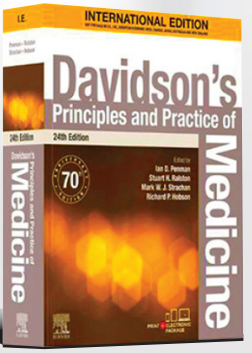
TABLE & CHARTS OF INFECTIOUS DISEASE

Davidson's Principles and Practice of Medicine 24th Edition

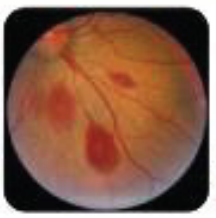


SK+F

Clinical examination of patients with infectious disease

5 Eyes

Conjunctival petechiae
Painful red eye in uveitis
Loss of red reflex in endophthalmitis
Roth's spots in infective endocarditis
Haemorrhages and exudates of cytomegalovirus retinitis
Choroidal lesions of tuberculosis



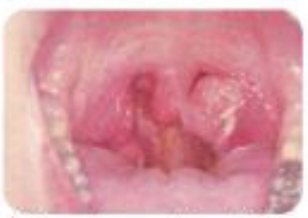
Roth's spots in endocarditis

4 Head and neck

Lymphadenopathy
Parotidomegaly
Abnormal tympanic membranes

3 Oropharynx

Dental caries
Tonsillar enlargement or exudate
Candidiasis



Streptococcal tonsillitis

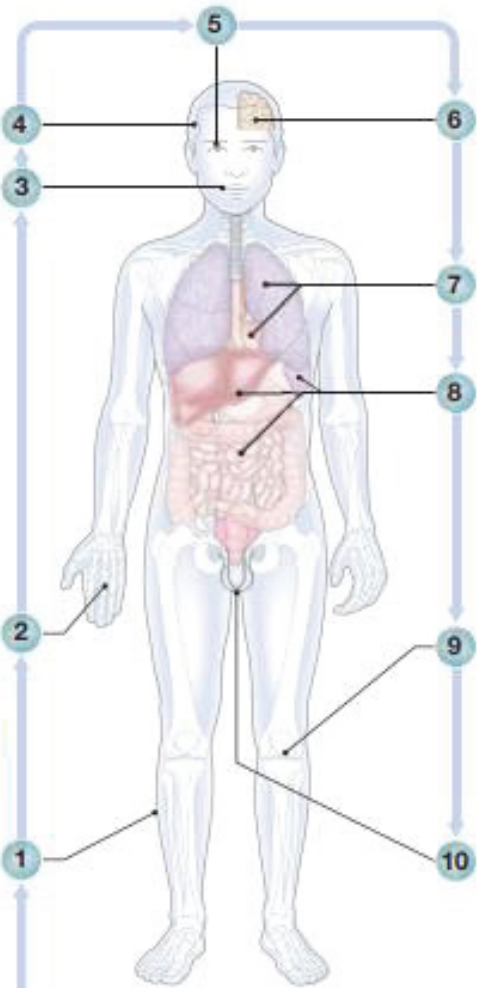
2 Hands and nails

Finger clubbing
Splinter haemorrhages
Janeway lesions
Signs of chronic liver disease
Vasculitis lesions

Splinter haemorrhages in endocarditis

1 Skin

Generalised erythema
Rash (see opposite)
IV injection track marks
Surgical scars
Prosthetic devices, e.g. central venous catheters
Tattoos



Observation

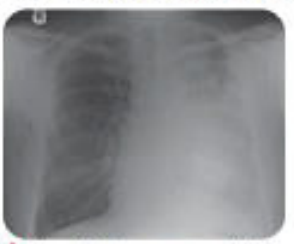
- Temperature
- Sweating
- Weight loss
- Respiratory distress
- Altered consciousness
- Pallor
- Jaundice

6 Neurological

Neck stiffness
Photophobia
Delirium
Focal neurological signs

7 Heart and lungs

Tachycardia, hypotension
Murmurs or prosthetic heart sounds
Pericardial rub
Signs of consolidation
Pleural or pericardial effusion



Chest X-ray consolidation in pneumonia

8 Abdomen

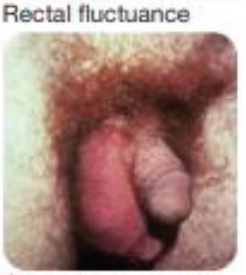
Hepatosplenomegaly
Ascites
Renal angle tenderness
Localised tenderness or guarding with decreased bowel sounds, e.g. in left iliac fossa with diverticulitis
Mass lesions
Surgical drains

9 Musculoskeletal

Joint swelling, erythema or tenderness
Localised tender spine suggestive of epidural abscesses or discitis
Draining sinus of chronic osteomyelitis

10 Genitalia and rectum

Ulceration or discharge
Testicular swelling or nodules
Inguinal lymphadenopathy
Prostatic tenderness
Rectal fluctuance



Testicular swelling in adult mumps

Insets (splinter haemorrhages) Courtesy of Dr Nick Beeching, Royal Liverpool University Hospital; (Roth's spots) Courtesy of Prof. Ian Rennie, Royal Hallamshire Hospital, Sheffield.

Figs A–C opposite Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield.

i Fever

Documentation of fever

- 'Feeling hot' or sweaty does not necessarily signify fever – diagnosed only when a body temperature of over 38.0°C is recorded
- Axillary and aural measurement is less accurate than oral or rectal
- Outpatients may be trained to keep a temperature chart

Rigors

- Shivering (followed by excessive sweating) occurs with a rapid rise in body temperature from any cause

Night sweats

- Associated with particular infections (e.g. TB, infective endocarditis); sweating from any cause is worse at night

Excessive sweating

- Alcohol, anxiety, thyrotoxicosis, diabetes mellitus, acromegaly, lymphoma and excessive environmental heat all cause sweating without temperature elevation

Recurrent fever

- There are various causes, e.g. *Borrelia recurrentis*, bacterial abscess

Accompanying features

- Severe headache and photophobia, although characteristic of meningitis, may accompany other infections.
- Delirium during fever is more common in young children or the elderly
- Myalgia may occur with viral infections, such as influenza, and with sepsis including meningococcal sepsis
- Shock may accompany severe infections and sepsis (p. 196)

i History-taking in suspected infectious disease

Presenting complaint

- Diverse manifestations of infectious disease make accurate assessment of features and duration critical; e.g. fever and cough lasting 2 days imply an acute respiratory tract infection but suggest TB if they last 2 months

Review of systems

- Must be comprehensive

Past medical history

- Define the 'host' and likelihood of infection(s)
- Include surgical and dental procedures involving prosthetic materials
- Document previous infections

Medication history

- Include non-prescription drugs, use of antimicrobials and immunosuppressants
- Identify medicines that interact with antimicrobials or that may cause fever

Allergy history

- Esp. to antimicrobials, noting allergic manifestation (e.g. rash versus anaphylaxis)

Family and contact history

- Note infections and their duration
- Sensitively explore exposure to key infections, e.g. TB and HIV

Travel history

- Include countries visited and where previously resident (relevant to exposure and likely vaccination history, e.g. likelihood of BCG vaccination in childhood)

Occupation

- e.g. Anthrax in leather tannery workers

Recreational pursuits

- e.g. Leptospirosis in canoeists and windsurfers

Animal exposures

- Include pets, e.g. dogs/hydatid disease

Dietary history

- Consider under-cooked meats, shellfish, unpasteurised dairy products or well water
- Establish who else was exposed, e.g. to food-borne pathogens

