national body NHS England.

Table 5.3.2 Other agencies with a role in communicable disease control

The Food Standards Agency (FSA)	A non-ministerial Government Department, governed by its own Board: members are appointed by Health Ministers in England, Wales and Northern Ireland. Responsible for protecting public health in relation to food. Particularly relevant to surveillance, investigation and control of food-borne pathogens, such as *Campylobacter*, *Salmonella* and STEC: FSA will be involved in the investigation and management of most significant food-borne outbreaks. Further information at: www.food.gov.uk
Animal and Plant Health Agency (APHA)	An executive agency, sponsored by the Department for Environment, Food & Rural Affairs (Defra), the Welsh Government and The Scottish Government. Works to safeguard animal and plant health for the benefit of people, the environment and the economy. Functions include following up reports of diseases that are notifiable in animals. Of particular relevance to zoonotic diseases, such as avian influenza, bovine TB, rabies, psittacosis and Q fever, and control of food-borne zoonoses in animals. Further information at: https://www.gov.uk/government/organisations/animal-and-plant-health-agency
Environment Agency (EA)	EA is an executive non-departmental public body, sponsored by the Department for Environment, Food and Rural Affairs. It works to create better places for people and wildlife, and support sustainable development in England. Responsible for assessing, monitoring and reporting on waste disposal and the impact of the environment on human health. May be involved in incidents in which there is environmental contamination. Further details at: https://www.gov.uk/government/organisations/environment-agency
Health and Safety Executive (HSE)	HSE is a non-departmental government body sponsored by the Department for Work and Pensions (DWP). Responsible for the encouragement, regulation and enforcement of workplace health, safety and welfare. Reduces risks to workers and the public from work activities. Controls infectious disease risks in the workplace, including investigating Legionnaires' disease. Many NHS premises are subject to HSE regulation. Further details at: www.hse.gov.uk
The Drinking Water Inspectorate (DWI)	Ensures safety of public water supplies and regulates the performance of water companies in England and Wales. Particularly relevant to control of water-borne pathogens, such as *Cryptosporidium*. Further information at: www.dwi.gov.uk
Occupational Health Services	Provided by employers. Advise managers and employees about the effect of work on health and of health on work, minimises infectious hazards at work, including advising on NHS occupational health (the NHS employs about 1.6 million people in the UK). This includes advising on immunisation of staff to protect themselves and vulnerable patients, advising workers with infectious diseases (e.g. blood-borne viruses) and ensuring access to advice, testing and prophylaxis for exposure to infections or hazards (e.g. needlestick injuries).
Defence Medical Services (DMS)	An umbrella organisation within the Ministry of Defence, which organises all medical, dental and nursing services across the British Armed Forces. Led by the Surgeon-General. Further information at: https://www.gov.uk/government/groups/defence-medical-services

Table 5.3.3 Agencies and individuals involved in local health protection

Public Health England	Consultant for Communicable Disease Control Consultant/Specialist in Health Protection Health Protection Nurse Regional Public Health, National Reference and FWE laboratories Field Epidemiologist Chemical and radiation hazard specialists Health Emergency Planning Adviser
Local authority departments (environmental health, public health, education, social services)	Environmental Health Officers Director of Public Health and support staff Health and Wellbeing Board members Trading Standards Officers Teachers, social workers, home carers Residential home managers, safety managers
NHS Trusts	Director for Infection Prevention and Control Infection Control Doctor Medical microbiologist and local laboratory staff Infection Control Nurses Infectious disease specialist TB specialist, TB nurse advisers Genito-urinary medicine specialist, GUM health adviser Health Visitors, School Nurses, District Nurses
NHS Clinical Commissioning Groups	Medical Director CCG Board Commissioning staff Community Infection Control Nurse
Primary care providers	General practitioners, practice nurses and other practice staff, community pharmacists, general dental practitioners
Private nursing homes, residential homes	Managers, nursing staff, carers
Occupational health departments	Occupational health doctors and nurses
Day nurseries	Managers, nursery nurses
General public	Citizens, consumers, newspapers, radio, TV
Water companies	Quality managers

5.4 Austria

Austria (population 8726000) is a federal republic with nine federal states (*Bundesländer*), subdivided into 95 districts (*Bezirke*) and 15 autonomous cities (*Statutarstädte*).

The prevention, control and surveillance of infectious diseases are regulated by federal law. The responsibility for the public health services, including control of communicable diseases, is shared between the Ministry of Health and Women's Affairs at the federal level, and the states and local health departments within the states. The Ministry of Health and Women's Affairs has a key role, with responsibility for implementation of the legislation, national surveillance and international contacts (EU and WHO).

In each federal state, the infectious disease control concerning food-borne infections, including surveillance, is the responsibility of a State Department for Health, led by the State Health Director. Despite the lack of a formal legal mandate, the State Health Director also co-ordinates control of non-food-borne outbreaks affecting more than one district. At the level of districts and autonomous cities there are District/City Health Offices. Specific public health functions are carried out by antenatal clinics, vaccination centres, AIDS help centres, and so on.

The Austrian Agency for Health and Food Safety (AGES) is a state-owned enterprise that carries out expert tasks in the area of food safety and communicable disease control on behalf of the Austrian Government. The agency has activities in the area of epidemiology, microbiology (reference laboratory functions), threat detection, outbreak control and supports the national surveillance system for infectious diseases.

National competent authorities for communicable disease control

- Ministry of Health and Women's Affairs (Ministerium für Gesundheit und Frauen; BMG): http://www.bmgf.gv.at
- Austrian Agency for Health and Food Safety (Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH; AGES): https://www.ages.at/startseite/

Surveillance of communicable diseases

Surveillance of communicable diseases is regulated by federal law, and the Ministry of Health and Women's Affairs is responsible for introducing changes in the statutory notification system. Some 71 diseases are notifiable by physicians and laboratories. No financial incentives are given.

The reporting is hierarchical with first-level reporting to the District Health Offices which report into an electronic reporting system, which can be accessed at any time by the health authorities at state and national level within the data protection rules. Data processing is performed by AGES and dissemination is carried out by the Ministry of Health and Women's Affairs, and annual and monthly reports are available on the ministry website (http://www.bmgf.gv.at/home/Gesundheit/Krankheiten/Epidemiologie). There is a separate reporting system for AIDS.

Outbreak investigation and control

In the case of an outbreak affecting more than one state, the Ministry of Health has to be informed. District administrations (and in the case of food-borne infections, the state health administrations) have the legal responsibility for detection and investigation of outbreaks and for public health action on outbreaks in co-operation with regional food and veterinary administration and AGES.

Childhood vaccination schedule

Updated data on the Austrian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes Rota, DTP, IPV, HiB, HepB, PCV, Men B, MenC, MCV4, MMR, Var, HPV, IIV3, HepA (ahead of nursery), and TBE (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates in 2014 were: DTP1 (95%), DTP3 (87%), IPV1 (95%), IPV3 (87%), HepB3 (87%), Hib3 (87%), MMR1 (95%), and MMR2 (89%).

5.5 Belgium

Belgium (population 11 251 000) is a federal state with three levels of government: (i) federal; (ii) regional (Brussels: Capital Region, Flanders and Wallonia); and (iii) linguistic communities (Flemish Community, French Community and German Community). Each federated entity has its own administration of public health and different responsibilities are shared in a complex way.

Surveillance and control of communicable diseases is mainly the responsibility of the federated entities, which have their own infectious disease control units. The German

speaking Community is located entirely within the Province of Liège in Wallonia. The Flemish and French Communities share the responsibilities for communicable disease control in Brussels in a separate commission with its own infectious disease control unit.

Emergency planning, crisis management and health security issues (e.g. bioterrorism) are the responsibility of the federal government (Federal Public Service, Health, Food Chain Safety and Environment) in consultation with federated entities. The Scientific Institute of Public Health is, on behalf of the federal and federated entities, responsible for the co-ordinated surveillance of communicable diseases, including HIV/STI surveillance, influenza sentinel surveillance and surveillance based on data from reference laboratories.

National competent authorities for communicable disease control

- Flemish Agency for Care and Health (Vlaams Agentschap Zorg en Gezondheid): http://www.zorg-en-gezondheid.be
- French Agency for a Life in Quality. Walloon Region, https://www.aviq.be
- Commission communautaire commune of the Brussels-Capital Region. http://www.ccc-ggc.irisnet.be/fr
- Federal Public Service, Health, Food Chain Safety and Environment (Le service public fédéral (SPF) Santé publique, Sécurité de la Chaîne alimentaire et Environnement /De Federale overheidsdienst (FOD) Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu): http://www.health.belgium.be
- The Scientific Institute of Public Health (Institut Scientifique de la Santé Publique/ Wetenschappelijk Instituut Volksgezondheid): https://www.wiv-isp.be

Surveillance of communicable diseases

The Ministry of Health of each federated entity is responsible for introducing changes in the statutory notification system. About 35 diseases are notifiable in the regions. The responsibility for case management is held by the treating physician. No financial incentives are given to notifying physicians or laboratories. The local reporting is to the health inspector of the respective infectious disease unit.

Surveillance data are available from the Scientific Institute of Public Health online interactive tools (https://epistat.wiv-isp.be) and also in weekly report for influenza and annual reports for all other diseases (https://epidemio.wiv-isp.be/ID/Pages/Publications.aspx). The *Flemish Infectious Disease Bulletin* (quarterly, print and online in Flemish with summaries in English) (https://www.zorg-en-gezondheid.be/vlaamsinfectieziektebulletin) is published by the Department of Infectious Diseases Control, Flanders. A monthly letter is also written by the Scientific Institute of Public Health together with the infectious diseases units of the Federated entities (https://epidemio.wiv-isp.be/ID/Pages/flashs.aspx).

Outbreak investigation and control

The Scientific Institute of Public Health performs epidemic intelligence gathering and is in charge of the co-ordination of risk assessment in case of a threat falling under IHR or Decision 1082/2013/EU. The infectious diseases units of the Federated entities have the legal responsibility for detection, investigation and public health action within their territory in co-operation with other local/regional authorities (environmental health, veterinarians, etc.). The Federal Public Service, Health, Food Chain Safety and Environment is involved whenever there is a health issue with an international dimension (e.g. pandemic, bioterrorism) and provides the IHR focal point.

Childhood vaccination schedule

Updated data on the Belgian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national

child immunisation programme includes Rota, DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR (spec. groups), HPV, IIV (spec. groups), and HepA (spec. groups) (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP 1 (99%), DTP3 (98%), DTP4 (93%), IPV1 (99%), IPV3 (99%), HepB3 (97%), Hib3 (97%), MMR1 (96%), MMR2 (85%), PCV1 (98%), PCV2 (97%), PCV3 (94%), Rota1 (90%), and RotaC (87%).

5.6 Bulgaria

Bulgaria is a republic (population 7 202 000) divided into 28 provinces (*oblasts*) named after their main city, and subdivided into 264 municipalities.

The Bulgarian public health system is supervised by the Ministry of Health. The Chief State Health Inspector (within the Ministry of Health) is responsible for preparing guidelines and issues related to preparedness and response. At provincial level, 28 Regional Health Inspectorates have important roles in communicable disease surveillance and control.

The National Centre for Infectious and Parasitic Diseases acts under the Ministry as the main national research and reference centre on infectious diseases. It provides the evidence-base for the control of communicable diseases, it runs the national microbiological reference laboratories, analyses the epidemiological surveillance data on communicable diseases and antimicrobial resistance, issues guidelines, supports the national immunisation programme and provides graduate and postgraduate training in the field.

National competent authorities for communicable disease control

- Bulgaria Ministry of Health, Directorate of Public Health: http://www.mh.government.bg
- Bulgaria National Center of Infectious and Parasitic Diseases (NCIPD): www.ncipd.org

Surveillance of communicable diseases

The surveillance of communicable diseases in Bulgaria is regulated by the Law on Health from 2005. All physicians and microbiological laboratories are obliged to report 60 mandatory notifiable diseases (suspected and confirmed cases) within 24 hours to the Regional Health Inspectorate. These reports are passed on as aggregated information (number of cases and place of origin) to the NCIPD on a daily basis. These reports are followed up on a monthly basis with aggregated information on confirmed cases, outcome and place of origin.

Data analysis is performed both at the regional and national level (NCIPD). The surveillance system is supported by a network of microbiology laboratories and the reference laboratories at the NCIPD, and the NCIPD provides necessary support. A weekly bulletin on the epidemiological situation is issued by NCIPD: https://www.ncipd.org/index.php?option=com_biuletin&view=view&layout=enversion&Itemid=1193&lang=en.

Specific diseases, such as tuberculosis, influenza, acute respiratory tract infections, STIs and healthcare-associated infections are reported through parallel vertical systems.

Outbreak investigation and control

The Regional Health Inspectorates are responsible for outbreak investigations and control measures with support from national level when necessary. They are obliged to immediately inform the Ministry of Health of any communicable disease outbreak.

Childhood vaccination schedule

Updated data on the Bulgarian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.

eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, DTP, IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: BCG (96%), DTP1 (94%), DTP3 (92%), DTP4 (90%), IPV1 (94%), IPV3 (92%), HepB3 (91%), Hib3(92%), MMR1 (92%), MMR2 (88%), PCV1 (94%), PCV (93%) and PCV3 (90%).

5.7 Croatia

Croatia (population 4 284 889) is a republic divided into 20 counties and the capital city of Zagreb (with the authority and legal status of both a county and a city) and 127 local cities and municipalities.

The Ministry of Health (Ministarstvo zdravstva) has the overriding responsibility for the public health system, including public health policy, preparation of legislation and supervision of its implementation, and overall monitoring of the public health systems.

The Croatian Institute of Public Health (HZJZ) acting under the Ministry of Health, is a broad national expert and reference institution dealing both with communicable and non-communicable diseases. It is responsible for the surveillance of communicable diseases, co-ordinating outbreak response activities and also planning, supervising and evaluating the national immunisation programme. HZJZ issues recommendations and guidelines on all aspects of communicable disease prevention and control and performs microbiology reference activities. It is also involved in research and training.

National competent authorities for communicable disease control

- Ministry of Health (Ministarstvo zdravstva): https://zdravstvo.gov.hr
- Croatian Institute of Public Health (Hrvatski zavod za javno zdravstvo): www.hzjz.hr

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. Ninety-nine diseases are notifiable. Reporting is an obligation of both physicians and laboratories. HZJZ carries out epidemiological surveillance and proposes, organises and undertakes preventive and counter-epidemic measures. It also plays a crucial role in planning, supervision and evaluation of immunisation.

National surveillance is co-ordinated by the Department of Infectious Disease Control at HZJZ.(http://www.hzjz.hr/sluzba-epidemiologija-zarazne-bolesti). The Department operates the national registry of infectious diseases, and publishes an annual infectious disease report (in Croatian), available at http://www.hzjz.hr/cat/hrvatski-zdravstveno-statisticki-ljetopis

Outbreak investigation and control

The responsibility for case management is held by the notifier. Outbreaks are detected at regional level by various information sources, including surveillance data and laboratory results. Reporting of suspected outbreaks to the HZJZ is obligatory.

