Key Points Revision

1 Structure and classification of bacteria

- Bacteria contain unique structures that differentiate them from eukaryotes
- Bacteria are known by their genus and species name e.g. *Salmonella* (genus name) *enterica* (species name)
- Species of bacteria cause a recognized spectrum of infectious syndromes, so identification is important in predicting their pathogenicity and epidemiology
- Bacterial structure is used to separate species of bacteria
- Serological and biochemical characteristics and increasingly gene sequencing are used to definitively identify bacterial species

2 Innate immunity and normal flora

- Commensal bacteria form the normal flora and may help to prevent invasion by pathogens
- Antibiotics may destroy the natural bacterial balance and allow infection by naturally resistant pathogens
- The innate immune system is the first line of defence and prevents a wide range of infections efficiently
- Congenital deficiencies in components of the innate immune system result in susceptibility to particular infections e.g. complement membrane attack complex deficiency makes neisserial infection more likely
- Medical practice can bypass or compromise the innate immune system e.g. a cannula breaching the skin

3 Pathogenicity and pathogenesis of infectious diseases

- Pathogenicity is the ability to cause disease
- Virulence is the ability of an organism to cause severe disease
- Pathogens can be obligate (always cause disease) or opportunist (cause disease when circumstances allow)
- All pathogens must be transmitted, invade, attach and evade the immune response
- Pathogens produce pathogenicity factors that cause harm through a variety of mechanisms e.g. toxin release or an intense immune response such as the lipopolysaccharide response

4 The laboratory investigation of infection

- Almost all biological samples can be used for the diagnosis of infection and it is essential that these are collected and transported to the laboratory in a way that preserves the pathogen to be detected
- It is important to choose a sample in which, from your knowledge of the natural history of infection, the pathogen, its antigens or the immune response is likely to be present
- Gross examination, microscopy, culture, serology and molecular detection are used to detect the presence of pathogens
- Susceptibility testing allows treatment to be tailored to individual patients

Medical Microbiology and Infection at a Glance, Fourth Edition. Stephen H. Gillespie, Kathleen B. Bamford.

5 Antibacterial therapy

- Antibiotics aim to kill the infecting organism without harming the host: selective toxicity
- Choice of therapy depends on the infecting organism, site of infection, the susceptibility pattern, severity of infection, allergy and other medical issues
- Antibiotics can be administered parenterally, orally or locally e.g. skin, rectally or in pessaries
- Therapy can be monitored to reduce toxicity, ensure adequate tissue concentrations in difficult sites or when the infecting organism is partially resistant
- Antibiotics can have adverse events in all body systems and additionally can disturb the normal flora causing diarrhoea or superinfection with resistant organisms

6 Antibiotics in clinical use

- Antibiotics in clinical use act by inhibiting bacterial metabolism specifically
- Each agent has a unique spectrum of activity
- The main classes include penicillins, cephalosporins, fluoroquinolones, aminoglycosides and tetracyclines
- New agents are being introduced to improve the pharmacokinetic characteristics of the drugs and to overcome resistance

7 Resistance to antibacterial agents

- Bacteria can rapidly become resistant to antibiotics because of their fast growth rate, mutation rate and the ability to exchange DNA between organisms
- Antibiotic use favours organisms that have acquired resistance determinants so antibiotics should be prescribed carefully
- Resistance emerges through chromosomal mutation, transformation, transduction or conjugation
- Bacteria can acquire multiple resistance elements that can make them difficult to eradicate
- Resistance develops through enzymic destruction or modification, altering the target site or metabolic pathway, pumping the antibiotic out of the cell or blocking its entry

8 Sources and transmission of infection

- The source of infection can be endogenous: from the host's flora or exogenous from a source outside the body
- The main source of infection is other humans
- Other important sources are animals, whether as food or by direct contact and the environment e.g. *Legionella*
- Organisms may have specialist survival structures such as spores in some bacteria or a tough outer coat in the case of some parasites
- The main routes of transmission are oral, airborne, sexual, parenteral and via vectors

9 Principles of infection control

- Outbreaks must be recognized by effective diagnosis and synthesis of clinical and laboratory data
- Infecting organisms must be studied in sufficient detail to allow closely related organisms to be identified and distinguished from unrelated organisms
- Typing can be achieved by biochemical, serological, phage-based and molecular/genomic methods
- The main aim of infection control is to prevent spread of infection from infected to uninfected individuals
- There are different forms of isolation that break critical components of the transmission route: wound and enteric, respiratory, protective and strict isolation

10 Infection in the hospital environment

- The hospital environment favours infection transmission due to the presence of individuals with reduced defences who are often subjected to invasive procedures
- Communal air supply, catering and water may be a source of infection
- Indwelling catheters, parenteral cannulae and endotracheal tubes can bypass host defences and allow invasive infection
- Peroperative antibiotics may reduce the risk of infection
- Operations may be classified into clean, contaminated and infected; these classifications change the prescription of antibiotic given