History of intravenous drug injection or receipt of blood products

- Risks for blood-borne viruses, e.g. HIV-1, HBV and HCV

Sexual history

- Explore in a confidential manner (Ch. 13); remember that the most common mode of HIV-1 transmission is heterosexual (Ch. 12)

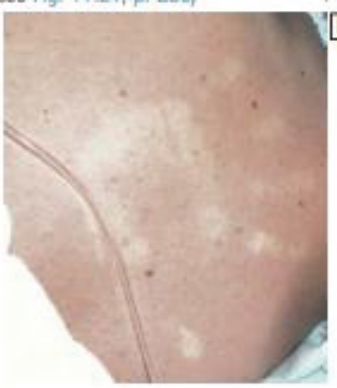
Vaccination history and use of prophylactic medicines

- Consider occupation- or age-related vaccines
- In a traveller or infection-predisposed patient, establish adherence to prophylaxis

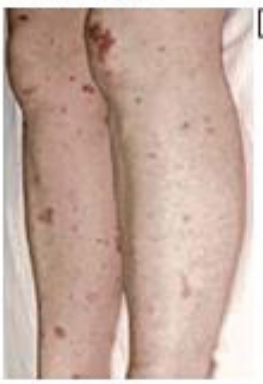
*Always consider non-infectious aetiologies in the differential diagnosis. (HBV/HCV = hepatitis B/C virus; HIV-1 = human immunodeficiency virus-1; TB = tuberculosis)

1 Skin lesions in infectious diseases

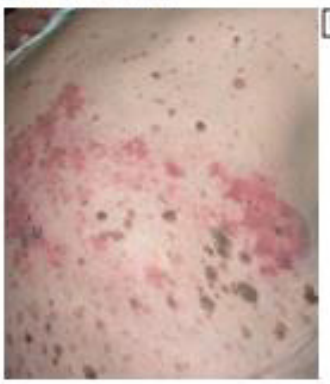
- Diffuse erythema, e.g. A
- Migrating erythema, e.g. enlarging rash of erythema migrans in Lyme disease (see Fig. 11.21, p. 256)
- Purpuric or petechial rashes, e.g. B
- Macular or papular rashes, e.g. primary infection with HIV (see Box 12.8, p. 312)
- Vesicular or blistering rash, e.g. C
- Erythema multiforme (see Fig. 29.53 and Box 29.32, pp. 1264 and 1265)
- Nodules or plaques, e.g. Kaposi's sarcoma (p. 315)
- Erythema nodosum (D and Box 29.33, p. 1265)

A 

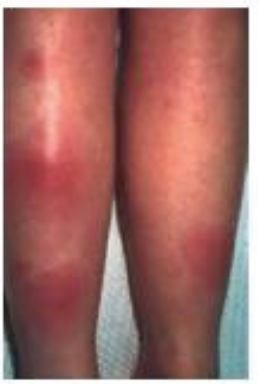
Streptococcal toxic shock syndrome.

B 

Meningococcal sepsis.

C 

Shingles.

D 

Erythema nodosum.

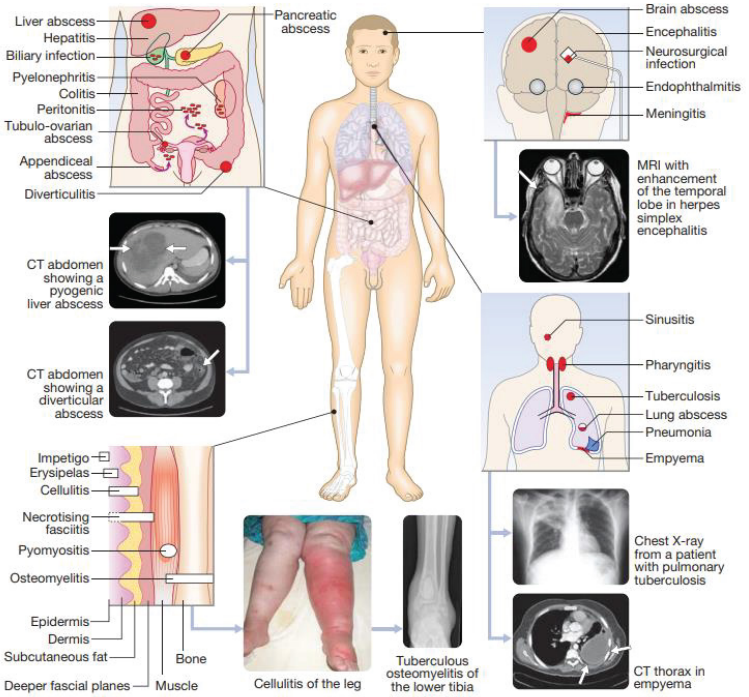


Fig. 11.1 Common infectious syndromes presenting with fever and localised features. Major causes are grouped by approximate anatomical location and include central nervous system infection; respiratory tract infections; abdominal, pelvic or urinary tract infections; and skin and soft tissue infections (SSTIs) or osteomyelitis. For each site of infection, particular syndromes and their common causes are described elsewhere in the book. The causative organisms vary, depending on host factors, which include whether the patient has lived in or visited a tropical country or particular geographical location, has acquired the infection in a health-care environment or is immunocompromised. *Insets (cellulitis of the leg) Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield; (pulmonary tuberculosis) Courtesy of Dr Ann Chapman, Royal Hallamshire Hospital, Sheffield; (empyema, pyogenic liver abscess, diverticular abscess, tuberculous osteomyelitis) Courtesy of Dr Robert Peck, Royal Hallamshire Hospital, Sheffield.*

11.2 Aetiology of pyrexia of unknown origin (PUO)

Infections (~30%)

Specific locations
- Abscesses: hepatobiliary, diverticular, urinary tract (including prostate), pulmonary, CNS
- Infections of oral cavity (including dental), head and neck (including sinuses)
- Bone and joint infections
- Infective endocarditis*

Specific organisms
- TB (particularly extrapulmonary)*
- HIV-1 infection
- Other viral infections: cytomegalovirus (CMV), Epstein–Barr virus (EBV)
- Fungal infections (e.g. *Aspergillus* spp., *Candida* spp. or dimorphic fungi)
- Infections with fastidious organisms (e.g. *Bartonella* spp., *Tropheryma whipplei*)

Specific patient groups
- Recently spent time in a region with geographically restricted infection:
  Malaria*, dengue, rickettsial infections, *Brucella* spp., amoebic liver abscess, enteric fevers (Africa, Asia, Oceania, Central and South America), *Leishmania* spp. (southern Europe, India, Africa and Latin America), *Burkholderia pseudomallei* (South-east Asia), Middle East respiratory syndrome coronavirus (MERS-CoV; Arabian Peninsula)
- Residence in or travel to a region with endemic infection:
  TB* (Africa, Asia, Central and South America), extensively drug-resistant TB (XDR-TB; South Africa), *Brucella* spp. (Africa, Asia, Central and South America), HIV-1 (Africa, Asia), *Trypanosoma cruzi* (Central and South America)
- Nosocomial infections:
  Pneumonia*, infections related to prosthetic materials and surgical procedures, urinary tract infections, central venous catheter infections
- HIV-positive individuals:
  Acute retroviral syndrome
  AIDS-defining infections (disseminated *Mycobacterium avium* complex (DMAC), *Pneumocystis jirovecii* pneumonia, CMV and others)