Childhood vaccination schedule

Updated data on the Croatia childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The mandatory national immunisation programme includes BCG, DTP, IPV, HiB, HepB, HPV and IIV (risk groups) (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary).

Vaccine coverage rates for 2016 were: BCG (99%), DTP3 (93%), DTP4 (87%), HepB3 (93%), Hib3 (93%), IPV3 (93%), MMR1 (90%) and MMR2 (96%).

5.8 Cyprus

Cyprus (population 1 141 000) is a republic, administratively divided in six districts. Since 1974, when Turkey invaded Cyprus, 36% of the country's territory is not under the effective control of the Government of the Republic of Cyprus. The areas under Turkish occupation are thus not included in the national public health and surveillance systems.

The responsibility for communicable disease control in the country lies with the Department of Medical and Public Health Services of the Ministry of Health, specifically within its Unit for Surveillance and Control of Communicable Diseases. The Director of Medical and Public Health Services (or a person authorised by him/her) is responsible for issuing guidelines, surveillance, threat detection, preparedness, outbreak control and communication, as well as contacts with the EU on communicable diseases.

National competent authority for communicable disease control

- Ministry of Health, Directorate Medical and Public Health Services: www.moh.gov.cy/moh/moh.nsf/medpub_en/medpub_en?OpenDocument

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated in the Quarantine Law. A total of 60 communicable diseases are notifiable; 12 to be notified within 24 hours. All physicians are obliged to report these diseases to the District Medical Officers who forward the information to the Medical and Public Health Services. For diseases notifiable within 24 hours, simultaneous reporting is to the District Medical Officer and to the Medical and Public Health Services.

Surveillance data are disseminated via the *Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus* (biannual, print and online in Greek), published by the Medical and Public Health Services.

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is generally the responsibility of the District Medical Officer and his/her team, supported when necessary by the Medical and Public Health Services.

Childhood vaccination schedule

Updated data on the Cypriot childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR, HPV, IIV (specific groups) and HepA (specific groups) (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP3 (97%), HepB3 (97%), Hib3 (96%), IPV1 (99%), IPV3 (97%), MMR1 (90%), PCV1 (98%), PCV2 (95%) and PCV3 (81%).

5.9 Czech Republic

The Czech Republic (population 10 553 000) is divided in 13 administrative regions and the capital city of Prague. All public health

services (central governmental and regional) are centralised under the Ministry of Health. The Ministry of Health is responsible for issuing guidelines, threat detection, preparedness, outbreak control and communication.

The National Institute of Public Health (SZÚ) is a scientific institute directly managed by the Ministry of Health. The Institute works with both communicable and chronic diseases. A main task is communicable disease control; epidemiology, microbiology and hygiene. The NIPH provides scientific advice and is responsible for surveillance of infectious diseases. Furthermore, it provides methodological support and operates most of the national reference laboratories in the country.

Regional public health offices are responsible for the basic public health services, including surveillance and implementation of the general immunisation programmes.

National competent authorities for communicable disease control

- Ministry of Health (Ministerstvo zdravotnictví): www.mzcr.cz
- National Institute of Public Health (Státní zdravotní ústav – SZÚ): www.szu.cz

Surveillance of communicable diseases

All communicable diseases are by law notifiable by physicians, laboratories and detached Regional Public Health Offices. The notifications are sent to the Regional Public Health Offices, which forward the information, usually within a week, to the NIPH who coordinates the national reporting system (EPIDAT). The responsibility for case management is held by the notifier. Dissemination of surveillance data is done by NIPH through the monthly print and online Bulletin of Centre for Epidemiology and Microbiology (Zprávy CEM) in Czech with abstracts in English http://www.szu.cz/publications-and-products/zpravy-epidemiologie-a-mikrobiologie and as online tabular notifications (Infekce v ČR – EPIDAT): http://www.szu.cz/publikace/data/infekce-v-cr.

Outbreak investigation and control

Directors of all healthcare facilities are required by law to notify unusually high occurrence or severity. Control measures including contact tracing and outbreak investigation is generally the responsibility of the Public Health Service, primarily at regional level with support from national level (national outbreak management team) when necessary.

Childhood vaccination schedule

Updated data on the Czech childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), Rota, DTP, IPV, HiB, HepB, PCV, MCV, MMR, VAR, HPV, IIV (spec. groups) and TBE (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: DTP3 (96%), DTP4 (96%), HepB3 (96%), Hib3 (96%), MMR1 (98%), MMR2 (93%) and IPV3 (96%).

5.10 Denmark

Denmark (population 5 707 000) is a constitutional monarchy, administratively divided into five regions. The Danish healthcare system is universal and based on the principles of free and equal access to healthcare for all citizens. The healthcare system offers

high-quality services, the majority of which are financed by general taxes. Healthcare is predominantly managed at the regional level. The Ministry of Health is in charge of the administrative functions in relation to the organisation and financing of the healthcare system, psychiatry and health insurance as well as the approval of pharmaceuticals and the pharmacy sector.

The Ministry of Health oversees the following authorities

- Danish Health Authority
- Danish Medicines Authority
- Danish Patient Safety Authority
- The Danish Health Data Authority
- Statens Serum Institut

The Danish Health Authority is the supreme healthcare authority in Denmark, and has an important role in overseeing all communicable disease control activities, issuing guidelines, providing scientific advice, and reviewing the national immunisation programme. The Danish Health Authority is also responsible for preparedness, risk management and communication.

The Statens Serum Institut (SSI) is a public enterprise under the Ministry of Health. It is the main national expert agency working with communicable disease control and is the main adviser to the Danish Health Authority. Main tasks of the SSI are research, scientific advice, national surveillance of infectious diseases, specialised microbiological diagnostics (including reference laboratories), technical assistance in outbreak management, vaccine procurement, biosecurity and preparedness against bioterrorism.

Regional Medical Officers of Health are employed by the Danish Patient Safety Authority. These officers have a large array of medical-legal and public health duties, including tasks in relation to prevention and control of infectious diseases amongst others coordinating local efforts to control outbreaks, primarily in relation to notifiable diseases.

Additional tasks in relation to control and prevention of infectious disease are carried out at the municipalities being responsible for institutions for child care, for the elderly, water supply and sanitation.

National competent authorities for communicable disease control

- Ministry of Health (Sundheds- og Ældreministeriet): www.sum.dk
- Danish Health Authority (Sundhedsstyrelsen): www.sst.dk
- Statens Serum Institut (SSI): www.ssi.dk

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. Forty-five diseases are notifiable on a person-identifiable basis. Laboratories report identification of nine specific microbial agents as well as all gastrointestinal bacteria to the SSI. In addition, the number of positive and negative HIV test results are reported. Reporting is primarily done by automatic real time reporting to a national microbiology database called MiBa. All physicians and laboratories are obliged to notify cases of notifiable diseases in parallel to the Regional Medical Officers of Health and to the SSI. Surveillance data are disseminated by SSI via a weekly bulletin available in Danish (*Epi-Nyt)* and in English (*Epi-News*) http://www.ssi.dk/English/News/EPI-NEWS.aspx

Outbreak investigation and control

Physicians are required by law to report any abnormal event or outbreak of any disease immediately by phone to the Medical Officers of Health. They also have to notify to the national level (SSI) by mail using a written form. Local and national reference laboratories also detect and report outbreaks. The Medical Officers of Health have responsibility for outbreak control at regional and local level, including contact-tracing. The SSI has national responsibility as a reference centre for surveillance and is involved in outbreak investigation and control on request. SSI hosts a national outbreak centre with

cross-disciplinary skills in public health microbiology and epidemiology. There is a permanent committee for the management of food-borne outbreaks, including the Danish Veterinary and Food Administration, the National Food Institute DTU and SSI.

Childhood vaccination schedule

Updated data on the Danish childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes DTP, IPV, HiB, HepB (specific groups), MMR, PCV and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/global summary). Vaccine coverage rates for 2016 were: DTP1 (97%), DTP3 (94%), DTP4 (84%), IPV1 (97%), HiB3 (94%), MMR1 (94%), MMR2 (85%), PCV1 (97%), PCV2 (94%) and PCV3 (94%).

5.11 Estonia

Estonia (population 1 317 000) is a republic, administratively divided in 15 counties. The main bodies responsible for communicable disease control are the Ministry of Social Affairs and its agencies. The Ministry has a supervising role and responsibility for public health policy and strategies and introduction of new legislation, while surveillance and control activities are carried out by the Health Board under the Ministry.

The Health Board is the main public health institution working with communicable diseases. It is responsible for surveillance of infectious diseases, outbreak management, preventive measures, supervision, and monitoring of the national immunisation programme. It also organises public health microbiology, as well as being responsible for early warning and response, national stockpile of vaccines and antiretrovirals. Four regional Health Board Services are part of the organisation

Surveillance and control of tuberculosis and HIV are carried out by the National Institute for Health Development.

In each of the 15 counties, local communicable disease control is carried out by the County Health Board Offices.

National competent authorities for communicable disease control

- Ministry of Social Affairs (Sotsiaalministeerium; SoM): http://www.sm.ee/et
- Health Board (Terviseamet; TA): http://www.terviseamet.ee
- National Institute for Health Development (Tervise Arengu Instituut; TAI) HIV/AIDS and TB surveillance: http://www.tai.ee/?lang=en

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law (Communicable Diseases Prevention and Control Act). A total of 58 communicable diseases (except tuberculosis) with full patient identification are notifiable to the County Health Board Offices or to the web-based CD Information System (NAKIS). Cases of tuberculosis are reported to the Tuberculosis Registry (National Institute for Health Development). Electronic or telephone reporting is carried out for designated serious infectious diseases or their suspicion (priority list) and clusters with water-borne and food-borne transmission. All physicians and laboratories are obliged to notify cases that fulfil the criteria for notifiable diseases. No financial incentives are given for notifying. The responsibility for case management is held by the physicians (including contact tracing), supported by the County Health Board Office.

Surveillance data are disseminated monthly via *EstEpi Report* (*Estonian Communicable Disease Bulletin*) http://www.terviseamet.ee/en/cdc/communicable-disease-bulletin.html.

Outbreak investigation and control

A variety of information sources are used to detect possible outbreaks. The information is forwarded to County Health Board Offices, responsible for investigation and public health action at local level. The County Health Board Offices report to the Health Board, responsible for outbreak detection, and management at national level.

Childhood vaccination schedule

Updated data on the Estonian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, Rota, DTP, IPV, HiB, HepB, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: BCG (95%), DTP1 (95%), DTP3 (93%), DTP4 (91%), HepB3 (93%), Hib3 (93%), MMR1 (93%), MMR2 (92%), IPV1 (95%), IPV3 (93%), Rota1 (88%) and RotaC (87%).

5.12 Finland

Finland (population 5 489 000) is a republic, divided into six administrative regions. The main bodies responsible for communicable disease control are the Ministry of Social Affairs and Health and the National Institute for Health and Welfare. The Ministry has a supervising role with responsibility for public health policy and strategies, proposing legislation and monitoring its implementation.

The National Institute for Health and Welfare (THL), acting under the Ministry of Social Affairs and Health, is the main scientific and public health institute working with communicable disease control. In addition, the Food Safety Authority (EVIRA), acting under the Ministry of Agriculture and Forestry, has a role in zoonotic disease control and food-borne and water-borne disease prevention. With a strong research base, the THL is responsible for epidemiological surveillance and response, threat detection, the Finnish vaccination programme, scientific advice and communication. THL and EVIRA work closely together for outbreak investigations and AMR prevention.

Finland is a devolved democracy, in which municipalities have a strong role in terms of the application of administrative authorities. At the local level, Municipal Health and Environmental Health Authorities are in primary charge of control measures. Hospital district infection control teams are responsible for regional surveillance and control support. State regional offices carry oversight functions. However, it should be noted that due to an ongoing major national social- and health service reform, CD surveillance and control functions will most likely be transferred from the 300+ municipalities to 18 provinces to be formed in 2020: http://alueuudistus.fi.

National competent authorities for communicable disease control

- Ministry of Social Affairs and Health (Department for Promotion of Welfare and Health): www.stm.fi
- National Institute for Health and Welfare (Terveyden ja hyvinvoinnin laitos; Institutet för hälsa och välfärd; THL): https://www.thl.fi/en/web/thlfi-en
- Food Safety Authority (Elintarviketurvallisuusvirasto; Livsmedelssäkerhetsverket; EVIRA): https://www.evira.fi/en

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by the Law and Act of Communicable Diseases http://finlex.fi/fi/laki/alkup/2016/20161227. The notifiable diseases are classified into three categories. For some diseases both the physician and the laboratory must report the case, for others only laboratory reports are collected (more than half of all infections). The information is entered into the National Infectious Disease Register (NDR) and duplicate notifications are merged. Data from individual cases are linked by the unique personal identifying number. There are no financial incentives for notifying physicians.

Laboratory notifications are sent directly to the national level at THL. In addition, laboratories send microbes to a national strain collection. Physician notifications are sent through the regional level to the national level. The notifying physicians are responsible for detection and notification of cases and for necessary action to stop spread. They are assisted by infectious disease specialists and microbiologists.

All registry data are compiled and arranged at THL and accessible through encrypted www-communication to health authorities in charge at district and municipal levels. Tabular data down to district level from NDR is available on the THL website (in Finnish and Swedish) https://www.thl.fi/ttr/gen/rpt/tilastot.html.

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation are generally the responsibility of the municipal health centre and environmental health authorities, primarily on local level with support from regional and national level, when necessary. In suspected outbreak situations, local health authorities (i.e. Human health and veterinary health/food inspection authorities working as joint teams) are primarily responsible for situation analysis and action. In cases where several municipalities are involved, the hospital district specialist and/or the regional veterinary and food authorities act as co-ordinator and consultant. The THL is involved in wider outbreaks and provides co-ordination, national guidance and expert help, as necessary. All suspected food- and water-borne outbreaks are notified to an electronic notification system, jointly operated by EVIRA and THL.

Childhood vaccination schedule

Updated data on the Finnish childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (spec. groups), Rota, DTP, IPV, HiB, HepB (spec. groups), PCV, MMR, VAR, HPV, IIV and TBE (residents on the island of Åland) (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP3 (92%), EDTP4 (85%), IPV1 (99%), IPV3 (92%), Hib3 (92%), MMR1 (95%), MMR2 (85%), PCV1 (95%), PCV3 (87%), Rota1 (93%) and RotaC (84%).

5.13 France

France (population 66842000) is a republic, which after the 2016 reform of the French regional organisation is divided into 12 metropolitan and 12 overseas territories (5 overseas regions, 6 overseas collectivities and 1 special status collectivity), and subdivided into 101 departments.

The main bodies responsible for communicable disease control are the Ministry of Social Affairs and Health with its General Directorate of Health (DGS) and The French Public Health Agency (Santé publique France). The DGS has

a supervising role with responsibility for public health policy and strategies, proposing legislation and monitoring its implementation. The DGS is further responsible for issuing guidelines, preparedness and response, health emergencies including bioterror threats, risk communication and EU contacts on risk management issues.