11 Immunization

- Immunization is the process whereby immunologically naïve individuals are provided with immunity without the risk of complications of natural infection
- Immunization can be achieved by giving protective antibodies (Passive Immunization) or by giving vaccination that will stimulate an effective immune response (Active Immunization)
- Vaccine may consist of killed whole organism, toxoids, cellular subunits, live attenuated organisms or genetically engineered antigens
- Vaccines are administered according to national guidelines to provide immunity against the range of preventable diseases
- Individual vaccines may be required for rarer diseases for those individuals at higher risk than the general population

12 Emerging infections

- The speed at which organisms spread depends on the route of transmission and the basic reproductive number
- Pathogens may be ‘emerging’ because they are isolated for the first time in the human host, are an established organism invading a new territory or an organism that has been controlled previously but returns
- Organisms may emerge because of changes that humans make, agricultural methods or the way in which food is handled
- Organism may emerge because they acquire novel pathogenicity determinants

- Some organisms may be emergent because they have acquired multiple resistance and are now difficult to eradicate

13 *Staphylococcus*

- There are more than 26 staphylococcal species of which *S. aureus* and *S. epidermidis* are most important in clinical practice that can act as either commensals or pathogens
- *S. aureus* has a range of pathogenicity factors including toxins, lytic enzymes, coagulase, adhesion molecules and capsular structures
- *S. aureus* can become resistant to flucloxacillin by the acquisition of a cassette encoding an alternative penicillin-binding protein (mecA).
- Methicillin-resistant *S. aureus* can pose a considerable infection risk in hospitals and the community
- *S. aureus* is an important cause of skin, bone and joint infection, also rarely endocarditis and pneumonia
- *S. epidermidis* may act as a pathogen for patients with indwelling venous cannulae

14 Streptococcal infections

- *Streptococcus pyogenes* colonises the throat and can cause pharyngitis, skin sepsis, septicaemia, puerperal sepsis, septic arthritis osteomyelitis and toxic shock syndrome
- *S. pyogenes* immune responses may cause glomerulonephritis or rheumatic fever
- *S. pyogenes* has a range of pathogenicity factors including the antiphagocytic M protein, toxins, adhesins and tissue destroying enzymes e.g. hyaluronidase
- *S. agalactiae* colonises the gut and vagina and is an important cause of neonatal sepsis
- Enterococci are part of the normal flora but may cause urinary tract infection and septicaemia. Strains that have acquired resistance to glycopeptide can be important hospital pathogens

15 *Streptococcus pneumoniae*, other Gram-positive cocci and alpha-haemolytic streptococci

- *S. pneumonia* is the most important bacterial cause of pneumonia and a common cause of meningitis
- Its pathogenicity is defined by its antiphagocytic capsule (more than 90 types) and antibodies to the capsule are protective
- Although ideally treated with penicillin, an increasing number have reduced susceptibility due to the acquisition of small components of DNA from related organism to form a mosaic genes
- To protect younger children a vaccine consisting of capsular polysaccharide conjugated to protein from the commonest serotypes is used
- Oral streptococci are an important cause of endocarditis and the *S. anginosus–intermedius–constellatus* group of organisms may cause multiple abscesses

16 *Listeria, Bacillus Corynebacterium and* environmental mycobacteria

- *Listeria* is an environmental organism that can contaminate food and can both survive and multiply at refrigeration temperatures
- It can be transmitted from the mother to baby and is an important cause of perinatal sepsis in both mother and baby where it may cause septicaemia or meningitis
- *Bacillus anthracis* is the causative organism of anthrax a rapidly fatal cattle infection that can rarely spread to humans, presenting as skin lesions or septicaemia
- *Bacillus anthracis* is an important potential bioterrorism weapon and considerable efforts have been made to be able to detect it and manage deliberate releases
- Non-tuberculosis mycobacteria are increasingly recognized as important pathogens in individuals who are immunocompromised or have anatomic disturbance of lung architecture

17 Diphtheria, tetanus and pertussis

- All three of these infections are prevented by vaccines given as part of the primary vaccination schedule
- Diphtheria is a severe disease mediated by a phage-encoded toxin gene
- Diphtheria presents with a severe pharyngitis followed by toxaemia and neuropathy
- The toxin of tetanus produces severe muscle spasms that may compromise respiration
- Pertussis is a chronic infection causing a paroxysmal cough complicated by secondary bacterial infections