Malignancy (~20%)

Haematological malignancy
- Lymphoma*, leukaemia and myeloma

Solid tumours
- Renal, liver, colon, stomach, pancreas

Connective tissue disorders (~15%)

Older adults
- Temporal arteritis/polymyalgia rheumatica*

Younger adults
- Still's disease (juvenile rheumatoid arthritis)*
- Systemic lupus erythematosus (SLE)
- Vasculitic disorders, including polyarteritis nodosa, rheumatoid disease with vasculitis and granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis)
- Polymyositis
- Behçet's disease
- Rheumatic fever (in regions where still endemic, e.g. Asia, Oceania and parts of Africa)

Miscellaneous (~20%)

Cardiovascular
- Atrial myxoma, aortitis, aortic dissection

Respiratory
- Sarcoidosis, pulmonary embolism and other thromboembolic disease, extrinsic allergic alveolitis

Gastrointestinal
- Inflammatory bowel disease, granulomatous hepatitis, alcoholic liver disease, pancreatitis

Endocrine/metabolic
- Thyrotoxicosis, thyroiditis, hypothalamic lesions, phaeochromocytoma, adrenal insufficiency, hypertriglyceridaemia

Haematological
- Haemolytic anaemia, paroxysmal nocturnal haemoglobinuria, thrombotic thrombocytopenic purpura, myeloproliferative disorders, Castleman's disease, graft-versus-host disease (after allogeneic haematopoietic stem cell transplantation)

Inherited
- Familial Mediterranean fever and periodic fever syndromes

Drug reactions*
- e.g. Antibiotic fever, drug hypersensitivity reactions etc.

Factitious fever

Idiopathic (~15%)

*Most common causes within each group.

11.1 Fever in old age

- **Temperature measurement**: fever may be missed because oral temperatures are unreliable. Rectal measurement may be needed but core temperature is increasingly measured using eardrum reflectance.
- **Delirium**: common with fever, especially in those with underlying cerebrovascular disease or dementia.
- **Prominent causes of pyrexia of unknown origin**: include tuberculosis and intra-abdominal abscesses, complicated urinary tract infection and infective endocarditis. Non-infective causes include polymyalgia rheumatica/temporal arteritis and tumours. A smaller fraction of cases remain undiagnosed than in young people.
- **Pitfalls in the elderly**: conditions such as stroke or thromboembolic disease can cause fever but every effort must be made to exclude concomitant infection.
- **Common infectious diseases in the very frail** (e.g. nursing home residents): pneumonia, urinary tract infection, soft tissue infection and gastroenteritis.

11.3 Clues to the diagnosis of factitious fever

- A patient who looks well
- Bizarre temperature chart with absence of diurnal variation and/or temperature-related changes in pulse rate
- Temperature >41°C
- Absence of sweating during defervescence
- Normal erythrocyte sedimentation rate and C-reactive protein despite high fever
- Evidence of self-injection or self-harm
- Normal temperature during supervised (observed) measurement
- Infection with multiple commensal organisms (e.g. enteric or mouth flora)

11.4 Microbiological investigation of pyrexia of unknown origin

Location-independent investigations

Microscopy
- Blood for atypical lymphocytes (EBV, CMV, HIV-1, hepatitis viruses or *Toxoplasma gondii*)
- Respiratory samples for mycobacteria and fungi
- Stool for ova, cysts and parasites
- Biopsy for light microscopy (bacteria, mycobacteria, fungi) and/or electron microscopy (viruses, protozoa (e.g. microsporidia) and other fastidious organisms (e.g. *Tropheryma whipplei*))
- Urine for white or red blood cells and mycobacteria (early morning urine ×3)

Culture
- Aspirates and biopsies (e.g. joint, deep abscess, debrided tissues)
- Blood, including prolonged culture and special media conditions
- Sputum for mycobacteria
- CSF
- Gastric aspirate for mycobacteria
- Stool
- Swabs
- Urine ± prostatic massage in older men

Antigen detection
- Blood, e.g. HIV p24 antigen, cryptococcal antigen, *Aspergillus* galactomannan ELISA and for *Aspergillus* and other causes of invasive, fungal infection (1,3)-β-D-glucan
- CSF for cryptococcal antigen
- Bronchoalveolar lavage fluid for *Aspergillus* galactomannan
- Nasopharyngeal aspirate/throat swab for respiratory viruses, e.g. IAV or RSV
- Urine, e.g. for *Legionella* antigen

Nucleic acid detection
- Blood for *Bartonella* spp. and viruses
- CSF for viruses and key bacteria (meningococcus, pneumococcus, *Listeria monocytogenes*)
- Nasopharyngeal aspirate/throat swab for respiratory viruses
- Sputum for *Mycobacterium tuberculosis* (MTB) and rifampicin (RIF) resistance with geneXpert MTB/RIF cartridge-based nucleic acid amplification test
- Bronchoalveolar lavage fluid, e.g. for respiratory viruses
- Tissue specimens, e.g. for *T. whipplei*
- Urine, e.g. for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*
- Stool, e.g. for norovirus, rotavirus

Immunological tests
- Serology (antibody detection) for viruses, including HIV-1, and some bacteria
- Interferon-gamma release assay for diagnosis of exposure to tuberculosis (but note this will not distinguish latent from active disease and can only be used to trigger further investigations of active disease)

Geographically restricted tests[2]

Microscopy
- Blood for trypanosomiasis, malaria and *Borrelia* spp.
- Stool for geographically restricted ova, cysts and parasites
- Biopsy for light microscopy (dimorphic fungi, *Leishmania* spp. and other parasites)
- Urine for red blood cells and schistosome ova

Antigen detection
- Blood, e.g. dengue virus NS1 antigen, *Histoplasma* antigen (restricted availability) and malaria antigen (e.g. HRP-2 for *Plasmodium falciparum* or parasite-specific LDH for *P. falciparum* and *P. vivax*)

Nucleic acid detection
- Blood for causes of viral haemorrhagic fever
- CSF for geographically restricted viruses, e.g. Japanese encephalitis virus
- Nasopharyngeal aspirate/throat swab or bronchoalveolar lavage fluid for geographically restricted respiratory viruses, e.g. MERS-CoV

Immunological tests
- Serology (antibody detection) for viruses, dimorphic fungi and protozoa

[1]This list does not apply to every patient with a pyrexia of unknown origin. Appropriate tests should be selected in a stepwise manner, according to specific predisposing factors, epidemiological exposures and local availability, and should be discussed with a microbiologist. [2]Addition of these tests should be guided by the location of presentation or travel history.
(CMV = cytomegalovirus; CSF = cerebrospinal fluid; EBV = Epstein–Barr virus; ELISA = enzyme-linked immunosorbent assay; HIV-1 = human immunodeficiency virus-1; HRP-2 = histidine-rich protein 2; IAV = influenza A virus; LDH = lactate dehydrogenase; MERS-CoV = Middle East respiratory syndrome coronavirus; NS1 = non-structural 1; RSV = respiratory syncytial virus)