Santé publique France was created in 2016 in a merger of the French Institute for Public Health Surveillance (InVS), the French Institute for Prevention and Health Education (Inpes), the Establishment for Preparedness and Response to Health Emergencies (Eprus) and a public interest grouping (Adalis) in charge of helplines and online support for the public in relation to addictions, drugs and alcohol. Santé publique France has national responsibility for threat detection and alert, surveillance of diseases in all areas of public health, preparedness and response, prevention and health promotion. It provides advice to decision makers more particularly to the DGS at the national level and to the Regional Health Agencies (ARS) recommending measures against detected threats. Santé publique France also contributes to the management of health crises to support the DGS at national level and the ARS at regional level. The mission of the Agency covers the overseas departments.

In each region a Regional Health Agency (ARS) is responsible for carrying out public health actions at regional and sub-regional levels. Santé publique France has regional offices (Cellule d'intervention en région – CIRe) located at the regional health agency (ARS). The regional offices develop surveillance and investigation activities and support response to public health threat, including those of infectious origin at the regional level.

National competent authorities for communicable disease control

- Ministry of Social Affairs and Health, General Directorate of Health (Ministère des Affaires Sociales et de la Santé, Direction Générale de la Santé; DGS): http://social-sante.gouv.fr/ministere/organisation/directions/article/dgs-direction-generale-de-la-sante
- Santé publique France: www.santepubliquefrance.fr
- Web portal of the Regional Health Agencies: http://www.ars.sante.fr

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. The Ministry of Social Affairs and Health has the responsibility for modifications in the notification system based on proposals made by Santé publique France. While DGS is responsible for policy and decision, the Santé publique France is responsible for managing surveillance activities at the national level. The agency performs trend analysis, outbreak detection based on the surveillance and epidemic intelligence and carries out outbreak investigation.

All physicians, biologists and hospitals are obliged by law to notify all cases that fulfil the criteria for mandatory notification. No financial incentive is given to the notifiers. Individual cases are anonymously notified to the ARS that forwards the notifications to the Santé publique France (usually within one to two days). The responsibility for case management is held by the notifier. According to the disease, a case detection may lead to two levels of action. All the diseases, except for HIV/AIDS, acute hepatitis B and tetanus, have to be notified for immediate action.

Further to the surveillance of notifiable diseases, the surveillance of communicable diseases is also implemented through voluntary surveillance networks, the use of health and administrative data from the national health data system, a national network of laboratories, and a network of national reference centres. In total, there are about 70 communicable diseases surveillance systems operated by Santé publique France.

Surveillance data are disseminated via annual surveillance reports (http://invs.

santepubliquefrance.fr/Dossiers-thematiques/Maladies-infectieuses) at the national and regional level and the *Bulletin Épidemiologique Hebdomadaire* (*Weekly Epidemiological Bulletin*) (print and online in French): http://invs.santepubliquefrance.fr//Publications-et-outils/BEH-Bulletin-epidemiologique-hebdomadaire.

Outbreak investigation and control

Besides notifiable communicable diseases, all health professionals also are obliged to inform the ARS of any abnormal health event or outbreak of any disease. The ARS is responsible for investigation and control with the assistance from Santé publique France by its regional offices (CIRe) with the support of the headquarters of Santé publique France when necessary

Control of the outbreak is the responsibility of the ARS and the DGS. The Ministry of Agriculture is involved in food-borne outbreaks.

Childhood vaccination schedule

Updated data on the French childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (spec. groups), DTP, IPV, HiB, HepB, PCV, MenC, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP3 (97%), HepB3 (88%), HiB3 (96%), IPV3 (97%), MMR1 (91%), MMR2 (79%), PCV2 (92%) and PCV3 (91%).

5.14 Germany

Germany (population 82 176 000) is a federal republic, administratively divided into 16 states (*Bundesländer*), and subdivided into 439 districts (*Kreise*) and cities (*kreisfreie Städte*). The decision-making power is shared between the federal and the state governments, and the responsibility for health is at state level. The main national authorities responsible for communicable disease control are the Federal Ministry of Health (BMG) and the Robert Koch Institute (RKI).

The BMG has a supervising role with responsibility for public health policy and strategies, drafting legislation and monitoring its implementation, as well as for preparedness, health protection, disease prevention, risk communication and EU contacts on risk management issues.

The RKI is the central federal expert institution responsible for communicable disease prevention and control. The RKI work is research-based, and includes compiling scientific findings as a basis for political decisions, infectious disease surveillance (including surveys and sentinel studies), and threat detection (national and international), as well as identification and prevention of bioterror attacks. To achieve its objectives, the RKI co-operates closely with the federal ministries, with the state governments, local authorities and European and international institutions.

The Federal Centre for Health Education (BZgA) is responsible for the implementation of health educational programmes of national importance.

At state level, communicable disease control is carried out by the state health department (*Landesgesundheitsamt*), and at district level by the local health department (*Gesundheitsamt*).

National competent authorities for communicable disease control

- Federal Ministry for Health (Bundesministerium für Gesundheit; BMG): https://www.bundesgesundheitsministerium.de
- Robert Koch Institute (RKI): www.rki.de
- Federal Centre for Health Education (Bundeszentrale für gesundheitliche Aufklärung; BZgA): www.bzga.de

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law, with a new law in force since 2001. Some 57 diseases/infections are notified with identifiers of the patient. Six other diseases/infections are notified without personal identifiers. All physicians and medical microbiology laboratories are obliged to report notifiable diseases, and no financial incentives are given for notifying physicians.

For most notifiable diseases, notifications from physicians and laboratories go to local health departments. From there they are forwarded via the state health departments to the RKI at federal level. The notifications usually reach the state level within three days and the RKI within one week.

Surveillance data are disseminated via annual surveillance reports (http://www.rki.de/DE/Content/Infekt/Jahrbuch/jahrbuch_node.html) and the *Epidemiologisches Bulletin* (*Epidemiological Bulletin*) (weekly online in German) (http://www.rki.de/DE/Content/Infekt/EpidBull/epid_bull_node.html), published by the RKI. The data can also be accessed and used via an Internet application, SurvStat@RKI (https://survstat.rki.de).

Outbreak investigation and control

Outbreak investigation and management, including contact tracing, is generally the responsibility of the local health department with support from the state health department and RKI when necessary.

Childhood vaccination schedule

Updated data on the German childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes Rota, DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP3 (95%), IPV1 (98%), IPV3 (95%), HepB3 (88%), Hib3 (93%), MMR1 (97%), MMR2 (93%), PCV3 (86%) and RotaC (66%).

5.15 Greece

Greece (population 10 955 000) is a parliamentary republic, administratively divided into 13 peripheries and subdivided into 51 prefectures. The main national authorities responsible for communicable disease control are the Ministry of Health and Social Solidarity with its Directorate of Public Health and the Hellenic Centre for Disease Control and Prevention (HCDCP/KEELPNO).

The Ministry of Health and Social Solidarity has a supervising role with responsibility for public health policy and strategies, proposing legislation and monitoring its implementation. The Directorate of Public Health is further responsible for preparedness, risk communication, and EU contacts on risk management issues.

The KEELPNO is an independent expert institution working under the supervision of the Ministry, collaborating closely with other public health authorities. The KEELPNO provides scientific advice, preparing guidelines, organising educational campaigns, and is responsible for the national surveillance of communicable diseases. It also intervenes in cases of outbreaks of national significance (in collaboration with local public health authorities), provides information to the general public (including travel advice), provides risk assessment for communicable diseases and works on bioterror preparedness. Finally, KEELPNO together with the National School of Public Health co-ordinates the function of the National and District Public Health laboratories.

National competent authorities for communicable disease control

- Ministry of Health and Social Solidarity, Directorate of Public Health: www.ermis.gov.gr/portal/page/portal/ermis/publicBodies?p_topic=8669
- Hellenic Centre for Disease Control and Prevention (KEELPNO): www.keelpno.gr

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. The notifiable diseases are divided into three categories (depending on urgency of notification). No financial incentive is given to physicians to notify. The responsibility for case management is held by the notifier. Physicians notify cases to the Prefecture Public Health Division, being responsible for case investigation. Monthly aggregate data are sent to the Ministry of Health and to the KEELPNO. The KEELPNO is responsible for the analysis of the data. Separate surveillance and other action programmes are established within the KEELPNO to assess and intervene in surveillance issues with migrants, HIV and STIs, viral hepatitis and nosocomial infections.

Tabulated surveillance data are accessible on the KEELPNO website: http://www.keelpno.gr/en-us/epidemiologicalstatisticaldata.aspx. The Centre also publishes a monthly on line newsletter in Greek and English: http://www2.keelpno.gr/blog/?lang=en.

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is generally the responsibility of the Public Health Service, primarily on local level with support from the HCDCP when necessary.

Childhood vaccination schedule

Updated data on the Greek childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, Rota, DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR, HPV, IIV (spec. groups) and HepA (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP2 (99%), DTP3 (96%), IPV1 (99%), IPV3 (99%), HepB3 (96%), Hib3 (99%), MMR1 (97%), PCV1 (99%), PCV3 (96%), Rota1 (25%) and RotaC (20%).

5.16 Hungary

Hungary (population 9 856 000) is a parliamentary republic, administratively divided into 19 counties and the capital city (Budapest). These are further subdivided into 174 sub-regions, with Budapest comprising its own sub-regions. The counties and Budapest are grouped into seven planning and statistical regions.

Directly under the Ministry of Human capacities, the Chief Medical Officer of Hungary leads the Hungarian National Public Health and Medical Officers' Service (NPHMOS), which operates as a public administration agency. The NPHMOS is organised at national, regional and local levels and is responsible for controlling, coordinating and supervising all public health activities. The NPHMOS includes the Office of the Chief Medical Officer (OCMO), a number of national scientific institutes as well as regional and sub-regional institutions.

The National Centre for Epidemiology (NCE) is part of NPHMOS, but acts as a scientifically independent expert institution with main responsibilities including surveillance, threat detection, prevention and control of

infectious diseases, vaccine safety, laboratory and reference laboratory functions, training of the health officers and postgraduate training. The NCE also provides expertise for epidemiological preparedness and emergency situations (including bioterror events) of national importance, and is the leading institution against nosocomial infections. NCE is responsible for the development of the national immunisation programme.

The Korányi National Institute of Tuberculosis and Pulmonology is responsible for surveillance and control of tuberculosis.

The implementation of communicable disease surveillance and control at county and municipality level is carried out by the regional and sub-regional institutions of the NPHMOS.

National competent authorities for communicable disease control

- Ministry of Human Capacities (Emberi Erőforrások Minisztériuma): http://www.kormany.hu/hu/emberi-eroforrasok-miniszteriuma
- Hungarian National Public Health and Medical Officer Service (Állami Népegészségügyi és Tisztiorvosi Szolgálat – NPHMOS/ÁNTSZ): https://www.antsz.hu
- National Centre for Epidemiology (Országos Epidemiolgiai Központ): www.oek.hu
- Korányi National Institute of Tuberculosis and Pulmonology: www.koranyi.hu

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by legislation from 1997. The basis for the national surveillance system (except TB) is the NPHMOS. Communicable diseases, even the suspicion of the disease, are reported on paper forms by mail by health service providers to the sub-regional level of the NPHMOS where data are entered immediately into the electronic database of NPHMOS. Access to the database is provided online for the sub-regional, regional and national level of NPHMOS.

Mandatory notification is required for 72 diseases with personal identifying data and for 13 diseases without identifying data.

The NCE issues a weekly epidemiological bulletin Epinfo (*Az Országos Epidemiológiai Központ epidemiológiai információs hetilapja*) in Hungarian: (http://www.oek.hu/oek.web?to=,839&nid=41&pid=1&lang=hun).

Outbreak investigation and control

Control measures including contact tracing and outbreak investigations are generally the responsibility of the sub-regional and regional institutes of the NPHMOS, with the support of the NCE.

Childhood vaccination schedule

Updated data on the Hungarian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, DTP, IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: BCG (99%), DTP1 (99%), DTP3 (99%), IPV1 (99%), IPV3 (99%), Hib3 (99%), MMR1 (99%), PCV1 (99%), PCV2 (99%) and PCV3 (98%).

5.17 Iceland

Iceland (population 332 000) is a republic divided into seven health regions. The Ministry of Welfare is responsible for health

services including public health, policy issues and strategic planning. The main national health authority is the Directorate of Health. Within the Directorate is a specific Unit for Communicable Disease Control, headed by the Chief Epidemiologist who acts under the Act on Health Security and Communicable Diseases from 1997. This act applies to diseases and agents that can cause epidemics and pose a health threat to the public. In addition to infectious agents, these agents include chemical agents, radio-nuclear materials and unusual and unexpected events.

The Chief Epidemiologist has a broad mandate including organising and co-ordinating communicable disease prevention and control in the country, surveillance of communicable diseases, monitoring use of and resistance to antimicrobial agents, and to keep a register of human use of antimicrobial drugs, supervision of preventive measures, including the national immunisation programme, health information, providing advice and guidelines, and risk assessment and measures in the case of outbreaks of communicable diseases.

The Chief Epidemiologist works closely with Civil Protection, which is a department of the National Commissioner of Police, on preparedness planning on, for example pandemic influenza, preparedness plans of airports, ports and harbours and on CBRN preparedness. The Chief Epidemiologist is the IHR national focal point for Iceland.

Under the Chief Epidemiologist, seven regional epidemiologists and 11 district epidemiologists in selected healthcare centres have local responsibility for preventive measures and control measures against infectious diseases.

National competent authorities for communicable disease control

- Ministry of Welfare (Velferðarráðuneytið): www.velferdarraduneyti.is
- Chief Epidemiologist at the Directorate of Health (Embætti landlæknis): www.landlaeknir.is

Surveillance of communicable diseases

The national surveillance is regulated in regulation no. 221/2012 on reporting of communicable diseases and agents posing a threat to public health under the Act on Health Security and Communicable Diseases. Physicians and laboratories are obliged to report statutory reportable infectious diseases, acute symptoms caused by chemical or radio nuclear material and unexpected events with full identity to the Chief Epidemiologist. Data dissemination is done through the website of the Directorate of Health, with statistical information and a quarterly bulletin available in English: http://www.landlaeknir.is/english/epi-ice.

Childhood vaccination schedule and national vaccination registry

Updated data on the Icelandic childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes DTP, IPV, HiB, PCV, MenC, MMR and HPV (see list of Abbreviations at front of book).

The Chief Epidemiologist is responsible for keeping a registry of immunisations. Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (96%), DTP3 (91%), DTP4 (87%), IPV1 (96%), IPV3 (91%), Hib3 (91%), MMR1 (91%), MMR2 (95%), PCV1 (96%), PCV2 (95%) and PCV3 (90%).