18 Pathogenic mycobacteria

- Mycobacteria have an unusual cell wall with a high proportion of lipid that, when stained, resists decolouration giving rise to the popular name of these organisms ‘acid fast’
- Tuberculosis and leprosy are global infections caused by the pathogenic mycobacteria
- Tuberculosis is a chronic progressive infection of the lung. There are approximately 10 million new infections diagnosed each year and more than 1 million deaths
- Treatment is made difficult by their slow growth rate and their ability to mutate to become resistant, which means that treatment needs to be with multiple anti-tuberculous antibiotics taken for at least 6 months
- Leprosy is a chronic infection that affects the neurological system causing a sensory neuropathy followed by digital destruction and ‘Charcot’s’ joints

19 *Clostridium*

- Clostridia cause disease due to the production of one or more exotoxins
- *Clostridium difficile* produces pseudomembranous colitis. It often presents when a colonized patient is given antibiotics and this organism becomes dominant in the gut

- *C. difficile* can be responsible for outbreaks of disease in hospitals and elderly-care facilities and control of spread and rapid treatment is an important priority
- *Clostridium botulinum* contaminating food may produce a toxin which, if it survives the preparation process, can produce a flaccid paralysis that may compromise respiration
- *Clostridium perfringens* and other related clostridia can invade necrotic tissues causing rapidly progressive necrosis: gas gangrene

20 Non-sporing anaerobic infections

- Non-sporing anaerobes are an important part of the normal flora and provide protection against invading pathogens
- Infection is usually endogenous and occurs when anaerobic conditions are created that allow these organisms to invade e.g. a strangulated hernia
- Intra-abdominal sepsis, sepsis of the female genital tract and pelvic inflammatory disease are the major syndromes associated with these organisms
- Treatment is directed towards correcting tissue anoxia by operative intervention and drainage of pus
- Such infections can be reduced by optimizing operative technique and providing preoperative antibiotic prophylaxis

21 *Neisseria* and *Moraxella*

- *Neisseria gonorrhoeae* is a sexually transmissible agent responsible for urethritis cervicitis and pelvic inflammatory disease
- Rapid diagnosis and syndromic treatment is essential to control transmission of the organism
- The multiplicity of strain types makes vaccination impossible at present
- *Neisseria meningitis* is usually part of the normal flora but from time to time some strains can cause meningitis and septicaemia. Large epidemics, notably in Africa, can be associated with high attack rates and mortality
- Diagnosis depends on clinical suspicion, clinical features and rapid diagnosis
- Protein conjugates with capsular polysaccharide have made effective vaccines for two major serotypes: meningitis A and meningitis C

22 Small Gram-negative coccobacilli: *Haemophilus*, *Brucella*, *Francisella*, *Yersinia* and *Bartonella*

- *Haemophilus influenzae* colonises the nasopharynx and is responsible for respiratory infections in patients with chronic obstructive pulmonary disease.
- *Brucella* are pathogens of animals that spread to humans through direct contact (farmers and vets) or from products e.g. milk or cheese
- *Francisella tularensis* is a rare zoonotic infection acquired from rodents or dear causing a syndrome that resembles typhoid
- *Yersinia pestis* is the causative organism of plague a potentially pandemic disease that can spread rapidly and cause high mortality
- *Bartonella* are rare pathogens acquired by vectors (ticks, lice or sandflies) or from domesticated animals

23 Pathogenicity of enteric Gram-negative bacteria

- Enterobacteriaciae are found in the flora of humans and animals as well as in soil and water
- The main pathogenicity factors are capsules, lipopolysaccharide and toxins
- They can gain attachment through pili and specialised complex machinery – enteroadherent *E. coli*
- Enterobacteriaciae readily exchange genetic material including genes encoding pathogenicity determinant using plasmids and integrons
- Operons containing complex pathogenicity determinants such as type III secretion mechanisms can be exchanged

24 Enterobacteriaceae clinical syndromes

- *Salmonella* are responsible for two main syndromes: enteric fever and localized intestinal infection
- *E. coli* are important causes of intestinal infections
- *E. coli* are also responsible for septicaemia, meningitis in neonates and urinary tract infection
- *Klebsiella* are an important cause of ventilator-associated pneumonia, urinary tract infection, wound infection and bacteraemia
- Enterobacteriaceae have gained a wide range of resistance determinants so treatment should be guided by antibiotic susceptibility patterns

25 *Vibrio, Campylobacter* and *Helicobacter*

- *Vibrio cholera* O1 and O139 are the main types associated with cholera
- Disease is mediated by the expression of cholera toxin that causes fluid secretion from the intestine
- Cholera is characterized by severe diarrhoea and is managed by oral rehydration
- *Campylobacter* are the most common bacterial cause of intestinal infection, usually self-limiting and spread to humans from chickens
- *Helicobacter pylori* infection is responsible for peptic ulceration and is able to colonize the stomach because of a urease that raises the local pH