11.5 Additional investigations in PUO

- Serological tests for connective tissue disorders:
  - Autoantibody screen
  - Complement levels
  - Immunoglobulins
  - Cryoglobulins
- Ferritin
- Echocardiography
- Ultrasound of abdomen
- CT/MRI of thorax, abdomen and/or brain
- Imaging of the skeletal system:
  - Plain X-rays
  - CT/MRI spine
  - Isotope bone scan
- Labelled white cell scan
- Positron emission tomography (PET)/single-photon emission computed tomography (SPECT)
- Biopsy:
  - Bronchoscopy and lavage ± transbronchial biopsy
  - Lymph node aspirate or biopsy
  - Biopsy of radiological lesion
  - Biopsy of liver
  - Bone marrow aspirate and biopsy
  - Lumbar puncture
  - Laparoscopy and biopsy
  - Temporal artery biopsy

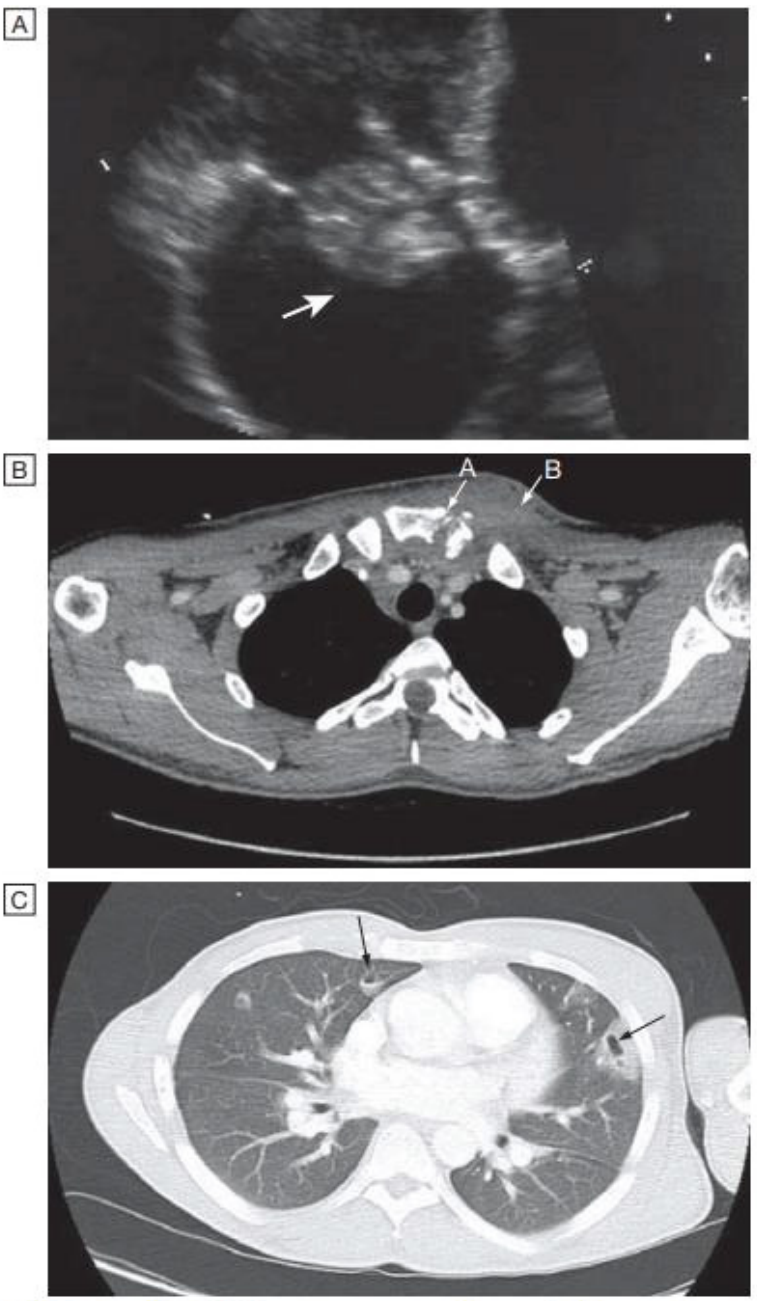


Fig. 11.3 Causes of fever in injection drug-users. A Endocarditis: large vegetation on the tricuspid valve (arrow). B Septic arthritis of the left sternoclavicular joint (arrow A) (note the erosion of the bony surfaces at the sternoclavicular joint) with overlying soft tissue collection (arrow B). C Tricuspid valve endocarditis caused by *Staphylococcus aureus*. Thoracic CT scan shows multiple embolic lesions with cavitation (arrows). The patient presented with haemoptysis. *C, Courtesy of Dr Julia Greig, Royal Hallamshire Hospital, Sheffield.*

11.6 Infections in transplant recipients

Time post transplantation	Infections
Solid organ transplant recipients	
0–1 month	Bacterial or fungal infections related to the underlying condition or surgical complications
1–6 months	CMV, other opportunistic infections (e.g. *Pneumocystis jirovecii* pneumonia)
>6 months	Bacterial pneumonia, other bacterial community-acquired infections, shingles, cryptococcal infection, PTLD
Myeloablative haematopoietic stem cell transplant recipients	
Pre-engraftment (typically 0–4 weeks)	Bacterial and fungal infections, respiratory viruses or HSV reactivation
Post-engraftment:	
Early (<100 days)	CMV, *Pneumocystis jirovecii* pneumonia, moulds or other opportunistic infections
Late (>100 days)	Community-acquired bacterial infections, shingles, CMV, PTLD

(CMV = cytomegalovirus; HSV = herpes simplex virus; PTLD = post-transplant lymphoproliferative disorder)

11.7 Common causes of blood-stream infection

Community-acquired

- *Escherichia coli*
- *Staphylococcus aureus*, including MRSA
- *Streptococcus pneumoniae*
- Other streptococci

Nosocomial

- *Staph. aureus*, including MRSA
- Coagulase-negative staphylococci
- Enterococci, including VRE
- Gram-negative bacteria
- *Candida* spp.

(MRSA = meticillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant enterococci)

11.8 Causes of sepsis

Infection	Setting
Bacterial	
Staphylococcus aureus, coagulase-negative staphylococci	Bacteraemia may be associated with endocarditis, intravascular cannula infection, or skin or bone foci
Streptococcus pneumoniae	Invasive pneumococcal disease, usually with pneumonia or meningitis; asplenia
Other streptococci	Invasive streptococcal disease, especially necrotising fasciitis Viridans streptococci in neutropenic host with severe mucositis
Staphylococcal or streptococcal toxic shock syndrome	Toxin-mediated, blood cultures negative; clues include erythrodermic rash and epidemiological setting
Enterococci	Most often with abdominal focus
Neisseria meningitidis	Sepsis in children or young adults with petechial rash and/or meningitis
Escherichia coli, other Gram-negative bacteria	Urinary or biliary tract infection, or other abdominal infections
Pseudomonas aeruginosa, multidrug-resistant Gram-negative bacteraemia	Nosocomial infection
Salmonella Typhi or Paratyphi	In countries with a high incidence of enteric fever
Yersinia pestis	In plague
Burkholderia pseudomallei	Endemic in areas of Thailand; more likely to involve patients with diabetes mellitus or immunocompromised
Capnocytophaga canimorsus	Associated with dog bites and asplenic individuals
Clostridium difficile	Severe colitis, particularly in the elderly
Polymicrobial infection with Gram-negatives and anaerobes	Bowel perforation, bowel ischaemia
Mycobacterium tuberculosis, *M. avium* complex (MAC)	HIV-positive or immunocompromised with miliary tuberculosis or disseminated MAC
Fungal	
Candida spp.	Line infection or post-operative complication, nosocomial or immunocompromised host
Histoplasma capsulatum, other dimorphic fungi	Immunocompromised host
Parasitic	
Falciparum malaria	Malaria with high-level parasitaemia and multi-organ failure or as a complication of bacterial superinfection
Babesia microti	Asplenic individual
Strongyloides stercoralis hyperinfection syndrome	Gram-negative infection complicating *Strongyloides* infection in immunocompromised host