5.18 Ireland

Ireland (population 4 761 865) is a republic, administratively divided in four provinces and 26 counties. For public health purposes the country is divided into eight Department

of Public Health areas (http://www.hse.ie/eng/services/list/5/publichealth/publichealthdepts/about/aboutus.html), each with a responsible Medical Officer of Health (MOH). The main bodies responsible for communicable disease control are the Department (Ministry) of Health, the Health Service Executive (HSE) national office for Health Protection and national MOH, regional MOHs and the Health Protection Surveillance Centre (HPSC). The Ministry has a supervising role with responsibility for public health policy and strategies, proposing legislation and monitoring its implementation.

The HPSC is the national specialist institution for surveillance of communicable diseases, including HCAI and AMR, and for monitoring immunisation uptake. Other key tasks of the centre are providing independent advice to government departments and other agencies, issuing guidelines, epidemiological investigations, applied research, communication and training in communicable disease control. The HPSC is part of the Health Service Executive (HSE) and works closely with the regional Medical Officers of Health.

National competent authorities for communicable disease control

- Department of Health: http://health.gov.ie
- Health Service Executive: http://www.hse.ie/eng/about/Who/healthwellbeing/About-Us/HWteam.html
- Health Protection Surveillance Centre (HPSC): http://www.hpsc.ie/hpsc

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. The Department of Health has the responsibility for modifications. A total of 84 diseases are notifiable (20 with immediate preliminary notification). The responsibility for case management is held by the notifier. The reporting is done by clinicians and the microbiology laboratories and linked through the Computerised Infectious Disease Reporting (CIDR) system, which is a shared system between HSE departments of Public Health, laboratories and HPSC.

Surveillance data are disseminated via Epi-Insight, a monthly electronic report on infectiousdiseases(http://www.hpsc.ie/EPI-Insight), five weekly electronic reports (on infectious diseases, HIV and STI, outbreaks, influenza and Clostridium difficile) (http://www.hpsc.ie/NotifiableDiseases/WeeklyIDReports), disease specific quarterly reports (e.g. http://www.hpsc.ie/a-z/vaccinepreventable/tuberculosistb/epidemiology/annualreports/2016) and an annual epidemiological report (http://www.hpsc.ie/AboutHPSC/AnnualReports).

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is generally the responsibility of the HSE public health Departments, primarily at a local level with support, if required, from the national level. The HPSC investigates and controls national outbreaks on behalf of the national MOH, liaising with laboratories the Food Safety Authority and other bodies as appropriate.

Childhood vaccination schedule

Updated data on the Irish childhood vaccination schedule are available from the National Immunisation Office (https://www.hse.ie/eng/health/immunisation/pubinfo/pcischedule/immschedule/) and from

ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, DTP, IPV, HiB, HepB, PCV, MenC, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016

were: DTP3 (95%), HepB3 (95%), Hib3 (95%), IPV3 (95%), MMR1 (92%) and PCV3 (91%).

5.19 Italy

Italy (population 60 665 551) is a republic divided in 19 regions and 2 autonomous provinces, 14 metropolitan cities and 95 provinces. The regions have large autonomy in terms of healthcare organisation (including public health). The main national authorities responsible for communicable disease control are the Ministry of Health, with its General Directorate of Health Prevention, and the National Health Institute (ISS).

The Ministry of Health is the national authority in the Italian National Health Service (NHS) and has a supervising role with responsibility for public health policy and planning, proposing legislation and regulations and monitoring their implementation. The Directorate General of Health Protection within the Ministry of Health has the overall national responsibility for infectious disease control including surveillance, issuing guidelines, preventive measures, bioterrorism, antimicrobial resistance, hospital-acquired infections and international co-operation.

The ISS is the leading national scientific institution of the NHS, active on many issues related to human health. It has a broad public health mandate. Activities related to communicable diseases are mainly carried out within the Department of Infectious Diseases and the National Centre for Global Health. The main tasks of ISS in this field include national surveillance, threat detection, rapid response, scientific advice (including on vaccines), training and applied research. Support to the local health authorities in outbreak investigations and public health activities is provided upon request.

To co-ordinate the activities between the Ministry of Health, the ISS and the regions on issues related to surveillance, prevention and health emergencies, a co-ordinating body, The National Centre for Prevention and Disease Control (CCM), is established within the General Directorate of Health Protection.

The hospital Lazzaro Spallanzani is a national reference institution for the diagnosis and care of severe infectious diseases, including HIV/AIDS, and rare imported infections. A biosafety level four laboratory is available at the hospital.

Regional public health agencies have an important role in guiding the activity of the 101 local health units, in charge of delivering primary health care and prevention.

National competent authorities/bodies for communicable disease control

- Ministry of Health (Ministero della Salute): www.salute.gov.it
- National Centre for Prevention and Disease Control (Centro Nazionale per la Prevenzione e il Controllo della Malattie – CCM): http://www.ccm-network.it/home.html
- National Health Institute (Istituto Superiore di Sanità – ISS): www.iss.it
- National Institute for Infectious Diseases (Istituto Nazionale per le Malattie Infettive L. Spallanzani): www.inmi.it

Surveillance of communicable diseases

Reporting of communicable diseases is regulated by law. All detected infections posing a risk to public health are principally notifiable; however, a list of specific diseases are noted in the national regulation. These are divided into five classes, which differ by flow of information, timeliness of reporting and by the degree of ascertainment requested. Diagnosing physicians are obliged by law to notify all cases that fulfil the criteria for these notifiable diseases.

Cases of notifiable diseases are reported to the public hygiene departments of local

health units, which have to check and carry out additional investigations (e.g. in case of outbreaks). Data from individual notification forms are entered in a computerised database and a common subset of data is periodically extracted and forwarded to the regional health authorities who in turns forward the aggregated data set to the Ministry of Health.

Data on relevant communicable diseases that are not included in the notification list, as well as on 'emerging' issues, are obtained by means of 'special' surveillance systems set up by ISS in collaboration with the regional authorities and the Ministry of Health. In these systems, data are collected at ISS and made available via EpiCentro, the epidemiological portal of ISS (http://www.epicentro.iss.it).

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation are generally the responsibility of the local health units, with support from regional and national level when deemed necessary. ISS performs field investigations only upon request of the Ministry of Health or the regional authority.

Childhood vaccination schedule

Updated data on the Italian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes Rota, DTP, IPV, HiB, HepB, PCV, MenB, MenC, MCV, MMR, VAR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: DTP3 (93%), HepB3 (93%), Hib3 (93%), IPV3 (93%), MMR1 (85%), MMR2 (83%), PCV3 (89%) and Rota1 (7%).

5.20 Latvia

Latvia (population 1950000) is a republic administratively divided in 9 cities and 110 municipalities. For public health purposes epidemiologists are situated in the eight largest cities of the country. The Ministry of Health has a leading role with responsibility for public health policy and strategies, health promotion, proposing legislation and monitoring its implementation, as well as overseeing the work of its subordinate institutions.

The Centre for Disease Prevention and Control of Latvia (SPKC) is a government institution under the Ministry of Health. The SPKC is responsible for threat detection, control, prevention and national surveillance of all communicable diseases, including STI, HIV/AIDS and tuberculosis, as well as overseeing the national immunisation programme. The SPKC gives scientific advice, prepares guidelines, provides training and conducts applied research.

Diagnostic and reference laboratory functions are performed by the National Reference Laboratory of the Latvian Centre of Infectious Diseases of the Riga East University Hospital.

The State Emergency Medical Service is responsible for co-ordination of emergency management for public health threats, and acts as the WHO liaison point for International Health Regulations.

National competent authorities for communicable disease control

- Ministry of Health (Veselības ministrija): www.vm.gov.lv
- The Centre for Disease Prevention and Control of Latvia (Slimību profilakses un kontroles centrs – SPKC): www.spkc.gov.lv
- Latvian Centre of Infectious Diseases of the Riga East University Hospital (Rīgas Austrumu klīniskās universitātes slimnīcas stacionārs Latvijas Infektoloģijas centrs): https://www.aslimnica.lv/en/saturs/latvian-centre-infectious-diseases

- State Emergency Medical Service (Neatliekamās medicīniskās palīdzības dienests, NMPD): www.nmpd.gov.lv/en/sems
- Health Inspectorate of Latvia (Veselības inspekcija): www.vi.gov.lv/en/start/_142

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by the Epidemiological Safety Law. Physicians and laboratories are obliged to report notifiable diseases and pathogens. Case notifications of notifiable diseases from physicians or laboratories are made within 12–72 hours depending on disease (condition). Notifications (except HIV/AIDS and tuberculosis) are processed by local epidemiologists; they organise epidemiological investigations and control measures, as well as forward the reports to the central level. Notifications of HIV/AIDS and tuberculosis are processed by epidemiologists at the central level. Surveillance data are disseminated in Latvian via the *Epidemiological Bulletin* (www.spkc.gov.lv/lv/statistika-un-petijumi/infekcijas-slimibas/epidemiologijas-bileteni1).

Outbreak investigation and control

Epidemiologists working at the municipality level are responsible for epidemiological investigation and control of outbreaks.

Childhood vaccination schedule

Updated data on the Latvian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, Rota, DTP, IPV, HiB, HepB, PCV, MMR, VAR and HPV (see list of Abbreviations at front of book). TBE vaccination is state funded for children in the territories with the highest TBE morbidity, as well as for orphans and children left without parental care.

Updated data on vaccine coverage are available from the WHO Regional Office for Europe (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: BCG (96%), DTP1 (99%), DTP3 (98%), DTP4 (95%), IPV1 (99%), IPV3 (98%), HepB3 (98%), HiB3 (98%), MMR1 (93%), MMR2 (89%), PCV1 (93%), PCV2 (93%), PCV3 (82%), Rota1 (98%), RotaC (83%) and HPV1 (44%).

5.21 Lithuania

Lithuania (population 2 853 000) is a republic, administratively divided into 10 counties, further subdivided into 60 municipalities. The Ministry of Health of the Republic of Lithuania is responsible for general supervision of the healthcare system. The Public Health Department of the Ministry of Health is responsible for public health policy and strategies, drafting and implementation of legislation and co-ordination of the activities of institutions under the Ministry of Health.

The Centre for Communicable Diseases and AIDS (ULAC) is a governmental institution under the Ministry of Health, organising and implementing prevention and management of communicable diseases, including national surveillance and the national immunisation programme. The national public health centre under the Ministry of Health has 10 departments in every county. Healthcare institutions report to departments of the National Public Health Centre about cases of communicable diseases, they investigate outbreaks and are responsible for prevention and control of communicable diseases at local and regional level.

The Health Emergency Situation Centre is responsible for emergency preparedness and response. This institution is a 24/7 focal point in Lithuania and is responsible for information and co-ordination during non-working hours, weekends and holidays. It also fulfils the functions of the WHO International Health Regulations National Focal Point.

The Lithuanian Institute of Hygiene is responsible for prevention of healthcare-associated infections and rational use of antimicrobials, including surveillance in these areas.

National competent authorities for communicable disease control

- Ministry of Health (Sveikatos apsaugos ministerijos – SAM): http://sam.lrv.lt
- Centre for Communicable Diseases and AIDS (Užkrečiamųjų ligų ir AIDS centras – ULAC): www.ulac.lt
- National Public Health Centre under the Ministry of Health (Nacionalinis visuomenės sveikatos centras – NVSC): https://nvsc.lrv.lt
- National Public Health Surveillance Laboratory (Nacionalinė visuomenės sveikatos priežiūros laboratorija – NVSPL): www.nvspl.lt
- Lithuania Health Emergency Situations Centre (Ekstremaliųjų sveikatai situacijų Centras – ESSC): http://www.essc.sam.lt
- Institute of Hygiene (Higienos Institutas – HI): www.hi.lt

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by Law on Communicable Diseases Prevention and Control. Physicians are obliged to report cases (within 12 hours) to NVSC which reports to ULAC by a computerised notification system. Aggregated surveillance data are disseminated via monthly and annual surveillance overviews on the ULAC website (http://www.ulac.lt/ataskaitos).

Outbreak investigation and control

NVSC is responsible for outbreak investigations and control measures. For food-borne outbreaks, the State food and veterinary service is also involved. The ULAC supports outbreak investigations and informs media and the Ministry of Health.

Childhood vaccination schedule

Updated data on the Lithuanian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, DTP, IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: BCG (98%), DTP1 (97%), DTP3 (94%), DTP4 (90%), HepB3 (95%), Hib3 (94%), IPV1 (97%), IPV3 (94%), MMR1 (94%), MMR2 (92%), PCV1 (82%), PCV2 (66%) and PCV3 (82%).

5.22 Luxembourg

Luxembourg (population 576 000) is a constitutional monarchy (grand duchy), administratively divided into 3 districts, which are further divided into 12 cantons. Public health is the responsibility of the Ministry of Health, and interventions are provided by a few public services and by private practitioners and non-profit associations paid for out of the Ministry budget.

The Health Directorate within the Ministry of Health is responsible for communicable disease control, especially policy issues, preparing and implementing guidelines, threat detection, preparedness and response, as well as training and communication. The national surveillance is carried out by the Division of Health Inspection within the Health Directorate, supported by experts in the National Health Laboratory (also responsible

for sentinel surveillance of influenza and food poisoning) and the National Service of Infectious Diseases within the Central Hospital of Luxembourg.

National competent authorities for communicable disease control

- Ministry of Health (Ministère de la Santé): http://www.sante.public.lu
- Ministry of Health, Health Directorate (Direction de la Santé): http://www.sante.public.lu/fr/politique-sante/ministere-sante/direction-sante/index.html
- National Health Laboratory: http://www.lns.public.lu

Surveillance of communicable diseases

The infectious or communicable diseases subject to compulsory notification are regulated in law. The notifiable diseases are grouped into eight classes. A small fee per notified patient is given to physicians as financial incentive to notify. Notifications are submitted to the Health Directorate, which publishes surveillance data every month with a yearly summary report.

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is the responsibility of the Health Directorate.

Childhood vaccination schedule

Updated data on the Luxembourgian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes Rota, DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (99%), DTP3 (99%), DTP4 (95%), IPV1 (99%), IPV3 (99%), HepB3 (94%), HiB3 (99%), MMR1 (99%), MMR2 (86%), PCV1 (97%), PCV2 (95%), Rota1 (91%) and RotaC (89%).

5.23 Malta

Malta (population 445 000) is a republic at the centre of the Mediterranean consisting of three islands; Malta, Gozo and Comino. The country is administered directly from the capital Valletta, and subdivided into 6 districts (mainly for statistical purposes) and 68 local councils. The Maltese government provides comprehensive health care that is free at the point of delivery for all Maltese residents.

The Ministry of Health has the overall responsibility for the health care services, including public health. Within the Ministry, the responsibility for communicable disease surveillance and control rests with the Infectious Disease Prevention and Control Unit (IDCU) which is part of the Health Promotion and Disease prevention directorate which falls under the Department of the Superintendent of Public Health. The IDCU is responsible for the national surveillance of communicable diseases, for the preparedness and response to new and emerging threats, data dissemination, epidemiological research, as well as managing outbreaks. The unit also provides advice to health professionals and the general public and contributes to training in communicable disease control.