26 Environmental pathogens: *Pseudomonas, Burkholderia* and *Legionella*

- *Pseudomonas*, found commonly in the hospital environment, is an important cause of hospital-acquired infection
- It is naturally resistant to many antibiotics making it difficult to treat
- *Burkholderia cepacia* and *Stenotrophomonas maltophilia* can cause chronic pulmonary infection in cystic fibrosis whereas *Burkholderia pseudomallei* is a primary pathogen found in the tropics causing a tuberculosis like syndrome or acute septicaemia
- *Legionella pneumophila* is an environmental organism that can colonize air-conditioning systems that are not properly maintained and can be a source of infection for humans
- Legionnaire's disease presents as an acute, often severe, pneumonia and is more common in patients with pulmonary or liver disease

27 *Chlamydia*, *Mycoplasma* and *Rickettsia*

- These organisms do not grow on conventional bacterial media and so are often overlooked
- *Chlamydia* spp. are responsible for trachoma, the commonest infectious form of blindness, urethritis and pelvic inflammatory disease
- To reduce community transmission, national screening programmes for *Chlamydia* are required
- *Mycoplasma pneumoniae* is one of the most important bacterial causes of lower respiratory tract infection
- There are a large number of rickettsial species, some of which are vector borne, which cause typhus, spotted fever or scrub typhus
- *Coxiella burnetii* is a zoonotic organism that causes lower respiratory tract infection or more rarely culture-negative endocarditis

28 Spiral bacteria

- Leptospirosis is a zoonosis acquired when humans come in contact with the natural host or its urine
- The central nervous system, liver and kidneys are the main organs damaged in the infection
- *Borrelia* are transmitted to humans via arthropods (lice or ticks) throughout the world, with a well-defined geographical territory and host specificity
- Relapsing fever is episodic and can be complicated by myocarditis, cerebral haemorrhage or hepatic failure leading to significant mortality
- *Borrelia burgdorferi* and related species, which cause Lyme disease, are tick borne and cause migratory rashes complicated by arthritis and chronic neurological symptoms
- Untreated *Treponema pallidum* infection is characterized by three phases: the primary chancre; later a disseminated infection with rash; followed after a long latent period by neurological and arterial complications. It can be transmitted from mother to infant

29 Virus structure, classification and antiviral therapy

- Viruses can be classified on the basis of their nucleic acid, in particular whether it is single or double stranded
- DNA viruses usually replicate using a virally encoded polymerase
- The nucleic acid of RNA viruses can act as messenger (positive/sense), can be transcribed into message (negative/antisense) or transcribed into DNA by reverse transcriptase and incorporated into the host DNA (single strand/sense)
- Capsids, repetitive protein units, allow viral structure to be encoded by a small number of genes
- Antivirals can interfere with viral uncoating, nucleotide replication by chain termination or reverse transcriptase inhibition, protease inhibition, fusion inhibition, release inhibition or integrase inhibition

30 Herpesviruses I

- Herpes viruses are divided into α-herpesviruses (fast-growing cytolytic viruses that establish latent infections in neurons), β-herpesviruses (slow-growing viruses that become latent in secretory glands and kidneys,) and γ-herpesviruses (latent in lymphoid tissues)

- Cytomegalovirus is a common asymptomatic infection with approximately 50% of adults having been infected
- It can be transmitted congenitally where it may cause deafness and developmental delay
- Epstein–Barr virus usually causes a self-limiting infectious mononucleosis syndrome but also Burkitt's lymphoma in malarial areas, and nasopharyngeal carcinoma and a lymphoproliferative disease in transplant recipients
- HHV-6 causes a self-limiting erythematous infection 'slapped cheek' syndrome that is associated with febrile convulsions
- HHV-8 is an infection that, should the individual develop HIV or another condition that causes immune compromise, can cause Kaposi's sarcoma

31 Herpesviruses II

- Herpes simplex causes an acute mucosal infection in the mouth or genital tract and then becomes latent and may relapse in later life
- Herpes simplex may cause a severe encephalitis in neonates (if infected perinatally) or in individuals of all ages
- Diagnosis is by NAAT; treatment is with aciclovir and related drugs
- Varicella zoster virus causes chickenpox in children and, like herpes simplex, can become latent, emerging in later life in one dermatome as a painful blistering rash 'shingles'
- Non-immune individuals can catch chickenpox from a patient with shingles but not the other way round
- Early treatment of shingles with aciclovir or related drugs may reduce the risk of postherpetic neuralgia