11.9 Severe necrotising soft tissue infections

- Necrotising fasciitis (primarily confined to subcutaneous fascia and fat)
- Clostridial anaerobic cellulitis (confined to skin and subcutaneous tissue)
- Non-clostridial anaerobic cellulitis
- Progressive bacterial synergistic gangrene (*Staphylococcus aureus* + micro-aerophilic streptococcus) ('Meleney's gangrene', primarily confined to skin)
- Pyomyositis (discrete abscesses within individual muscle groups)
- Clostridial myonecrosis (gas gangrene)
- Anaerobic streptococcal myonecrosis (non-clostridial infection mimicking gas gangrene)
- Group A streptococcal necrotising myositis

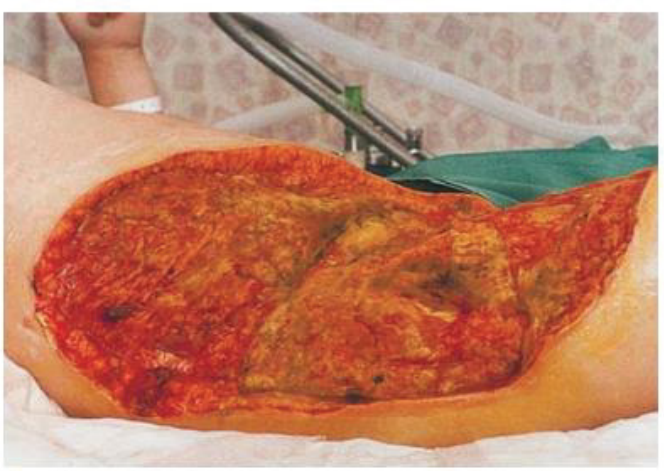


Fig. 11.4 Excision following necrotising fasciitis in an injection drug-user.

11.10 Causes of infectious gastroenteritis

Toxin in food: <6 hrs incubation

- *Bacillus cereus* (p. 262)
- *Staphylococcus aureus* (p. 262)
- *Clostridium* spp. enterotoxin (p. 262)

Bacterial: 12–72 hrs incubation

- Enterotoxigenic *Escherichia coli* (ETEC, p. 263)
- Shiga toxin-producing *E. coli* (EHEC, p. 263)*
- Enteroinvasive *E. coli* (EIEC, p. 263)*
- *Vibrio cholerae* (p. 264)
- *Salmonella* (p. 262)
- *Shigella** (p. 265)
- *Campylobacter** (p. 262)
- *Clostridium difficile** (p. 264)

Viral: short incubation

- Rotavirus (p. 249)
- Norovirus (p. 249)

Protozoal: long incubation

- Giardiasis (p. 287)
- Cryptosporidiosis (pp. 287 and 317)
- Microsporidiosis (p. 317)
- Amoebic dysentery (p. 286)*
- Cystoisosporiasis (p. 233)

*Associated with bloody diarrhoea.

11.12 Infectious diarrhoea in old age

- **Incidence**: not increased but the impact is greater.
- **Mortality**: most deaths due to gastroenteritis in the developed world are in adults aged over 70. Most are presumed to be caused by dehydration leading to organ failure.
- ***Clostridium difficile* infection (CDI)**: more common, especially in hospital and nursing home settings, usually following antibiotic exposure.

11.11 Differential diagnosis of acute diarrhoea and vomiting

Infectious causes

- Gastroenteritis
- *Clostridium difficile* infection (p. 264)
- Acute diverticulitis (p. 833)
- Sepsis (p. 196)
- Pelvic inflammatory disease (p. 336)
- Meningococcaemia (p. 1119)
- Pneumonia (especially 'atypical disease', p. 582)
- Malaria (p. 273)

Non-infectious causes

Gastrointestinal

- Inflammatory bowel disease (p. 813)
- Bowel malignancy (p. 827)
- Overflow from constipation (p. 834)
- Enteral tube feeding

Metabolic

- Diabetic ketoacidosis (p. 735)
- Thyrotoxicosis (p. 635)
- Uraemia (p. 414)
- Neuro-endocrine tumours releasing (e.g.) VIP or 5-HT

Drugs and toxins

- NSAIDs
- Cytotoxic agents
- Antibiotics
- Proton pump inhibitors
- Dinoflagellates (p. 149)
- Plant toxins (p. 150)
- Heavy metals
- Ciguatera fish poisoning (p. 149)
- Scombrotoxic fish poisoning (p. 150)

(5-HT = 5-hydroxytryptamine, serotonin; NSAIDs = non-steroidal anti-inflammatory drugs; VIP = vasoactive intestinal peptide)

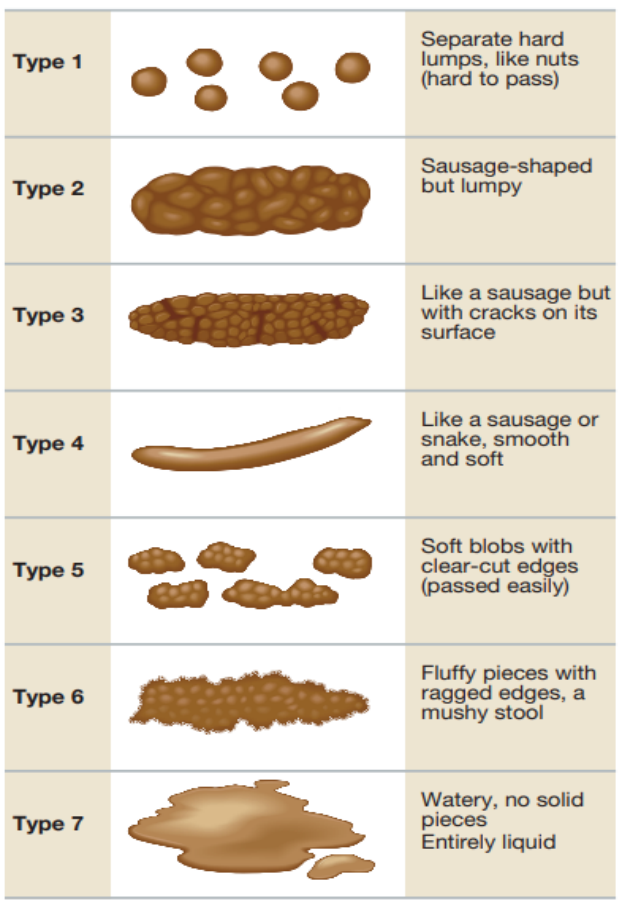


Fig. 11.5 Bristol stool chart. The stool is given a 'score' of 1–7 by reference to the verbal and visual description. This is recorded on a chart (usually known as a 'Bristol stool chart') or in a patient monitoring database. *Adapted from Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997; 32:920–924.*