National competent authority for communicable disease control

- Infectious Disease Prevention and Control Unit (IDCU) within the Ministry for Health: http://health.gov.mt/en/health-promotion/idpcu/Pages/introduction.aspx

Surveillance of communicable diseases

Communicable disease control is governed by the Prevention of Disease Ordinance Act and the Public Health Act. There are 71 communicable diseases or conditions (including nosocomial infections) which doctors (in the public and private sector) are obliged to notify by law. Clinical notification, except for HIV/AIDS, can be done electronically through a web platform. In addition, the main state public medical diagnostic laboratory and all licensed private medical diagnostic laboratories are obliged to report all positive infectious disease results. Monthly and annual tables are reported for all confirmed cases on the IDCU website: (http://health.gov.mt/en/health-promotion/idpcu/Pages/librarymenu.aspx).

Outbreak investigation and control

Outbreak investigation including when necessary the setting up of outbreak control teams is the remit of IDCU, being responsible for issuing timely control measures. Annual reports of all outbreaks are reported on the IDCU website.

Childhood vaccination schedule

Updated data on the Maltese childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), DTP, IPV, HiB, HepB, MMR, HPV and IIV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (97%), DTP3 (97%), DTP4 (98%), HepB3 (97%), Hib3 (97%), IPV3 (97%), MMR1 (93%) and MMR2 (86%).

5.24 The Netherlands

The Netherlands (population 17256397 according to the Central Bureau of Statistics on October 8, 2018) is a constitutional monarchy divided into 12 provinces and subdivided into 380 municipalities (01 January, 2018). The Ministry of Health, Welfare and Sports has the overall responsibility for the provision and infrastructure of public health in the country. Public health is regulated in the revised Dutch Public Health Act of 2008.

Public health is executed by 25 Municipal Health Services (GGDs), each under the responsibility of a group of collaborating municipalities. The regions coincide with the 25 Safety Regions. The Municipal Health Services take care of infectious disease control, child health examinations, vaccinations, environmental health, medical disaster relief, health protection and health promotion activities. Local public health includes all aspects of infectious disease control, general hygiene, school health and public health education.

The centralised steering of outbreak control by the Minister is limited in the law to outbreaks of category A diseases (e.g. SARS, poliomyelitis, smallpox, haemorrhagic fevers) and incidents/outbreaks with international impact. The Health Care Inspectorate (IGZ) under the Ministry monitors and assesses public healthcare, primarily on quality and safety.

The National Institute for Public Health and the Environment (RIVM) is a broad public health research institute acting in the fields of health, nutrition and environmental protection. RIVM is an agency of the Ministry of Health and mainly works for the Dutch government. RIVM has an important role in the co-ordination, prevention and control of infectious diseases, through its Centre for Infectious Disease Control (CIb), which hosts laboratories, epidemiology and a national co-ordination and response department (LCI). RIVM/CIb is responsible for the national surveillance of infectious diseases. It is the designated national focal point for communication

with the WHO and the EU, and it provides advice, support and co-ordination of outbreak management between the 25 municipal health services. LCI issues guidelines for communicable disease prevention and control (https://lci.rivm.nl/richtlijnen) and is responsible for the national child immunisation programmes as well as for emergency vaccination campaigns.

National competent authorities for communicable disease control

- Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport), Directorate-General of Public Health, policy issues and preparedness: http://www.rijksoverheid.nl/ministeries/vws
- The Dutch Health Care Inspectorate (Inspectie voor de Gezondheidszorg; IGZ): www.igz.nl
- Netherlands National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu; RIVM): http://www.rivm.nl/en
- RIVM, Centre for Infectious Disease Control (Centrum Infectieziektebestrijding; CIb), national focal point, research, surveillance, secondary diagnostics, preparedness and response: https://www.rivm.nl/en/

Surveillance of communicable diseases

Notification and surveillance of communicable diseases is regulated by the Public Health Act 2008. The Ministry of Health is responsible for changes in statutory notification. The system is based on notifications from both physicians and laboratories to the Municipal Health Services (GGD). The national surveillance system (Osiris) at CIb is updated on a daily basis from the GGDs.

A total of 42 diseases in three groups are notifiable, either instantly on suspicion (Group A diseases), within 24 hours after confirmation, or after one working day. No financial incentive is given to physicians to notify. A laboratory-based surveillance system for antimicrobial resistance (ISIS-AR) is run by RIVM-CIb together with the clinical microbiological laboratories run by the private sector.

Data dissemination is performed instantly through an electronic information system (inf@ct; labinf@ct; vetinf@ct) in the case of an emergency, a weekly signals report, a monthly zoonosis signals report, and two-monthly via a surveillance bulletin (*Infectieziekten Bulletin*) and through updates and reports on the RIVM-CIb website (http://www.rivm.nl/cib/publicaties/bulletin).

Outbreak investigation and control

Under supervision of the mayor, the Municipal Health Service (GGD) is responsible for control measures including source and contact tracing and outbreak investigation, with assistance and co-ordination from the RIVM/CIb when necessary. In the case of a category A disease (polio, SARS, smallpox, haemorrhagic fever), or when international implications are expected, RIVM/CIb is in charge and gives out directives to the GGDs under supervision of the Minister. Measures (to control an outbreak) that violate human rights are exhaustively described in the law and assessed by a court immediately after they are imposed.

Childhood vaccination schedule

Updated data on the Dutch childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes DTP, IPV, HiB, HepB, PCV, MenC, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP1 (95%), DTP3 (95%), HepB3

(93%), Hib3 (95%), IPV3 (95%), MMR1 (94%), MMR2 (91%) and PCV3 (94%).

5.25 Norway

Norway (population 5 258 317) is a constitutional monarchy, administratively divided into 19 counties (*fylker*) and subdivided in 426 municipalities (kommunar).

The Ministry of Health and Care Services (HOD) has the overall responsibility for public health services in Norway. Among the main tasks of the Department of Public Health within the Ministry are protection against communicable diseases, prevention of HIV/AIDS, and health promotion. The Directorate of Health is a specialist directorate under the Ministry of Health and Care Services. Headed by the Chief Medical Officer, it has regulatory and implementing functions in the areas of health and care policy, and it monitors the conditions that affect public health. The directorate provides advice and guidance, and has authority to apply and interpret laws and regulations in the health sector.

The Norwegian Institute for Public Health (FHI) is a broad public health agency, acting as a national competence centre. The Domain of Infectious Disease Control is responsible for prevention and control of communicable diseases. The activities include national surveillance of infectious diseases and infectious agents, specialised microbiological services, the national immunisation programme and vaccine supply. The Domain provides advice and recommendations and performs applied research.

National competent authorities for communicable disease control

- Ministry of Health and Care Services (Helse- og omsorgsdepartementet): https://www.regjeringen.no/en/dep/hod/id421
- Norwegian Directorate of Health (Helsedirektoratet): https://helsedirektoratet.no
- Norwegian Institute of Public Health (Folkehelseinstituttet – FHI): www.fhi.no

Surveillance of communicable diseases

The notifications in the Norwegian Surveillance System for Communicable Diseases (MSIS) are based on the Communicable Diseases Control Act of 1995 and Health Register Act of 2002. All physicians and medical microbiology laboratories are obliged to report notifiable diseases in writing directly to the FHI, with copies for some diseases to the municipal medical officer. Some 65 diseases are reported with full patient identification. HIV, gonorrhoea and syphilis are reported anonymously using non-unique identifier linking reports from clinicians and laboratories. Searchable surveillance data are directly accessible on the Internet (www.msis.no).

Outbreak investigation and control

The municipal medical officers have the legal responsibility for detection, investigation and public health actions within their municipality, in co-operation with other local authorities (e.g. food safety authorities). If more than one municipality is involved or otherwise needed FHI will provide assistance.

Childhood vaccination schedule

Updated data on the Norwegian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), Rota, DTP, IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.

int/immunization_monitoring/global summary). Vaccine coverage rates for 2015 were: DTP1 (99%), DTP3 (96%), DTP4 (94%), IPV1 (99%), IPV3 (96%), Hib3 (96%), MMR1 (96%), MMR2 (91%), PCV1 (99%), PCV2 (98%), and PCV3 (94%) and Rota1 (96%).

5.26 Poland

Poland (population 38 484 000) is a republic, administratively divided into 16 provinces (*voivodeships*) and further subdivided in 380 districts (*powiats*), including 66 cities with *powiat* status.

The Ministry of Health is responsible for national public health policy and implementing national public health programmes. The Chief Sanitary Inspectorate (GIS) is a central administration body under the Ministry of Health, with public health protection as the main mission. The GIS works with communicable disease control, and other issues related to public health, through a system of provincial, county and border sanitary-epidemiological stations. The GIS supervises the work of the 16 provincial (*voivodeship*) sanitary-epidemiological stations (WSSE), and 10 border sanitary-epidemiological stations (GSSE), while district (*powiat*) and city sanitary-epidemiological stations (PSSE) are under the provincial sanitary-epidemiological stations. The GIS is also responsible for preparedness, response, threat detection and communication to the public on the national level.

The National Institute of Public Health–National Institute of Hygiene (NIZP-PZH) has a broad public health mission including infectious disease surveillance, microbiological services, food safety, scientific research and training. NIZP-PZH provides expertise and advice to the government and conducts vaccine research.

Surveillance and laboratory work on antimicrobial resistance is the responsibility of the National Medicines Institute (NIL). The Polish National Tuberculosis and Lung Disease Institute (IGICHP) performs surveillance, research and gives scientific advice on all issues related to tuberculosis.

National competent authorities for communicable disease control

- Ministry of Health (Ministerstwo Zdrowia – MZ): www.mz.gov.pl/en
- Chief Sanitary Inspectorate (Główny Inspektorat Sanitarny – GIS): http://gis.gov.pl/en
- National Institute of Public Health/National Institute of Hygiene (Narodowy Instytut Zdrowia Publicznego/Państwowy Zaklad Higieny – NIZP-PZH): www.pzh.gov.pl/en
- National Medicines Institute (Narodowy Instytut Leków – NIL): www.nil.gov.pl
- Polish National Tuberculosis and Lung Disease Institute (Instytutu Gruźlicy i Chorób Płuc – IGICHP): www.igichp.edu.pl

Surveillance of communicable diseases

A defined list of diseases and syndromes, as well as hospital-acquired infections, are notifiable by law by physicians, some of them also by laboratories. For some of the diseases, specific case-based epidemiological information is collected. The information flow is hierarchical with first-level reporting of case data to the district Sanitary–Epidemiological Stations (PSSE). These pass on aggregated data bi-weekly to the Voivodeship (WSSE) level. The national level (NIZP-PZH) receives data (both aggregated and – for some diseases – case-base data) from the second level. Alert diseases are reported to national level in 24 hours. Data from the national level is disseminated by the NIZP-PZH through a biweekly epidemiological bulletin, including tables of notified diseases and an annual epidemiological report (http://wwwold.pzh.gov.pl/oldpage/epimeld/index_p.html).

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is generally the responsibility of the PSSE, with support at provincial and national level. The information is forwarded by the PSSE to the WSSE, which is responsible for outbreak detection and management at the provincial level. The WSSE reports to the NIZP-PZH and Chief Sanitary Inspectorate, which has national responsibility for outbreak control.

Childhood vaccination schedule

Updated data on the Polish childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, Rota, DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR (special groups) and IIV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO Regional Office for Europe (http://data.euro.who.int/cisid). Vaccine coverage rates for 2015 were: BCG (94%), DTP1 (98%), HepB3 (96%), Hib3 (98%) IPV3 (92%), MMR1 (96%) and MMR2 (94%).

5.27 Portugal

Portugal (population 10 341 000) is a republic, administratively divided into 18 districts in mainland Portugal and two autonomous regions (Azores and Madeira). For health purposes, the mainland country is divided in 5 regional health administrations, and 74 primary healthcare centres groups, covering between 80 000 and 200 000 inhabitants

Public health policy making and defining national legislation are important tasks for the Ministry of Health, while five Regional Health Administrations (mainland) and two Regional Health Directorates (Azores and Madeira) are in charge of implementing the policy and co-ordinating regional public health activities. National co-ordination of HIV/AIDS surveillance and prevention is a vertical programme.

The General Directorate of Health (DGS), under the Ministry of Health, is responsible for communicable disease prevention and control at the national level. DGS co-ordinates the national network of health authorities, responsible for the regional and local response to PH threats DGS also provides scientific advice, issues guidelines, organises the national surveillance, threat detection, training, preparedness and response, and communication about communicable diseases to the general public through its web portal.

The National Institute of Health 'Dr Ricardo Jorge' (INSA) is a state laboratory involved in microbiological surveillance and public health research. It acts under the Ministry of Health, and has as key areas of work food safety, infectious diseases, epidemiology, genetics, health promotion and chronic diseases and environmental health. INSA is the national public health reference laboratory for most communicable diseases. It is also tasked with health research and produces scientific advice for public health policy and action. As a state laboratory it is responsible for co-ordinating quality assurance programmes.

In each Regional Health Administration (ARS), the public health department co-operates technically with DGS and ensures co-ordination of local public health activities, and between regional and national level.

A network of local health authorities, consisting of public health doctors, is based in the primary healthcare centre groups. Among other tasks they are responsible for surveillance and control of communicable diseases.

National competent authorities for communicable disease control

- Ministry of Health (Ministério da Saúde): www.sns.gov.pt/institucional/ministerio-da-saude

- Directorate General of Health (Direcção–Geral da Saúde – DGS), Disease Prevention and Control Department: www.dgs.pt
- National Institute of Health 'Dr Ricardo Jorge' (Instituto Nacional de Saúde Dr. Ricardo Jorge; INSA): http://www.insa.pt/sites/INSA/English/Pages/NationalHealthInstituteDoutorRicardoJorge.aspx

Surveillance of communicable diseases

A total of 61 diseases are notifiable by law. Every physician identifying a case is responsible for reporting to the local health authority (done through a web platform – SINAVE: http://www.dgs.pt/servicos-on-line1/sinave-sistema-nacional-de-vigilancia-epidemiologica.aspx). DGS is responsible for national surveillance, and is supported by INSA on laboratory surveillance. Data dissemination is carried out by DGS, through periodic reports and yearly statistics on mandatory notifiable diseases, which are published on the internet (https://www.dgs.pt/portal-da-estatistica-da-saude/diretorio-de-informacao/diretorio-de-informacao/por-serie.aspx). Special bulletins are released when needed.

Outbreak investigation and control

Control measures including contact tracing and outbreak investigation is generally the responsibility of the Public Health Service, primarily on local level with support from regional (Public Health Departments of ARS) and national level (DGS). Public health emergencies (including communicable disease outbreaks and food-safety events) are co-ordinated at the national level by DGS through its Public Health Emergency Centre that connects all levels of public health care, including in interactions with other sectors and at international level within IHR and EU alert systems.

Childhood vaccination schedule

Updated data on the Portuguese childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), DTP, IPV, HiB, HepB, PCV, MenC, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: BCG (32%), DTP1 (99%), DTP3 (97%), HepB3 (98%), Hib3 (98%), IPV3 (98%), MMR1 (98%) and MMR2 (95%).