32 DNA viruses: adenovirus, parvovirus and poxvirus

- There are more than 50 serotypes of adenovirus
- Adenovirus cause a wide range of clinical syndromes including pharyngoconjunctival fever, respiratory infection, pharyngitis, epidemic conjunctivitis, haemorrhagic cystitis
- Parvovirus are small single-stranded DNA viruses that infect reticulocytes and cause 'slapped cheek' disease, a mild childhood exanthema
- They cause temporary arrest of red cell production, which can have disproportionate effects on patients with a high red cell turnover (e.g. in sickle cell disease) or pregnant women where hydrops fetalis may develop
- Papilloma viruses are responsible for simple warts but serotypes 6, 11, 16 and 18 predispose to cervical cancer
- Molluscum contagiosum is a common skin infection that produces multiple pearl-like skin lesions that can be slow to clear in patients with reduced cell-mediated immunity e.g. HIV

33 Measles, mumps and rubella

- Measles is caused by a highly infectious *Morbillivirus* that cause epidemics in populations not protected by the MMR vaccine
- The infection has a coryzal prodrome followed by a characteristic flat red rash accompanied by salt like lesions opposite the second molar tooth (Koplik's spots)

- It can be complicated by primary viral pneumonia, secondary bacterial pneumonia, early encephalitis or late subacute panencephalitis
- Mumps is often asymptomatic, but may produce parotitis, orchitis oophoritis or aseptic meningitis
- Rubella causes a mild exanthematous disease but has devastating effects on the growing fetus where infection can cause deafness, microcephaly and developmental arrest

34 Influenza virus

- Small negative-strand RNA viruses with eight segments that facilitate gene re-assortment and variability
- Influenza virus undergoes small genetic changes (drift) that allow infection to occur annually and shift (major genetic change caused by re-assortment), which triggers a global pandemic
- Immunity to pandemic strains is low and the attack rate, morbidity and mortality may be high and tends to occur in younger patients than is usual in seasonal 'flu
- Prevention is by vaccination of individuals who are especially vulnerable e.g. patients with chronic pulmonary obstructive disease, but during a pandemic widespread vaccination may be implemented if a suitable vaccine becomes available in a timely way
- Influenza can by treated with oseltamivir or zanamivir although resistance can develop rapidly

35 Parainfluenza and other respiratory viruses

- Paramyxoviruses are common as causes of respiratory infection associated with croup – laryngeal obstruction in younger children
- Infection is usually mild and treatment is supportive: antipyretics and humidification
- Respiratory syncytial virus (RSV) causes respiratory infections in young children worldwide
- It usually presents as a bronchitis in older children but bronchiolitis in younger individuals
- Coronaviruses usually cause a mild respiratory infection but a novel virus emerged from China causing a severe respiratory syndrome, severe acquired respiratory syndrome (SARS). Rapid response and good infection control brought the outbreak under control

36 Enterovirus and viruses that infect the intestinal tract

- These are small RNA viruses (picorna) divided into three groups: poliovirus, echovirus and coxsackie virus, although newly discovered organisms are now numbered enteroviruses
- Infection is transmitted by the faecal–oral route and infection occurs early in developing countries and later in developed countries
- Poliovirus infects and kills posterior horn cells causing motor paralysis
- A poliovirus eradication campaign is nearing completion so infection with this organism is confined to only a few countries
- Other enteroviruses can be responsible for aseptic meningitis, pharyngitis, hand food and mouth disease and myocarditis

37 Hepatitis viruses

- Hepatitis A virus is related to enteroviruses and spreads in the same way
- Hepatitis A virus is responsible for an acute febrile infection that, in a few cases is complicated by acute hepatitis. Infection is usually self-limiting but a few patients may suffer fulminant disease
- Hepatitis B is transmitted by blood, the sexual route or at birth
- Symptomatic disease is more common and more severe and can be complicated by fulminant liver failure, chronic infection, cirrhosis or liver cancer
- Infection is prevented by blood precautions, vaccination of those at risk and of neonates of hepatitis B-positive mothers
- Hepatitis C is caused by an RNA virus usually transmitted by blood and may cause chronic infection resulting in cirrhosis and liver cancer

38 Tropical exotic or arbovirus infections

- Rabies is caused by an enveloped RNA virus that infects warm-blooded animals worldwide
- Infection is by the bite of a rabid animal and the virus travels up the axons to cause an inevitably fatal encephalitis
- Infection can be prevented by the implementation of quarantine regulations, pre-exposure vaccination of high-risk individuals and postexposure vaccination of individuals who have received a potentially infected bite
- Yellow fever is a severe hepatitic viral infection transmitted by the bite of *Aedes* mosquitos
- Vaccination and mosquito control measures have made yellow fever an unusual infection
- Lassa fever is a haemorrhagic infection caused by an arenavirus and endemic in rural West Africa