11.13 Foods associated with infectious illness, including gastroenteritis

Raw seafood

- Norovirus
- *Vibrio* spp.
- Hepatitis A

Raw eggs

- *Salmonella* serovars

Undercooked meat or poultry

- *Salmonella* serovars
- *Campylobacter* spp.
- EHEC
- Hepatitis E (pork products)
- *Clostridium perfringens*

Unpasteurised milk or juice

- *Salmonella* serovars.
- *Campylobacter* spp.
- EHEC
- *Yersinia enterocolitica*

Unpasteurised soft cheeses

- *Salmonella* serovars
- *Campylobacter* spp.
- ETEC
- *Yersinia enterocolitica*
- *Listeria monocytogenes*

Home-made canned goods

- *Clostridium botulinum*

Raw hot dogs, pâté

- *Listeria monocytogenes*

(EHEC = enterohaemorrhagic *Escherichia coli*; ETEC = enterotoxigenic *E. coli*)

11.14 Composition of oral rehydration solution and other replacement fluids*

Fluid	Na	K	Cl	Energy
WHO	90	20	80	54
Dioralyte	60	20	60	71
Pepsi	6.5	0.8	–	400
7UP	7.5	0.2	–	320
Apple juice	0.4	26	–	480
Orange juice	0.2	49	–	400
Breast milk	22	36	28	670

*Values given in mmol/L for electrolyte and kcal/L for energy components. (WHO = World Health Organisation)

11.15 How to assess health needs in travellers before departure*

- Destination
- Personal details, including previous travel experience
- Dates of trip
- Itinerary and purpose of trip
- Personal medical history, including pregnancy, medication and allergies (e.g. to eggs, vaccines, antibiotics)
- Past vaccinations:
  - Childhood schedule followed? Diphtheria, tetanus, pertussis, polio, *Neisseria meningitidis* types B/C, *Haemophilus influenzae* B (HiB)
  - Travel-related? Typhoid, yellow fever, hepatitis A, hepatitis B, meningococcal ACW135Y, rabies, Japanese B encephalitis, tick-borne encephalitis
- Malaria prophylaxis: questions influencing the choice of antimalarial drugs are destination, past experience with antimalarials, history of epilepsy or psychiatric illness

*Further information is available at fitfortravel.nhs.uk.

11.16 How to obtain a history from travellers to the tropics with fever

Questions	Factors to ascertain
Countries visited and dates of travel	Relate travel to known outbreaks of infection or antimicrobial resistance
Determine the environment visited	Travel to rural environments, forests, rivers or lakes
Clarify where the person slept	Sleeping in huts, use of bed nets, sleeping on the ground
Establish what he/she was doing	Exposure to people with medical illness, animals, soil, lakes and rivers
History of insect bites	Type of insect responsible, circumstances (location, time of day etc.), preventive measures
Dietary history	Ingestion of uncooked foods, salads and vegetables, meats (especially if under-cooked), shellfish, molluscs, unpasteurised dairy products, unbottled water and sites at which food prepared
Sexual history	History of sexual intercourse with commercial sex workers, local population or travellers from other countries
Malaria prophylaxis	Type of prophylaxis
Vaccination history	Receipt of pre-travel vaccines and appropriateness to area visited
History of any treatments received while abroad	Receipt of medicines, local remedies, blood transfusions or surgical procedures

11.17 Specific exposures and causes of fever in the tropics

Exposure	Infection or disease
Mosquito bite	Malaria, dengue fever, Chikungunya, filariasis, tularaemia
Tsetse fly bite	African trypanosomiasis
Tick bite	Rickettsial infections including typhus, Lyme disease, tularaemia, Crimean–Congo haemorrhagic fever, Kyasanur forest disease, babesiosis, tick-borne encephalitis
Louse bite	Typhus
Flea bite	Plague
Sandfly bite	Leishmaniasis, arbovirus infection
Reduviid bug	Chagas' disease
Animal contact	Q fever, brucellosis, anthrax, plague, tularaemia, viral haemorrhagic fevers, rabies
Fresh-water swimming	Schistosomiasis, leptospirosis, *Naegleria fowleri*
Exposure to soil	Inhalation: dimorphic fungi Inhalation or inoculation: *Burkholderia pseudomallei* Inoculation (most often when barefoot): hookworms, *Strongyloides stercoralis*
Raw or under-cooked fruit and vegetables	Enteric bacterial infections, hepatitis A or E virus, *Fasciola hepatica*, *Toxocara* spp., *Echinococcus granulosus* (hydatid disease), *Entamoeba histolytica*
Under-cooked pork	*Taenia solium* (cysticercosis)
Crustaceans or molluscs	Paragonimiasis, gnathostomiasis, *Angiostrongylus cantonensis* infection, hepatitis A virus, cholera
Unpasteurised dairy products	Brucellosis, salmonellosis, abdominal tuberculosis, listeriosis
Untreated water	Enteric bacterial infections, giardiasis, *Cryptosporidium* spp. (chronic in immunocompromised), hepatitis A or E virus

11.18 Incubation times and illnesses in travellers

<2 weeks

Non-specific fever

- Malaria
- Chikungunya
- Dengue
- Scrub typhus
- Spotted group rickettsiae
- Acute HIV
- Acute hepatitis C virus
- *Campylobacter*
- Salmonellosis
- Shigellosis
- East African trypanosomiasis
- Leptospirosis
- Relapsing fever
- Influenza
- Yellow fever

Fever and coagulopathy (usually thrombocytopenia)

- Malaria
- VHF
- Meningococcaemia
- Enteroviruses
- Leptospirosis and other bacterial pathogens associated with coagulopathy

Fever and central nervous system involvement

- Malaria
- Typhoid fever
- Rickettsial typhus (epidemic caused by *Rickettsia prowazekii*)
- Meningococcal meningitis
- Arboviral encephalitis
- East African trypanosomiasis
- Other causes of encephalitis or meningitis
- Angiostrongyliasis
- Rabies

Fever and pulmonary involvement

- Influenza
- Pneumonia, including *Legionella* pneumonia
- Acute histoplasmosis
- Acute coccidioidomycosis
- Q fever
- SARS

Fever and rash

- Viral exanthems (rubella, measles, varicella, mumps, HHV-6, enteroviruses
- Chikungunya
- Dengue
- Spotted or typhus group rickettsiosis
- Typhoid fever
- Parvovirus B19
- HIV-1

2–6 weeks

- Malaria
- Tuberculosis
- Hepatitis A, B, C and E viruses
- Visceral leishmaniasis
- Acute schistosomiasis
- Amoebic liver abscess
- Leptospirosis
- African trypanosomiasis
- VHF
- Q fever
- Acute American trypanosomiasis
- Viral causes of mononucleosis syndromes

>6 weeks

- Non-*falciparum* malaria
- Tuberculosis
- Hepatitis B and E viruses
- HIV-1
- Visceral leishmaniasis
- Filariasis
- Onchocerciasis
- Schistosomiasis
- Amoebic liver abscess
- Chronic mycoses
- African trypanosomiasis
- Rabies
- Typhoid fever

(HHV-6 = human herpesvirus-6; SARS = severe acute respiratory syndrome; VHF = viral haemorrhagic fever)

Adapted from Traveller's Health Yellow Book, CDC Health Information for International Travel 2008.