5.28 Romania

Romania (population 19 511 000) is a republic divided into 41 counties (*județe*) and the capital Bucharest with equal status, and further subdivided into 319 cities and 2686 municipalities. Each county is governed by a county council.

The national public health system is under the responsibility of the Ministry of Health, and in the area of communicable disease control, the Ministry is responsible for initiation of legislative measures, implementation of surveillance systems, co-ordination of threat detection, preparedness and response, training, risk communication and international collaboration. This work is carried out through the co-ordination and supervision of a national network of communicable disease control and surveillance, consisting of several national, regional and district public health institutes and centres.

Under the Ministry of Health, the National Centre for Communicable Diseases Surveillance and Control (CNSCBT) at the National Institute of Public Health (INSP) in Bucharest co-ordinates the national epidemiological surveillance system and administers

the communicable diseases information system; it also monitors the national immunisation programme, co-ordinates the national early warning and response system and provides training.

Four regional centres (Centrul Regional de Sanatate Publica – CRSP), subordinate to the National Institute of Public Health, have responsibilities for regional surveillance and control of communicable diseases at regional level. The 42 district public health authorities (Direcţii de Sănătate Publica – DSP), in each district and the Bucharest Public Health Authority, have responsibility for control measures at the district level, including implementation of the immunisation programme and outbreak control.

The National Institute of Research Cantacuzino is an expert institute providing laboratory support in the area of communicable disease surveillance and control, including some reference laboratory support.

The National Institute for Infectious Diseases Prof. Dr. Matei Bals is a tertiary care infectious disease hospital, but is also responsible for HIV surveillance and the national HIV prevention programmes. The Institute of Pneumology Marius Nasta has the same role for tuberculosis. In its role of Co-ordinating Competence Body, the National Centre for Communicable Diseases Prevention Surveillance and Control relates with these institutes on surveillance matters and also in order to provide a single, co-ordinated response to the ECDC and the WHO.

National competent authorities for communicable disease control

- Ministry of Health (Ministrul Sănătăţii): www.ms.ro
- National Institute of Public Health (Institutul National de Sanatate Publica – INSP): www.insp.gov.ro
- National Centre for Communicable Diseases Surveillance and Control within the INSP (Centrul National de Supraveghere si Control al Bolilor Transmisibile – CNSCBT): www.cnscbt.ro
- Institute of Pneumology Marius Nasta (Institutul de Pneumoftiziologie Marius Nasta), surveillance: http://www.marius-nasta.ro
- National Institute for Infectious Diseases Prof. Dr. Matei Bals (Institutul National de Boli Infectioase Prof. Dr. Matei Bals), surveillance: www.mateibals.ro
- National Institute of Research Cantacuzino (Institutul National de Cercetare Cantacuzino), surveillance www.cantacuzino.ro

Surveillance of communicable diseases

The Romanian surveillance system is regulated by the Communicable Disease Control and Surveillance Action Plan 2004. The reporting system covers some 75 mandatory notifiable communicable diseases of which some are immediately notifiable, whereas for the others there is numerical reporting on a weekly, monthly, quarterly or annual basis. All health services' providers report to the DSPs.

The DSPs report further to the CRSP and for some communicable diseases, directly to CNSCBT. Data analysis is carried out at district, regional and national level. CNSCBT publishes weekly surveillance reports on its website.

There are separate systems for reporting on some diseases, for example HIV/AIDS, STI, and tuberculosis.

Outbreak investigation and control

The DSPs have the main responsibility for controlling outbreaks in their district. Control measures may include (preventive) treatment and hospitalisation. The CNSCBT-INSP holds the responsibility for co-ordination and control measures for outbreaks involving more than one district.

Childhood vaccination schedule

Updated data on the Romanian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG, DTP, IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: BCG (96%), DTP3 (89%), HepB3 (90%), Hib3 (89%), IPV3 (89%), MMR1 (86%) and MMR2 (87%).

5.29 Slovakia

Slovakia (population 5 435 343) is a republic divided into 8 regions (*krajov*) and further subdivided into 79 districts (*okresy*). The Ministry of Health has the overall responsibility for public health, including policy making, providing guidelines, health strategies, proposing legislation and co-ordinating preparedness, threat detection and response systems.

All the main activities in the area of communicable disease surveillance, prevention and control are carried out by the Public Health Authority of the Slovak Republic (UVZSR), an executive body under the Ministry of Health, and its network of 36 Regional Public Health Authorities. UVZSR is headed by the Chief Hygienist of the Slovak Republic. It is a broad public health agency, working on both communicable and non-communicable diseases. UVZSR is also responsible for the national immunisation programme, food safety, environmental hygiene, health education, health statistics, as well as for other public health functions. Within UVZSR, and selective Regional Public Health Authorities, are National Reference Centres, responsible for epidemiological and microbiological surveillance of specific infectious diseases. Surveillance is carried out closely together with the National Register of Communicable Diseases, located in the Regional Public Health Authority in Banská Bystrica. Surveillance and control activities on tuberculosis are carried out by the National Institute for Tuberculosis, Lung Diseases and Thoracic Surgery in Vyšné Hágy which runs the national TB registry.

National competent authorities for communicable disease control

- Ministry of Health of the Slovak Republic (Ministerstvo Zdravotníctva SR): www.health.gov.sk
- Public Health Authority of the Slovak Republic (Úrad Verejného Zdravotníctva Slovenskej Republiky; UVZSR): http://www.uvzsr.sk/en
- National Institute for Tuberculosis, Lung Diseases and Thorax Surgery/National Register of Tuberculosis in Vyšné Hágy: http://int.vhagy.sk/hagy
- Regional Public Health Authority in Banská Bystrica: http://www.vzbb.sk

Surveillance of communicable diseases

A total of 68 diseases are mandatory notifiable by law. Physicians and laboratories report to the Regional Public Health Authority which passes the information on to the National Register of Communicable Diseases in Banská Bystrica. The national analysis of data is carried out together with the experts in UVZSR. The basis for the surveillance system is the national Epidemiological Information System (EPIS), and dissemination of data (mainly in the Slovak language) is done through its portal: www.epis.sk.

Outbreak investigation and control

The physician who reports the case of communicable disease, is also responsible for case management. Outbreak detection and

control measures including contact tracing and outbreak investigation is generally the responsibility of the Regional Public Health Authorities, with support from UVZSR.

Childhood vaccination schedule

Updated data on the Slovakian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The national mandatory immunisation programme by law includes DTP, IPV, HiB, HepB, PCV, MMR, HPV and IIV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP3 (96%), DTP4 (97%), HepB3 (96%), Hib3 (98%), IPV3 (96%), MMR1 (95%) and MMR2 (97%).

5.30 Slovenia

Slovenia (population 2 064 000) is a republic divided into 12 'statistical' regions (without administrative functions), 58 administrative units and 211 local municipalities, 11 of which have urban status.

The Ministry of Health has the overall responsibility for the public health system, including public health policy, preparation of legislation and supervision of its implementation, and overall monitoring of public health systems.

The National Institute of Public Health (NIJZ), acting under the Ministry of Health, is a broad national expert and reference institution. It includes nine regional units and hosts the National Laboratory for Health, Environment and Food.

Within the NIJZ, the Centre for Communicable Diseases is responsible for surveillance of communicable diseases including healthcare-associated infections and the co-ordination of the activities of epidemiological teams in the nine regional units. The Centre is also involved in the preparation of proposals for legislation in the field of infectious diseases, and in the implementation and evaluation of preventive and control measures. It further issues recommendations and guidelines on all aspects of communicable disease prevention and control. It is also involved in research and training.

National competent authorities for communicable disease control

- Ministry of Health: www.mz.gov.si/en
- National Institute of Public Health (Nacionalni Inštitut za javno zdravje – NIJZ): http://www.nijz.si/en

Surveillance of communicable diseases

Surveillance of communicable diseases is regulated by law (Communicable Diseases Act and Law on Health Care Data Bases), and the Ministry of Health is responsible for proposing changes in the legislation. More than 80 diseases are notifiable. Reporting to the NIJZ is an obligation of all public healthcare institutions and other legal and physical entities providing healthcare.

National surveillance is co-ordinated by the Centre for Communicable Diseases at NIJZ. The Centre manages several national databases with reported data on communicable disease cases (including the communicable diseases data base, the HIV/STI/AIDS data base and the STI data base, as defined by the Law on Health Care Data Bases). Most of the results are disseminated through annual and quarterly disease surveillance reports available (in Slovenian) on the NIJZ website (http://www.nijz.si/sl/epidemiolosko-spremljanje-nalezljivih-bolezni-letna-in-cetrtletna-porocila). In addition, surveillance of healthcare-associated infections is being developed according to ECDC HAI-Net recommendations.

Outbreak investigation and control

The responsibility for case management is held by the notifier. Outbreaks are detected at regional level by various information sources, including surveillance data and laboratory results. Reporting of suspected outbreaks to the NIJZ is mandatory according to the Law on Communicable Diseases. Control measures such as contact tracing, clusters and outbreak investigation is under the responsibility of the Regional Units of the NIJZ (with the exception of HIV and STIs where it is the responsibility of the notifying physician).

Childhood vaccination schedule

Updated data on the Slovenian childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), DTP, IPV, HiB, HepB, PCV, MMR, HPV, IIV and TBE (endemic areas) (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP3 (94%), HepB3 (88%), Hib3 (94%), IPV3 (94%), MMR1 (92%), MMR2 (93%), PCV2 (49%) and PCV3 (50%).

5.31 Spain

Spain (population 46 423 000) is a constitutional monarchy. The country is divided into 17 autonomous regions and 2 autonomous cities, subdivided into 50 provinces. The regions have a large degree of autonomy with their own legislative assemblies, governments, supreme courts and public administrations. The public health services are organised regionally, and regional or local authorities are responsible for health protection, including surveillance and control of communicable diseases.

The Ministry of Health and Social Policy (MSSI) has the overall national responsibility to guarantee all inhabitants the right to health protection. Through its Directorate General for Public Health, the Ministry co-ordinates the health policies and is responsible for proposing and issuing legislation and regulations and for monitoring its implementation. In addition, the MSSSI acts as contact point for the International Health Regulations and is the Competent Body counterpart for the European Centre for Disease Prevention and Control (ECDC).

Co-ordination of public health is carried out in the Interterritorial Council of the National Health System (Consejo Interterritorial del Sistema Nacional de Salud), made up of national and regional Ministries of Health, where the decisions are taken by consensus. At provincial (health area) level there are Provincial Health Units. At local level, the public health services are integrated within primary healthcare, and the main part of preventive medicine and health promotion is carried out by GPs and nurses.

There are several national expert institutions including the Institute of Health Carlos III (ISCIII), the Health Research Fund (with national centres covering research and service in epidemiology and microbiology), the National Plan on AIDS (in charge of co-ordinating research, information, prevention and treatment of AIDS), the Spanish Medicines Agency and the Spanish Food Safety Agency.

The ISCIII is the key national public health research and scientific support institute supporting and advising the Ministry of Health and Social Policy and the national healthcare system. The tasks include epidemiological surveillance, reference, and diagnostic and control of communicable diseases and participating in the study of outbreaks and other biological or environmental health emergencies. The Institute operates a number of special departments and agencies, including the National Epidemiology Centre (CNE), the

National Centre for Tropical Medicine and the National Microbiology Centre.

The CNE is responsible for managing national surveillance and monitoring of both communicable and non-communicable diseases, as well as conducting research on health threats and providing training for experts in epidemiology and public health.

National competent authorities for communicable disease control

- Directorate-General for Public Health, Quality and Innovation (Dirección General de Salud Publica, Calidad e innovación), Ministry of Health and Social Policy (Ministerio de Sanidad, Servicios Sociales e Igualdad): https://www.msssi.gob.es
- Institute of Health Carlos III (Instituto de Salud Carlos III; ISCIII): www.isciii.es
- National Centre of Epidemiology (Centro Nacional de Epidemiología), ISCIII: http://www.isciii.es/ISCIII/es/contenidos/fd-servicios-cientifico-tecnicos/vigilancias-alertas.shtml

Surveillance of communicable diseases

All physicians are required by law to notify 60 diseases or agents to the regional health authorities. The notifications flow is: physicians to provincial/area authorities to regional authorities to the CNE to the Ministry of Health. The CNE manages surveillance at national level, through the national epidemiological surveillance network (Red Nacional de Vigilancia Epidemiológica de España; RENAVE). The Ministry of Health and Social Policy coordinates the network and coordinates the response to alerts and is responsible for preparedness and response plans.

A non-statutory laboratory reporting system (Sistema de Información Microbiológica; SIM) compiles at the national level information provided by clinical laboratories nationwide on a list of bacteria, viruses, fungi and intestinal parasites.

The CNE produces periodic reports and two bulletins, a weekly epidemiological bulletin (*Boletín Epidemiológico Semanal en red*) and the *Boletín Epidemiológico Semanal* http://www.isciii.es/ISCIII/es/contenidos/fd-servicios-cientifico-tecnicos/fd-vigilancias-alertas/boletines.shtml

Outbreak investigation and control

Outbreak investigations and control measures are undertaken by the health authorities at provincial or regional level, with support from national level in outbreaks involving more than one region. Regional and national reference laboratories also participate in investigations.

Childhood vaccination schedule

Updated data on the Spanish childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes DTP, IPV, HiB, HepB, PCV, MenC, MMR, VAR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: DTP3 (97%), DTP4 (95%), HepB3 (97%), Hib3 (97%), IPV3 (97%), MMR1 (97%), MMR2 (95%) and PCV3 (86%).

5.32 Sweden

Sweden (population 10 005 000) is a constitutional monarchy, divided into 20 county councils (*landsting and regioner*), and subdivided in 290 municipalities (*kommuner*). The county councils' responsibilities include

healthcare and public health including communicable disease control. The role of the central government is to establish principles and guidelines for healthcare and public health, while its implementation is to a large degree decentralised.

The Ministry of Health and Social Affairs (Socialdepartementet) has the overall responsibility for policy and introduction of new legislation, but the main part of national communicable disease control is carried out by the Public Health Agency of Sweden (Folkhälsomyndigheten).

Folkhälsomyndigheten has the overall national responsibility for protection and control of communicable diseases and a co-ordinating responsibility for public health, setting national standards, issuing guidelines, and co-ordinating outbreak control. Folkhälsomyndigheten is also in charge of national surveillance of communicable diseases, reference microbiology functions and research. Folkhälsomyndigheten also co-ordinates national and local actions against antimicrobial resistance; co-ordination, development and follow-up of vaccination programmes; and has the responsibility for preparedness for and management of health-threats (contact-point for IHR and EWRS).

At the county level, the County Medical Officer for Communicable Disease Control (*smittskyddsläkaren*) has a far reaching responsibility for local surveillance and for prevention and control of communicable diseases, including healthcare-associated infections.