39 Yeast infections

- *Candida* spp., of which *Candida albicans* is the most common isolate, are part of the normal flora that may cause invasive disease if immune defences are reduced
- Pathogenicity depends on melanin, adhesins, extracellular lipases and proteinases but they have modest capacity to invade
- By reducing the normal bacterial flora, antibiotics can allow *Candida* to cause mucosal or invasive infection
- *Cryptococcus neoformans* is a saprophyte and commensal in animal faeces that causes a subacute lymphocytic meningitis usually in patients with reduced cell mediated immunity e.g. HIV
- The azole group of compounds (clotrimazole, miconazole, fluconazole and itraconazole) act by blocking the action of cytochrome P450 and sterol 14□-demethylase and are used against a wide range of fungal pathogens

40 Filamentous fungal infections

- *Aspergillus* spp. are ubiquitous, free-living, saprophytic organisms. *A. fumigatus*, *A. niger*, *A. flavus* and *A. terreus* are associated with human infection.

- *Aspergillus* cause type I and III allergic reactions: bronchopulmonary allergic alveolitis and farmers' lung respectively as well as invasive disease in severely immunocompromised individuals
- Three filamentous fungi cause ringworm or nail infection: *Epidermophyton*, *Microsporum* and *Trichophyton*
- Ringworm presents as itchy, red, scaly, patch-like lesions that spread outwards leaving a pale, healed centre, with animal species causing much more severe inflammation
- Polyenes (amphotericin and nystatin) bind ergosterol in the fungal membrane forming a pore that leads to leakage of the intracellular contents and cell death. Resistance is rare

41 Intestinal protozoa

- *Entamoeba histolytica* invades the large intestine producing an infection characterized by frequent small volume stools
- In a small proportion of patients liver abscess can develop
- *Giardia* infects the small intestine causing infection characterized by infrequent large volume stools
- *Cryptosporidium* is an animal or human pathogen that typically causes large volume, watery diarrhoea and can be difficult to manage in immunocompromised individuals. There is no active treatment
- *Isospora belli* presents in a similar way to Cryptosporidium and treatment is with co-trimoxazole, fluoroquinolones or nitazoxanide

42 Malaria, leishmaniasis and trypanosomiasis

- *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae* cause malaria killing more than 1 million children under the age of 5 each year in Africa alone
- Fever and myalgia ('flu-like symptoms) are common but the diagnosis is made on the basis of exposure history
- Malaria is transmitted by the bite of female *anopheles* mosquitos and so control measures are directed to reducing mosquito numbers and preventing bites
- *Leishmania* infects cells of the reticuloendothelial system and bone marrow causing a chronic wasting disease associated with anaemia and secondary infections
- Trypanosome infection is transmitted by the tse tse fly. After an initial relapsing systemic infection, the meninges are invaded causing a chronic meningoencephalitis

43 Gut helminths

- Round worms cause disease by competing for nutrients or by loss of blood (hook worms)
- Transmission is faecal–oral although Strongyloides and hookworms can invade through intact skin
- Adult threadworms lay eggs around the anus causing itching. The scratching facilitates faecal–oral transmission
- *Strongyloides stercoralis* infection is associated with a migratory, itchy rash but overwhelming infection can follow immunosuppression

- Humans can act as both the intermediate and definitive host of the pork tapeworm, which means some patients acquire multiple disseminated lesions throughout the body including the brain – cysticercosis

44 Tissue helminths

- Three species infect humans: *Schistosoma mansoni* (Africa and South America); *S. japonicum* (Far East); and *S. haematobium* (Africa)
- Schistosomiasis symptoms occur in three phases: fever, hepatosplenomegaly, rash and arthralgia associated with infection; bloody diarrhoea or haematuria associated with egg expulsion; and later symptoms caused by the fibrotic reaction to the eggs
- Diagnosis is usually by visualizing the eggs and treatment is with praziquantel
- Filarial infections are transmitted by vectors, *Aedes* mosquitos and black flies
- Diagnosis depends on visualizing the parasite microscopically in blood or skin biopsy

45 Congenital and perinatal infections

- There is a 60% chance of congenital infection if rubella infection occurs in the first 20 weeks of pregnancy
- Jaundice, hepatitis, thrombocytopenic purpura, microcephaly and failure to make developmental milestones may result
- Congenital CMV infection affects around 1% of births with a 1% risk of congenital infection
- Neonates are at risk of severe infection if they acquire herpes or VZV infection around the time of birth. Steps to reduce the risk by giving specific globulin and aciclovir are necessary
- The risk of perinatal HIV transmission can be reduced by giving antiretroviral drugs to the mother and considering elective section if the viral load is not under control. Breast feeding should be avoided if possible.