11.19 Investigation of tropically acquired acute fever without localising signs

Features on full blood count	Further investigations
Neutrophil leucocytosis	
Bacterial sepsis	Blood culture
Leptospirosis	Culture of blood and urine, serology
Borreliosis (tick- or louse-borne relapsing fever)	Blood film
Amoebic liver abscess	Ultrasound
Normal white cell count and differential	
Malaria (may have low platelets or anaemia)	Blood film, antigen test
Typhoid fever	Blood and stool culture
Typhus	Serology
Lymphocytosis	
Viral fevers, including VHF	Serology, PCR
Infectious mononucleosis	Monospot test, serology
Malaria	Blood film, antigen test
Rickettsial fevers	Serology
Atypical lymphocytes	
Dengue and other VHF	Serology, antigen, PCR
Infectious mononucleosis-like syndromes	Serology, PCR
HIV (acute retroviral syndrome)	Serology, antigen
Hepatitis viruses	Serology, antigen, PCR
Parasitic, malaria, trypanosomiasis	Blood film, antigen test, PCR

(PCR = polymerase chain reaction; VHF = viral haemorrhagic fever)

11.20 Most common causes of travellers' diarrhoea

- Enterotoxigenic *E. coli* (ETEC)
- *Shigella* spp.
- *Campylobacter jejuni*
- *Salmonella* serovars
- *Plesiomonas shigelloides*
- Non-cholera *Vibrio* spp.
- *Aeromonas* spp.

11.21 Causes of chronic diarrhoea acquired in the tropics

- *Giardia lamblia*
- Strongyloidiasis
- Enteropathic *Escherichia coli*
- HIV enteropathy
- Intestinal flukes
- Tropical sprue
- Chronic intestinal schistosomiasis
- Chronic calcific pancreatitis
- Hypolactasia (primary and secondary)

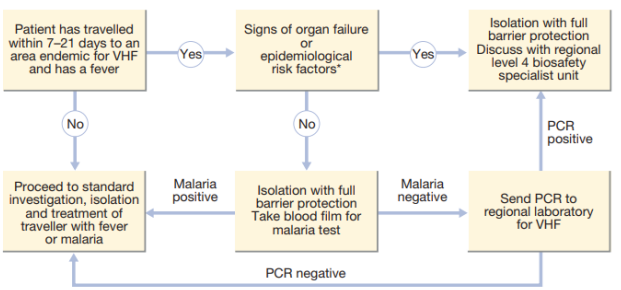


Fig. 11.6 Approach to the patient with suspected viral haemorrhagic fever (VHF). See page 245. *Epidemiological risk factors: staying with a febrile individual, caring for a sick individual, or contact with body fluids from a suspected human or animal case of VHF. (PCR = polymerase chain reaction)

11.22 Parasite infections that cause eosinophilia

Infestation	Pathogen	Clinical syndrome with eosinophilia
Strongyloidiasis	*Strongyloides stercoralis*	Larva currens
Soil-transmitted helminthiases		
Hookworm	*Necator americanus*	Anaemia
	Ancylostoma duodenale	Anaemia
Ascariasis	*Ascaris lumbricoides*	Löffler's syndrome
Toxocariasis	*Toxocara canis*	Visceral larva migrans
Schistosomiasis	*Schistosoma haematobium*	Katayama fever
	S. mansoni, S. japonicum	Chronic infection
Filariases		
Loiasis	*Loa loa*	Skin nodules
Wuchereria bancrofti	*W. bancrofti*	Lymphangitis, lymphadenopathy, orchitis, intermittent bouts of cellulitis, lymphoedema and elephantiasis
Brugia malayi	*B. malayi*	Brugian elephantiasis similar but typically less severe than that caused by *W. bancrofti*
Mansonella perstans	*M. perstans*	Asymptomatic infection, occasionally subconjunctival nodules
Onchocerciasis	*Onchocerca volvulus*	Visual disturbance, dermatitis
Other nematode infections	*Trichinella spiralis*	Myositis
	Gnathostoma spinigerum	Pruritus, migratory nodules, eosinophilic meningitis
Cestode infections	*Taenia saginata, T. solium*	Usually asymptomatic; eosinophilia associated with migratory phase
	Echinococcus granulosus	Lesions in liver or other organ; eosinophilia associated with leakage from cyst
Liver flukes	*Fasciola hepatica*	Hepatic symptoms; eosinophilia associated with migratory phase
	Clonorchis sinensis	As for fascioliasis
	Opisthorchis felineus	As for fascioliasis
Lung fluke	*Paragonimus westermani*	Lung lesions

11.23 Initial investigation of eosinophilia

Investigation	Pathogens sought
Stool microscopy	Ova, cysts and parasites
Terminal urine	Ova of *Schistosoma haematobium*
Duodenal aspirate	Filariform larvae of *Strongyloides*, liver fluke ova
Day bloods	Microfilariae *Brugia malayi*, *Loa loa*
Night bloods	Microfilariae *Wuchereria bancrofti*
Skin snips	*Onchocerca volvulus*
Slit-lamp examination	*Onchocerca volvulus*
Serology	Schistosomiasis, filariasis, strongyloidiasis, hydatid, trichinosis, gnathostomiasis etc.

11.24 Rash in tropical travellers/residents

Maculopapular rash

- Dengue
- HIV-1
- Typhoid
- *Spirillum minus*
- Rickettsial infections
- Measles

Petechial or purpuric rash

- Viral haemorrhagic fevers
- Yellow fever
- Meningococcal sepsis
- Leptospirosis
- Rickettsial spotted fevers
- Malaria

Vesicular rash

- Monkeypox
- Insect bites
- Rickettsial pox

Urticarial rash

- Katayama fever (schistosomiasis)
- *Toxocara* spp.
- *Strongyloides stercoralis*
- Fascioliasis

Ulcers

- Leishmaniasis
- *Mycobacterium ulcerans* (Buruli ulcer)
- Dracunculosis
- Anthrax
- Rickettsial eschar
- Tropical ulcer (*Fusobacterium ulcerans* and *Treponema vincentii*)
- Ecthyma (staphylococci, streptococci)

Papules

- Scabies
- Insect bites
- Prickly heat
- Ringworm
- Onchocerciasis

Nodules or plaques

- Leprosy
- Chromoblastomycosis
- Dimorphic fungi
- Trypanosomiasis
- Onchocerciasis
- Myiasis (larvae of tumbu fly or botfly)
- Tungiasis (*Tunga penetrans*)

Migratory linear rash

- Cutaneous larva migrans (CLM; dog hookworms)
- *Strongyloides stercoralis* (larva currens, more rapid than CLM)

Migratory papules/nodules

- *Loa loa*
- Gnathostomiasis
- Schistosomiasis

Thickened skin

- Mycetoma (actinomycetoma/eumycetoma)
- Elephantiasis (filariasis)