National competent authorities/ bodies for communicable disease control

- Ministry of Health and Social Affairs (Socialdepartementet): http://www.government.se/government-of-sweden/ministry-of-health-and-social-affairs
- Public Health Agency of Sweden (Folkhälsomyndigheten): www.folkhalsomyndigheten.se

Surveillance of communicable diseases

The surveillance of communicable disease is regulated by law. Some 66 infections are notifiable within 24 hours, both by the doctor treating the patient and the diagnostic laboratory. For 49 of these diseases, the diagnosing clinician has a responsibility to perform contact tracing, and for some serious diseases, the County Medical Officer could enforce individual restrictions to prevent further transmission. Complementary to the statutory notification system there is are various syndromic surveillance systems tracing communicable disease through alternative data resources (such as web searches and calls to the health-information system) and a more comprehensive voluntary laboratory reporting system for some diseases such as RSV.

Notifications are carried out in parallel to the County Medical Officer and to Folkhälsomyndigheten through the web-based electronic surveillance system, SmiNet, with detailed epidemiological information in the clinical case notification.

At county level, the surveillance information is used as a basis for direct public health action. At the national level, the information is analysed for outbreak detection and monitoring disease trends. Detailed epidemiological information (in Swedish) with trends and comments is available on the website of Folkhälsomyndigheten: https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/sjukdomsstatistik.

Outbreak investigation and control

The County Medical Officer is responsible for investigation, including contact tracing and control measures, assisted by the Folkhälsomyndigheten when necessary. Depending on the kind of the outbreak the National Veterinary Institute (www.sva.se), the Swedish Board of Agriculture

(www.jordbruksverket.se) and the National Food Agency (www.livsmedelsverket.se) are also involved.

Childhood vaccination schedule

Updated data on the Swedish childhood vaccination schedule are available from ECDC (http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx). The general national child immunisation programme includes BCG (risk groups), DTP, IIV (spec. groups), IPV, HiB, HepB, PCV, MMR and HPV (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2016 were: BCG (26%), DTP3 (98%), HepB3 (67%), Hib3 (98%), IPV3 (98%), MMR1 (97%), MMR2 (95%) and PCV3 (97%).

5.33 Switzerland

Switzerland (population 8 401 000) is a confederation, consisting of 26 cantons with a large degree of autonomy, and further subdivided into 2485 municipalities. Each canton has its own constitution, parliament, government and courts.

The confederation is limited to act in areas in which the constitution has granted it explicit powers, and health legislation is mainly a responsibility of the cantons. However, in the area of health protection, the federal constitution gives the confederation legislative powers in the area of combating transmissible diseases.

The responsibility for the control of infectious diseases lies with the federal authorities of the Swiss Confederation; the 26 cantons are the executive bodies. The Federal Office of Public Health (FOPH) is the integrated centre of excellence for public health with a mandate to promote public health in the country. Its broad public health mandate explicitly covers early detection, surveillance and prevention of communicable diseases; it also undertakes training, research and public campaigns.

The Communicable Diseases Division of the FOPH is responsible for the notification systems, epidemiological monitoring and assessment, strategies, principles and planning, vaccination programmes and control measures, prevention and promotion, as well as crisis management and international relations. The FOPH is also responsible for national public health programmes, including the national HIV/AIDS programme and general child immunisation programmes, and is also tasked with legislation and oversight in the field of biological safety and consumer safety.

National competent authority for communicable disease control

Swiss Federal Office of Public Health (Bundesamt für Gesundheit, BAG): https://www.bag.admin.ch/bag/en/home.html

Surveillance of communicable diseases

The surveillance of communicable diseases is regulated by law. Some 53 diseases are notifiable. There are no financial incentives for the notifying physician. The majority of diseases are to be reported both by clinicians and the laboratories to the cantonal physician and the FOPH (via fax or mail). An electronic notification system is in preparation. For diseases that may require prompt public health action (e.g. anthrax and haemorrhagic fevers), both the clinician and the laboratory should notify the cantonal physician and FOPH within two hours.

An epidemiological bulletin, BAG-Bulletin (OFSP-Bulletin) is published weekly in German

and French by FOPH (https://www.bag.admin.ch/bag/de/home/service/publikationen/bag-bulletin.html). Surveillance data by disease are also available on the FOPH website (https://www.bag.admin.ch/bag/de/home/service/zahlen-fakten/zahlen-zu-infektionskrankheiten.html).

Outbreak investigation and control

There is a national system for outbreak control in Switzerland. This system is activated when more than one canton is affected by the outbreak. Outbreak management is the responsibility of the 26 cantons. The role of the FOPH is mainly a coordinating one, and actions can only be taken by the FOPH in exceptional situations.

Childhood vaccination schedule

The Swiss childhood vaccination schedule is updated and is published on a yearly basis and available on the FOPH Website (https://www.bag.admin.ch/bag/de/home/themen/mensch-gesundheit/uebertragbare-krankheiten/impfungen-prophylaxe/informationen-rund-ums-impfen/impfungen-fuer-saeuglinge-und-kinder.html)

Updated data on the Swiss childhood vaccination schedule are available from the WHO vaccine-preventable diseases monitoring system. The general national child immunisation programme includes DTP, IPV, HiB, HepB, PCV, MenC and MMR, (see list of Abbreviations at front of book).

Updated data on vaccine coverage are available from the WHO (http://apps.who.int/immunization_monitoring/globalsummary). Vaccine coverage rates for 2015 were: DTP3 (96%), DTP4 (89%), HepB3 (17%), Hib3 (95%), IPV3 (96%), MMR1 (94%), MMR2 (87%), PCV1 (85%), PCV2 (84%) and PCV3 (80%).

5.34 United Kingdom

Overview

The United Kingdom of Great Britain and Northern Ireland (population 65 648 000) is a constitutional monarchy that consists of four countries: England, Scotland, Wales and Northern Ireland. Health matters are devolved to the four constituent nations and health protection arrangements therefore differ in each country.

England: The national Government's Department of Health and Social Care (DHSC) in London has overall responsibility for health and healthcare and sets national policy for England. At the local level, public health responsibilities are shared between Local Authorities, which employ local Directors of Public Health and Environmental Health Officers, and the NHS. Public Health England (PHE), an executive agency sponsored by DHSC, undertakes most specialised health protection functions through its local health protection teams, specialist regional and national teams, and specialist and reference laboratories.

Scotland: The Scottish Government is responsible for the development of health protection policy in Scotland. NHS Scotland is accountable to the Scottish Government and comprises 14 territorial NHS Boards responsible for the protection and improvement of their population's health and for delivering frontline services in their area: these Boards employ the local public health teams that undertake local health protection activities, supported by the relevant Local Authority environmental health teams. Health Protection Scotland (HPS) is the national centre for infectious diseases surveillance and health protection emergency response. It provides advice, support and information to health professionals, national and local government, the general public and other bodies that are involved in protecting health. It commissions specialist and reference laboratories. For certain priorities, when

requested by the Government, it co-ordinates and assures the implementation of health protection policy. It leads the management of the health protection response when an incident affects more than one NHS Board.

Wales: The Welsh Assembly Government is responsible for health legislation and policy in Wales. Public Health Wales provides specialist health protection services, including the national Communicable Disease Surveillance Centre, microbiology laboratories and local health protection teams that work with Local Authority environmental health departments and the NHS, which is organised into seven Health Boards and three NHS Trusts.

Northern Ireland: The Department of Health of the Northern Ireland Executive is responsible for health legislation and policy in Northern Ireland. The Public Health Agency (PHA) provides a specialist health protection service encompassing: operational health protection response to both communicable and non-communicable disease issues; surveillance; advice, information and support to health care professionals and related organisations, District Councils and the general public.

National competent authorities for communicable disease control

The UK lead agencies for most international functions, for example links to the WHO and ECDC, are DHSC and PHE, both based in London. PHE provides the IHR National Focal Point for the whole UK (ihr@phe.gov.uk). However, within the UK, DHSC and PHE will work closely with their counterparts in the devolved administrations, who will usually lead within their own nations.

England

Department of Health and Social Care https://www.gov.uk/government/organisations/department-of-health-and-social-care

Public Health England www.phe.gov.uk

Scotland

Scottish Government Health Directorates http://www.sehd.scot.nhs.uk

Health Protection Scotland http://www.hps.scot.nhs.uk

Wales

Health and Social Care Department, Welsh Assembly Government www.wales.gov.uk/topics/health/?lang=en

Public Health Wales http://www.wales.nhs.uk/sitesplus/888

Northern Ireland

Department of Health, Social Services and Public Safety, Northern Ireland Executive https://www.health-ni.gov.uk

Public Health Agency http://www.publichealth.hscni.net

Surveillance of communicable diseases

In *England*, notifications of communicable diseases are governed by the *Health Protection (Notification) Regulations 2010*, which make it compulsory for medical practitioners to notify selected disease, infection or contamination in patients (www.legislation.gov.uk/uksi/2010/659/schedule/1/made) to the proper officer of the relevant Local Authority (see Table 5.34.1). In addition, diagnostic laboratories must notify selected causative agents found in human samples (www.legislation.gov.uk/uksi/2010/659/schedule/2/made) to Public Health England.

Wales has similar arrangements to England, except that laboratory notifications are made to the proper officer of the Local Authority rather than to PHE. The list of notifiable diseases is slightly different in *Scotland*, where notification is to the local health board (www.legislation.gov.uk/asp/2008/5/contents) and, in the case of laboratory reporting, directly to HPS at the Common Services

Table 5.34.1 Notifiable diseases example: diseases notifiable in England under the Health Protection (Notification) Regulations 2010

Rare infections	Common infections
Acute encephalitis	Acute infectious hepatitis
Acute poliomyelitis	Acute meningitis
Anthrax	Enteric fever (typhoid or paratyphoid fever)
Botulism	Food poisoning
Brucellosis	Haemolytic uraemic syndrome (HUS)
Cholera	Infectious bloody diarrhoea
Diphtheria	Invasive group A streptococcal disease and scarlet fever
Leprosy	Rubella
Plague	Legionnaires' disease
Rabies	Malaria
SARS	Meningococcal septicaemia
Smallpox	Measles
Tetanus	Mumps
Typhus	Tuberculosis
Viral haemorrhagic fever (VHF)	Whooping cough
Yellow fever	

Agency (which also receives reports of the clinical notifications received by Health Boards). In *Northern Ireland*, notifications from clinicians are to the DPH of the Public Health Agency (https://www.niinfectioncontrolmanual.net/notifiable-diseases) and there is an informal system of laboratory reporting to PHA.

Other sources of surveillance data used in the UK are discussed in Chapter 4.1.

Surveillance data for England and Wales are disseminated via the weekly Health Protection Report (https://www.gov.uk/government/collections/health-protection-report-latest-infection-reports) and the HPS Weekly Report (http://www.hps.scot.nhs.uk/ewr/index.aspx) for Scotland. Data for Northern Ireland can be found at: http://www.publichealth.hscni.net/directorate-public-health/health-protection/surveillance-data.

Outbreak investigation and control

Outbreak investigation and management, including contact-tracing, is generally undertaken by the PHE/PHW/PHA local health protection team (local public health department in Scotland) with support from local NHS, local authority, other relevant agencies (e.g. Food Standards Agency, Health and Safety Executive, Animal and Plant Health Agency) and PHE/HPS/PHW/PHA specialist teams and laboratories as necessary.

Childhood vaccination schedule

Updated data on the UK childhood vaccination schedule is available from EUVAC·NET http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx or https://www.gov.uk/government/publications/the-complete-routine-immunisation-schedule. The national programme at the time of writing is shown in Table 4.7.1.

Updated data on vaccine coverage is available from http://apps.who.int/immunization_monitoring/globalsummary or https://www.gov.uk/government/collections/vaccine-uptake. The most recent vaccine coverage rates (from 2016): DTP3 (94%), DTP4 (87%), HiB3 (94%), MMR1 (92%), MMR2 (89%), PCV1 (94%), PCV2 (92%) and RotaC (90%) (see list of Abbreviations at front of book).

Appendix 1

Guidance documents and books

Please note that guidance documents are often updated and the documents given below are the most up to date that we could access at the time of writing. Checks for additional, more up to date or more local, guidance can be made by accessing the appropriate national centre website (see Section 5 chapters) or by checking the lists of websites at the end of this appendix and inside the covers of the book.

Guidance documents in this section are grouped by:

- Bloodborne viruses
- Gastrointestinal infections
- Immunisations
- Imported infections and travel advice
- Infection control and healthcare acquired infection
- Influenza
- Legionnaires' disease
- Meningitis and meningococcal infection
- Preparedness planning
- Tuberculosis
- Vector-borne diseases
- Other
- Websites containing infectious disease guidelines

Bloodborne viruses (BBV)

Guidance on BBVs and healthcare workers is available at: https://www.gov.uk/guidance/bloodborne-viruses-in-healthcare-workers-report-exposures-and-reduce-risks, including:

- UK Health Departments. *HIV infected health care workers: guidance on management and patient notification*. London: Department of Health, 2005.
- EAGA. *HIV post-exposure prophylaxis: guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS*. London: Department of Health, 2008.
- PHE. *The Management of HIV infected Healthcare Workers who perform exposure prone procedures: updated guidance, January 2014*. London: PHE, 2014.
- Health Protection Agency. *Standards for local surveillance and follow up of hepatitis B and C*. London: HPA, 2011.
- Department of Health. *Hepatitis B infected healthcare workers and antiviral therapy*. London: DH, 2007.
- Ramsay ME. Guidance on the investigation and management of occupational exposure to hepatitis C. *Commun Dis Public Health* 1999; **2**: 258-62.
- Department of Health. *Hepatitis C infected health care workers*. London: Department of Health Publications, 2002

Department of Health. *New healthcare workers: clearance for hepatitis B and C, TB, HIV*. London: DH, 2007. Available at URL: https://www.gov.uk/government/publications/new-healthcare-workers-clearance-for-hepatitis-b-and-c-tb-hiv

European Commission. *Recommendations for post-exposure prophylaxis against HIV infection in health care workers in Europe*. Project number SI2.322294, March 2002. Available at http://www.inmi.it/news/LineeGuida/RecommendationsHCW.htm

Cresswell F, Waters L, Eleanor Briggs H et al. UK guideline for the use of HIV Post-Exposure Prophylaxis Following Sexual Exposure, 2015. *International Journal of STD & AIDS 2016*; 27: &13–38. doi:10.1177/0956462416641813 Available at: https://www.bashhguidelines.org/media/1027/pepse-2015.pdf

Gastrointestinal infections

Up to date guidelines from PHE are available at: https://www.gov.uk/government/collections/gastrointestinal-infections-guidance-data-and-analysis, including the following:

Communicable Disease Control and Health Protection Handbook, Fourth Edition. Jeremy Hawker, Norman Begg, Ralf Reintjes, Karl Ekdahl, Obaghe Edeghere and Jim van Steenbergen.

- PHE. *Principles and Practice Recommendations for the Public Health Management of GI Infections*. London: PHE, 2018.
- PHE. *Public Health Operational Guidelines for Shiga toxin producing Escherichia coli (**STEC**) (previously known as VTEC) Including STEC (O157 and non-O157) infections*. London: PHE, 2018.
- PHE: *Public Health Operational Guidelines for **Shigellosis***. London: PHE, 2017.
- PHE. *Public Health Operational Guidelines for **Typhoid and Paratyphoid** (Enteric Fever)*. London: PHE, 2017.