46 HIV infection and AIDS

- HIV 1 and 2 are retroviruses: RNA viruses that are transcribed by reverse transcriptase and the DNA incorporated into the host genome
- Their tropism is for CD4 cells and ongoing infection results in progressive compromise of immunity
- If untreated, infections of low virulence can cause disease e.g. *Pneumocystis jiroveci*
- Highly active antiretroviral therapy is now available using drugs that target different stages of the replication cycle
- Eradication of infection is not possible so treatment is directed towards maintaining virus to less than 50 copies/mL, to preventing resistance emergence, restoring immunological function and preventing transmission

47 Pyrexia of unknown origin and septicaemia

- A pyrexia of unknown origin is a fever, intermittent or persistent, of greater than 38.2 °C for more than 2 weeks, for which there is no obvious cause
- Infection accounts for 45–55% of the cases e.g. endocarditis, tuberculosis, hidden abscess

- Patients require careful and repeated clinical examination
- Patients are usually severely ill with shock associated with depressed consciousness. Fever may be absent
- Puerperal fever is a bacteraemic illness caused by infection of the female genital tract after delivery. Common infectious agents include *S. pyogenes* and the normal flora of the female genital tract

48 Endocarditis, myocarditis and pericarditis

- Congenitally abnormal and damaged valves are most at risk of infection
- Low grade fever, malaise and heart murmurs are the cardinal signs of endocarditis
- Diagnosis is by echocardiography and at least three blood cultures should be taken
- Treatment is based on national or international treatment protocols
- Most myocarditis is caused by viruses of which enteroviruses are most common

49 Infections of the central nervous system

- Bacterial meningitis is characterized by fever and neck stiffness and may progress rapidly if not treated
- Bacterial meningitis can be complicated by recurrent fever, hydrocephalus, deafness and cranial nerve palsy
- Diagnosis of bacterial meningitis is made clinically and with blood culture, CSF and NAAT
- Some types of bacterial meningitis may be prevented by protein conjugate vaccines
- Encephalitis can be caused by wide range of viruses of which herpes simplex and arbovirus infections have the most severe outcome

50 Respiratory tract infections

- Patients with upper respiratory tract infection have fever and a painful infected throat that may have visible pus or exudate
- It is impossible to distinguish between viral and bacterial infections clinically
- Children under the age of seven are especially prone to otitis media. *Streptococcus pyogenes*, *S. pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* are the commonest bacterial causes
- Lower respiratory tract infection is a leading cause of death in children under 5 years
- *S. pneumoniae*, *Moraxella pneumoniae* and *Legionella pneumophila* are the commonest bacterial causes of lower respiratory tract infection

51 Urinary and genital infections

- Dehydration, obstruction, the disturbance of smooth urinary flow or the presence of a foreign body, such as a stone or urinary catheter, predisposes to urinary infection
- Lower urinary tract infection is characterized by urinary frequency, dysuria and suprapubic discomfort; fever may be absent
- The kidney can become infected (pyelonephritis) and this presents with fever, loin pain, renal angle tenderness and signs of septicaemia

- Therapy is based on the expected susceptibility patterns of the usual pathogens: *E. coli*, *K. pneumoniae* and *Proteus mirabilis*
- Genital ulcer disease increases the risk of HIV transmission and is caused by *T. pallidum*, *H. ducreyi* and *Herpes simplex* type 2

52 Infections of the bones and joints

- The bone can be infected by haematogenous spread, by direct extension from an infected joint, or following trauma, surgery or instrumentation
- *Staphylococcus aureus, Streptococcus pyogenes*, *Salmonella* spp., *Mycobacterium tuberculosis* and *Haemophilus influenzae* are the commonest bacterial causes
- Presentation is with fever and localized pain but in young children the pain may be poorly localized
- Diagnosis is usually clinical and changes on X ray, radioisotope scans or MRI may not become apparent for up to 2 weeks
- Chronic osteomyelitis may follow inadequately treated acute infection or may be secondary to surgery or fracture. Infection of prosthetic materials may occur with organisms with reduced virulence (e.g. coagulase-negative staphylococci)
- Septic arthritis is caused by similar organisms as osteomyelitis. *Neisseria gonorrhoeae* is another cause.

53 Bacterial diarrhoea

- The gut is protected by gastric acid, bile salts, the mucosal immune system and inhibitory substances produced by the normal flora
- Infectious diarrhoea is a very important cause of mortality and morbidity in children under 5 worldwide
- Organisms are transmitted by hands and fomites (faecal–oral route), by food or water. The infective dose can be as few as 10 organisms (*Shigella*). Some foods (e.g. milk) or drugs (e.g. H_2 antagonists and proton pump inhibitors) may reduce the infective dose
- The patient may have many small stools (typical of large-bowel infection), or infrequent large stools (small-intestine infection). Stools may be blood-stained when there is destruction of the intestinal mucosa or have a fatty consistency and offensive smell if malabsorption is present
- Diagnosis and typing of organisms is essential to link infective incidents if they are part of wider outbreaks
- The management of diarrhoeal disease is based on adequate fluid replacement and correction of electrolyte imbalances
- Prevention depends on good sanitation, animal husbandry, food storage and preparation

54 Zoonoses

- These are infections acquired from an animal source when humans enter the animal environment or via vectors such as mosquitoes (e.g. Japanese B encephalitis). Farming and pets are an important source of zoonotic infection
- Plague is caused by *Yersinia pestis*; the infection is endemic in rodents in remote rural areas. Rarely, epidemics may develop which may spread

worldwide (e.g. the Black Death). The organism is transmitted between rats and to humans, by the rat flea, *Xenopsylla cheopis*
- Toxoplasmosis is acquired by ingestion of oocysts from infected cat faeces or from tissue cysts in infected meat (e.g. undercooked beef)
- Cat scratch disease is caused by *Bartonella henselae.* A papular lesion may develop at the site and symptoms resolve slowly over a period of 2 months, but a more chronic course may ensue
- Two species of parasite are responsible for human hydatid disease: *Echinococcus granulosus* and *E. multilocularis*. Multiple cysts develop in the liver and lungs. Treatment is with albendazole and surgery when possible

55 Infection in immunocompromised patients

- Medical treatment or hereditary deficiency of components of the immune system may allow organisms with reduced virulence to cause infection and normal pathogens to cause severe infection
- Infection in severely neutropenic patients is prevented by: source isolation, filtered room air to remove fungal spores and antifungal prophylaxis; antibiotic prophylaxis with 4-fluoroquinolones is used in some centres
- T-cell deficiency is associated with mycobacterial infection, toxoplasmosis, *Listeria monocytogenes*, *Cryptococcus neoformans*, *Pneumocystis jiroveci,* herpes simplex, cytomegalovirus, varicella zoster virus and measles
- Patients with hypogammaglobulinaemia suffer recurrent respiratory tract infections with *Streptococcus pneumoniae* and non-capsulate *Haemophilus influenzae*, which lead to bronchiectasis. *Giardia*, *Cryptosporidium* and *Campylobacter* infections may be more persistent
- Patients with splenectomy are at excess risk of *Streptococcus pneumoniae* and *H. influenzae* infection. Malaria may run a fulminant course and *Capnocytophaga canimorsus* may arise after a dog bite

56 Ocular infection

- Bacterial conjunctivitis is common and caused by: *Staphylococcus aureus*, *Haemophilus influenzae*, *Streptococcus pneumoniae* or *Moraxella* spp.
- Adenovirus causes purulent conjunctivitis. Corneal involvement leads to punctate keratitis and subepithelial inflammatory infiltration, anterior uveitis and conjunctival haemorrhages
- Ocular infection with herpes simplex is the most common infectious cause of blindness in developed countries
- Trachoma, a chronic keratoconjunctivitis caused by infection with *Chlamydia trachomatis*, is now largely confined to the tropics. Symptoms develop 3–10 days after infection, with lacrimation, mucopurulent discharge, conjunctival infection and follicular hypertrophy
- Treatment is with oral macrolides, such as azithromycin. An international campaign plan to eradicate trachoma by 2020 is under way using the SAFE strategy (**S**urgery for in-turned lids, **A**ntibiotics, **F**ace-washing and **E**nvironmental improvement).
- Endophthalmitis develops after ocular operation, following trauma, presence of a foreign body and as a complication of systemic infection. Early postoperative infections are commonly due to *S. aureus*, *S. epidermidis*, streptococci and Gram-negative bacilli

57 Infections of the skin and soft tissue

- Cellulitis affects all layers of the skin and *S. pyogenes*, *S. aureus* and *Pasteurella multocida* are the most common cause
- Necrotising fasciitis is a rapidly progressive skin infection, involving skin and subcutaneous tissue, caused by mixed aerobic and anaerobic organisms or pure *S. pyogenes*
- Surgical resection of infected tissue is critical, supplemented with antibiotics targeted against streptococci and staphylococci, Gram-negative bacilli and obligate anaerobes e.g. benzylpenicillin, a third-generation cephalosporin or carbapenem and metronidazole
- Erysipelas is a streptococcal infection confined to the dermis
- Erysipeloid is a zoonosis found in pig handlers and fisherman caused by *Erysipelothrix rhusiopathiae*. It is usually self-limiting but treatment with oral penicillin or tetracycline speeds the response and is needed in rare septicaemic cases

Medical Microbiology and Infection at a Glance, Fourth Edition. Stephen H. Gillespie, Kathleen B. Bamford.