Norovirus Working Party. *Guidelines for the management of **norovirus** outbreaks in acute and community health and social care settings*. London: HPA, 2012. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/322943/Guidance_for_managing_norovirus_outbreaks_in_healthcare_settings.pdf

PHE *Public health control and management of **hepatitis A**. 2017 Guidelines*. London, PHE, 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/623036/Public_health_control_and_management_of_hepatitis_A_2017.pdf

PHE. ***Botulism**: clinical and public health management*. Available at: https://www.gov.uk/government/publications/botulism-clinical-and-public-health-management/botulism-clinical-and-public-health-management

Bouchier IT (Chairman). ***Cryptosporidium** in water supplies. Third report of the group of experts to: Department of Environment, Transport, and the Region and the Department of Health*. London: DETR, 1998. Available at: http://dwi.defra.gov.uk/research/bouchier/title.pdf

Immunisation

Department of Health. *Immunisation against Infectious Diseases*. London: DH, 2018. Available at: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

Immunisation schedules for other EU countries can be found at: http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx

Imported infection and travel advice

World Health Organization. *International travel and health*. Geneva: WHO, 2018. http://www.who.int/ith/en

European Centre for Disease Prevention and Control. Patient and case management for **Ebola** virus disease (various guidance documents).
https://ecdc.europa.eu/en/ebola-and-marburg-fevers/prevention-and-control/patient-and-case-management

Advisory Committee on Dangerous Pathogens. *Management of Hazard Group 4 **viral haemorrhagic fevers** and similar human infectious diseases of high consequence*. London: ACDP, 2015. Available at: *Management of Hazard Group 4 viral haemorrhagic fevers and similar human infectious diseases of high consequence*. London: ACDP, 2015.

Public Health England. *Investigation and public health management of people with possible Middle East Respiratory Syndrome Coronavirus (**MERS**-CoV) infection (v30 – January 2018)*. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/678219/Algorithm_case_Jan2018.pdf

Chiodini P et al. *Guidelines for **malaria** prevention in travellers from the United Kingdom 2017*. London: PHE, 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/660051/Guidelines_for_malaria_prevention_in_travellers_from_the_UK_2017.pdf

Diphtheria Guidelines Working Group. *Public health control and management of **diphtheria** (in England and Wales). 2015 Guidelines*. London: PHE, 2015.
Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/416108/Diphtheria_Guidelines_Final.pdf

Brown, K. *PHE guidelines on **rabies** post-exposure treatment (June 2017)*. London: PHE, 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/617521/PHE_guidelines_on_rabies_post-exposure_treatment.pdf.

HPA Centre for Infections. The Public Health Management of a Suspected Case of Human **Rabies**. A Standard Operating Procedure for Communication & Action. London: HPA, 2009. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/331162/Management_of_a_Suspected_Case_of_Human_Rabies.pdf

Infection control and healthcare acquired infection

Loveday HP, Wilson JA. Pratt RJ et al. *epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. J Hosp Inf* 2014; **86** suppl 1: S1–S70. https://doi.org/10.1016/S0195-6701(13)60012-2

Health Protection Agency. *Prevention and control of infection in care homes –an information resource*. London: HPA, 2013. Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214929/Care-home-resource-18-February-2013.pdf

NICE. *Infection Prevention and control of healthcare-associated infections in primary and community care (CG 139)*. Available at URL: https://www.nice.org.uk/guidance/cg139

SHEA/IDSA. *Strategies to Prevent **Clostridium difficile** Infections in Acute Care Hospitals: 2014 Update*. Available at URL: https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/strategies-to-prevent-clostridium-difficile-infections-in-acute-care-hospitals-2014-update/956D9777C4DA349B76F59E6A46553DC6

HCAI Operational Guidance Working Group). *Health Care Acquired Infection Operational Guidance and Standards for Health Protection Units*. London: HPA, 2013. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/332051/HCAI_Operationalguidancefinalamended_05July2012.pdf

APIC, 2010. *Guide to the Elimination of Methicillin-Resistant Staphylococcus aureus (**MRSA**) Transmission in Hospital Settings, 2nd Edition*. Available at URL: http://apic.org/Resource_/EliminationGuideForm/631fcd91-8773-4067-9f85-ab2a5b157eab/File/MRSA-elimination-guide-2010.pdf

European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2009. *Consensus statement. Prevention and control of **methicillin-resistant Staphylococcus aureus** (2009)*. Available at URL: https://www.escmid.org/fileadmin/src/media/PDFs/4ESCMID_Library/2Medical_Guidelines/other_guidelines/CMI_2009_15_2_120_Humphreys.pdf

Nathwani D et al on behalf of the British Society for Antimicrobial Chemotherapy Working Party on community-onset MRSA Infections. *Guidelines for UK practice for the diagnosis and management of methicillin-resistant Staphylococcus aureus (**MRSA**) infections presenting in the community 2008. J Antimicrob Chemotherapy* 2008; **61**: 976-994. doi:10.1093/jac/dkn096

HPA. *Guidance on the diagnosis and management of PVL-associated Staphylococcus aureus infections (**PVL-SA**) in England, 2nd Edition*. London, HPA, 2008. Available at: http://webarchive.nationalarchives.gov.uk/20140505135134/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1218699411960

Healing TD, Hoffman PN, Young SEJ. The infection hazards of human cadavers. *Commun Dis Rep CDR Rev* 1995; **5**: R61–68.

Influenza

World Health Organization. *Pandemic influenza risk management. A WHO guide to inform & harmonize national & international pandemic preparedness and response*. Geneva: WHO, 2017.

http://www.who.int/influenza/preparedness/pandemic/influenza_risk_management_update2017/en/

European Centre for Disease Prevention and Control. *Interim guidance. Public health use of influenza antivirals during influenza pandemics*. Stockholm: ECDC, 2009. Available at http://ecdc.europa.eu/en/publications/Publications/0907_GUI_Public_Health_use_of_Influenza_Antivirals_during_Influenza_Pandemic.pdf

Legionnaires' disease

PHE. *Guidance on investigating cases, clusters and outbreaks of Legionnaires' disease*. London: PHE, 2016. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/578018/LegionnairesDiseaseCasesClustersOutbreaks.pdf

World Health Organization. *Legionella and the prevention of legionellosis*. Geneva: WHO, 2007. Available at: http://www.who.int/water_sanitation_health/emerging/legionella.pdf

The Guidelines Working Group. *European technical guidelines for the prevention, control and investigation of infections caused by Legionella species. June 2017*. Available at: https://ecdc.europa.eu/en/publications-data/european-technical-guidelines-prevention-control-and-investigation-infections

Health and Safety Executive. *Legionnaires' disease. The control of legionella bacteria in water systems. Approved Code of Practice and guidance on regulations. 4th Edition*. London: HSE, 2013. Available at: http://www.hse.gov.uk/pubns/priced/l8.pdf

Meningitis and meningococcal infection

European Centre for Disease Prevention and Control. *Public health management of sporadic cases of invasive meningococcal disease and their contacts*. Stockholm: ECDC; 2010. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/1010_GUI_Meningococcal_guidance.pdf

Health Protection Agency Meningococcus and Haemophilus Forum. *Guidance for public health management of meningococcal disease in the UK*. London: HPA, 2012. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/322008/Guidance_for_management_of_meningococcal_disease_pdf.pdf

Public Health England and Universities UK. *Guidance on the prevention and management of meningococcal meningitis and septicaemia in higher education institutions*. London: PHE, 2016. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/582511/MenACWY_HEI_Guidelines.pdf

PHE. *Revised recommendations for the prevention of secondary Haemophilus influenzae type b (**Hib**) disease*. London: PHE, 2013. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/231009/Revised_recommendations_for_the_preventions_of_secondary_Haemophilus_influenzae_type_b_disease.pdf

Preparedness planning

European Centre for Disease Prevention and Control. *Operational guidance on rapid risk assessment methodology*. Stockholm: ECDC, 2011. http://ecdc.europa.eu/en/publications/Publications/1108_TED_Risk_Assessment_Methodology_Guidance.pdf

European risk assessment guidance for infectious diseases transmitted on aircraft – RAGIDA (various guidance documents). https://ecdc.europa.eu/en/infectious-diseases-public-health/travellers-health/infectious-diseases-aircraft

European Centre for Disease Prevention and Control. *ECDC tools to strengthen preparedness at migrant reception centres*. Stockholm: ECDC, 2016. http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?ID=1495&List=8db7286c-fe2d-476c-9133-18ff4cb1b568

European Centre for Disease Prevention and Control. *Handbook on implementing syndromic surveillance in migrant reception/detention centres and other refugee settings*. Stockholm: ECDC, 2016. https://ecdc.europa.eu/sites/portal/files/media/en/publications/

Publications/syndromic-surveillance-migrant-centres-handbook.pdf

European Centre for Disease Prevention and Control. *Safe use of personal protective equipment in the treatment of infectious diseases of high consequence*. Stockholm: ECDC, 2014. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/safe-use-of-ppe.pdf

European Centre for Disease Prevention and Control. *Use of personal protective equipment for safe first assessment of persons under investigation of Ebola virus disease in the EU/EEA*. Stockholm: ECDC, 2014. http://ecdc.europa.eu/en/publications/Publications/Use-of-PPE-for-safe-first-assessment.pdf

European Centre for Disease Prevention and Control. *Tutorial on the safe use of personal protective equipment (e-tutorial)*. Stockholm: ECDC, 2014. https://ecdc.europa.eu/en/publications-data/tutorial-safe-use-personal-protective-equipment

European Centre for Disease Prevention and Control. ECDC *Handbook on Simulation Exercises in EU public health settings*. Stockholm: ECDC, 2014. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Simulation-exercise-manual.pdf

Tuberculosis

National Institute for Health and Clinical Excellence. *Tuberculosis. NICE guideline*. London: NICE, 2016. Available at: https://www.nice.org.uk/guidance/ng33

European Centre for Disease Prevention and Control. *Management of contacts of MDR TB and XDR TB patients*. Stockholm: ECDC; 2012. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/201203-Guidance-MDR-TB-contacts.pdf

Getahun H, Matteelli A, Abubakar I et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. *European Respiratory Journal* 2015 46: 1563–1576; DOI: 10.1183/13993003.01245-2015. http://erj.ersjournals.com/content/46/6/1563

Public Health England Health Protection Services Prison Network. *Management of tuberculosis in prisons: Guidance for prison healthcare teams*. London: PHE, 2013. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/323325/TB_guidance_for_prison_healthcare.pdf

Vector-borne diseases

European Centre for Disease Prevention and Control. *Preparedness planning guide for diseases transmitted by Aedes aegypti and Aedes albopictus*. Stockholm: ECDC, 2016. http://ecdc.europa.eu/en/publications/Publications/zika-preparedness-planning-guide-aedes-mosquitoes.pdf

European Centre for Disease Prevention and Control. ***Zika*** *virus and safety of substances of human origin – A guide for preparedness activities in Europe*. Stockholm: ECDC, 2016. http://ecdc.europa.eu/en/publications/Publications/Zika-virus-safety-of-substances-of-human-origin.pdf

European Centre for Disease Prevention and Control. ***Zika*** *virus disease epidemic: Preparedness planning guide for diseases transmitted by Aedes aegypti and Aedes albopictus*. Stockholm: ECDC, 2016. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/zika-preparedness-planning-guide-aedes-mosquitoes.pdf

European Centre for Disease Prevention and Control. *Guidelines for the surveillance of invasive mosquitoes in Europe*. Stockholm: ECDC, 2012. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/TER-Mosquito-surveillance-guidelines.pdf

European Centre for Disease Prevention and Control. *Interim guidance for healthcare providers and* ***Zika*** *virus laboratory diagnosis*. Stockholm: ECDC, 2016. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/zika-virus-guidance-healthcare-providers-and-laboratory-diagnosis.pdf

European Centre for Disease Prevention and Control. ***West Nile virus*** *risk assessment tool*. Stockholm: ECDC, 2013. https://ecdc.europa.

eu/en/publications-data/west-nile-virus-risk-assessment-tool-0

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Pertussis Guidelines Group. *Guidelines for the Public Health Management of* ***Pertussis*** *in England*. London: PHE, 2016, Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/576061/Guidelines_for_the_Public_Health_Management_of_Pertussis_in_England.pdf

HPA Rash Guidance Working Group. *Guidance on Viral Rash in Pregnancy. Investigation, Diagnosis and Management of Viral Rash Illness, or Exposure to Viral* ***Rash Illness, in Pregnancy***. London: HPA, 2011. Avalable at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/322688/Viral_rash_in_pregnancy_guidance.pdf

Crowcroft NS et al. Guidance for the control of **parvovirus** B19 infection in healthcare settings and the community. *J Public Health Med* 1999; 21: 439-46. Available at: https://doi.org/10.1093/pubmed/21.4.439

PHE. *Managing* ***outbreaks of Sexually Transmitted Infections****: Operational guidance*. London: PHE, 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/584723/PHE_STI_outbreak_guidelinesNB180117.pdf

Health Protection Agency. *Initial investigation and management of* ***outbreaks and incidents of unusual illness.*** London: HPA, 2010. Available at: http://webarchive.nationalarchives.gov.uk/20140714100423/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1201265888951

WHO. Manual: *The public health management of* ***chemical incidents***. Geneva: WHO, 2009. Available at: http://www.who.int/environmental_health_emergencies/publications/Manual_Chemical_Incidents/en/

PHE. Health protection in **schools** and other childcare facilities. Available at https://www.gov.uk/government/publications/health-protection-in-schools-and-other-childcare-facilities.

PHE. PHE National **Measles** Guidelines August 2017. Available at: https://www.gov.uk/government/publications/national-measles-guidelines

NICE. *British National Formulary*. Available at: https://bnf.nice.org.uk/

BSAC. Antimicrobial stewardship. From principle to practice. Available at: http://bsac.org.uk/antimicrobial-stewardship-from-principles-to-practice-e-book/

UK Standards for Microbiology Investigations (SMI). Available at: https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi

Websites containing infectious disease guidelines

https://ecdc.europa.eu/en/publications-data

http://www.who.int/rpc/guidelines/en/index.html (plus some additional guidelines in disease sections of http://www.who.int/health-topics/)

https://www.gov.uk/topic/health-protection/infectious-diseases

https://www.nice.org.uk/guidance/health-protection http://www.neli.org.uk/IntegratedCRD.nsf/NeLI_Browse_Guidelines?OpenForm

https://www.cochranelibrary.com/browse-by-topic

http://www.library.nhs.uk/

https://www.cdc.gov/az/a.html

https://www.cdc.gov/infectioncontrol/guidelines/index.html

https://www.escmid.org/escmid_publications/medical_guidelines/

http://www.idsociety.org/PracticeGuidelines/

https://travelhealthpro.org.uk/

https://www.gov.uk/government/collections/immunisation

https://www.britishinfection.org/guidelines-resources/

https://www.ips.uk.net/professional-practice/guidance/

http://www.isid.org/education/guide-to-infection-control-in-the-healthcare-setting/

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