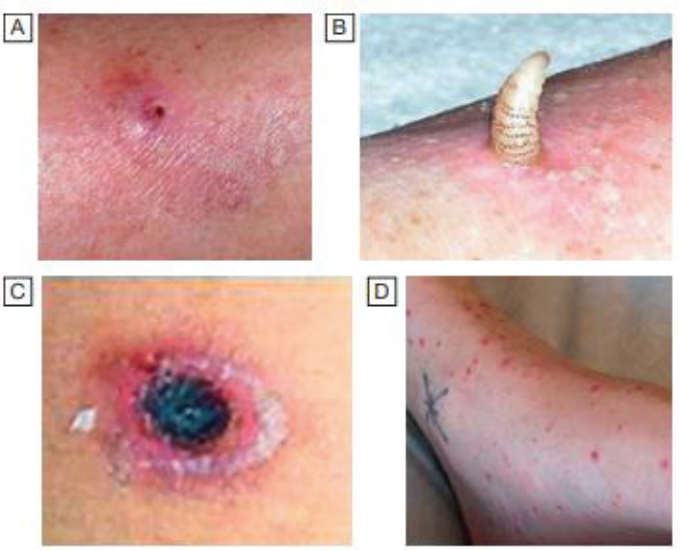


Fig. 11.7 Examples of skin lesions in patients with fever in the tropics. A Subcutaneous nodule due to botfly infection. B Emerging larva after treatment with petroleum jelly. C Eschar of scrub typhus. D Rat bite fever. *A, B and D, Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield. C, Courtesy of Dr Rattanaphone Phetsouvanh, Mahosot Hospital, Vientiane, PDR Laos.*

11.25 Key issues in infectious diseases in adolescence

- **Common infectious syndromes**: infectious mononucleosis, bacterial pharyngitis, whooping cough, pneumonia, staphylococcal skin/soft tissue infections, urinary tract infections, acute gastroenteritis.
- **Life-threatening infections**: meningococcal infection (sepsis and/or meningitis).
- **Sexually transmitted infections**: human papillomavirus (HPV), HIV-1, hepatitis B virus and chlamydia. These may reflect either voluntary sexual activity or sexual coercion/abuse.
- **Travel-related infections**: diarrhoea, malaria etc. are relatively common.
- **Infections in susceptible groups**: patients with cystic fibrosis, congenital immunodeficiency, acute leukaemia and other adolescent malignancies are vulnerable to specific groups of infections.
- **Infections requiring prolonged antimicrobial use**: adherence to chronic therapy is challenging, for both oral (antituberculous or antiretroviral) and systemic (osteomyelitis, septic arthritis or post-operative infections) treatments. Outpatient antimicrobial therapy is preferred to minimise hospitalisation.
- **Vaccination**: engagement with age-specific vaccine programmes should be ensured, e.g. HPV, childhood booster vaccines and meningococcal vaccine.
- **Risk reduction**: education relating to sexual health and alcohol and recreational drug usage is important.

11.27 Rubella infection: risk of congenital malformation

Stage of gestation	Likelihood of malformations
1–2 months	65–85% chance of illness, multiple defects/spontaneous abortion
3 months	30–35% chance of illness, usually a single congenital defect (most frequently deafness, cataract, glaucoma, mental retardation or congenital heart disease, especially pulmonary stenosis or patent ductus arteriosus)
4 months	10% risk of congenital defects, most commonly deafness
>20 weeks	Occasional deafness

11.26 Infections in pregnancy

Infection	Consequence	Prevention and management
Rubella	Congenital malformation	Childhood vaccination and vaccination of non-immune mothers post-delivery
Cytomegalovirus	Neonatal infection, congenital malformation	Limited prevention strategies
Zika virus	Congenital malformation	Avoidance of travel, delay in pregnancy if infected
Varicella zoster virus	Neonatal infection, congenital malformation, severe infection in mother	VZ immunoglobulin (see Box 11.31)
Herpes simplex virus (HSV)	Congenital or neonatal infection	Aciclovir and consideration of caesarean section for mothers who shed HSV from genital tract at time of delivery. Aciclovir for infected neonates
Hepatitis B virus	Chronic infection of neonate	Hepatitis B immunoglobulin and active vaccination of newborn
Hepatitis E virus	Fulminant hepatitis, pre-term delivery, fetal loss	Maintenance of standard food hygiene practices
HIV-1	Chronic infection of neonate	Antiretroviral drugs for mother and infant and consideration of caesarean section if HIV-1 viral load detectable. Avoidance of breastfeeding
Parvovirus B19	Congenital infection	Avoidance of individuals with acute infection if pregnant
Measles	More severe infection in mother and neonate, fetal loss	Childhood vaccination, human normal immunoglobulin in non-immune pregnant contacts and vaccination post-delivery
Dengue	Neonatal dengue if mother has infection <5 weeks prior to delivery	Vector (mosquito) control
Syphilis	Congenital malformation	Serological testing in pregnancy with prompt treatment of infected mothers
Neisseria gonorrhoeae* and *Chlamydia trachomatis	Neonatal conjunctivitis (ophthalmia neonatorum, p. 340)	Treatment of infection in mother and neonate
Listeriosis	Neonatal meningitis or bacteraemia, bacteraemia or pyrexia of unknown origin in mother	Avoidance of unpasteurised cheeses and other dietary sources
Brucellosis	Possibly increased incidence of fetal loss	Avoidance of unpasteurised dairy products
Group B streptococcal infection	Neonatal meningitis and sepsis. Sepsis in mother after delivery	Risk- or screening-based antimicrobial prophylaxis in labour (recommendations vary between countries)
Toxoplasmosis	Congenital malformation	Diagnosis and prompt treatment of cases, avoidance of under-cooked meat while pregnant
Malaria	Fetal loss, intrauterine growth retardation, severe malaria in mother	Avoidance of insect bites. Intermittent preventative treatment during pregnancy to decrease incidence in high-risk countries

11.28 Clinical features of parvovirus B19 infection

Affected age group	Clinical manifestations
Fifth disease (erythema infectiosum)	
Small children	Three clinical stages: a 'slapped cheek' appearance, followed by a maculopapular rash progressing to a reticulate eruption on the body and limbs, then a final stage of resolution. Often the child is quite well throughout
Gloves and socks syndrome	
Young adults	Fever and an acral purpuric eruption with a clear margin at the wrists and ankles. Mucosal involvement also occurs
Arthropathies	
Adults and occasionally children	Symmetrical small-joint polyarthropathy. In children it tends to involve the larger joints in an asymmetrical distribution
Impaired erythropoiesis	
Adults, those with haematological disease, the immunosuppressed	Mild anaemia; in an individual with an underlying haematological abnormality it can precipitate transient aplastic crisis, or in the immunocompromised a more sustained but often milder pure red cell aplasia
Hydrops fetalis	
Transplacental fetal infection	Asymptomatic or symptomatic maternal infection that can cause fetal anaemia with an aplastic crisis, leading to non-immune hydrops fetalis and spontaneous abortion

11.29 Herpesvirus infections

Virus	Infection
Herpes simplex virus (HSV)	
HSV-1 (p. 247)	Herpes labialis ('cold sores') Stomatitis, pharyngitis Corneal ulceration Finger infections ('whitlows') Eczema herpeticum Encephalitis
HSV-2 (p. 247)	Genital ulceration and neonatal infection (acquired during vaginal delivery) Acute meningitis or transverse myelitis; rarely, encephalitis
Varicella zoster virus (VZV)	Chickenpox (varicella) Shingles (herpes zoster)
Cytomegalovirus (CMV) (p. 242)	Congenital infection Infectious mononucleosis (heterophile antibody-negative) Hepatitis Disease in immunocompromised patients: retinitis, encephalitis, pneumonitis, hepatitis, enteritis Fever with abnormalities in haematological parameters
Epstein–Barr virus (EBV) (p. 241)	Infectious mononucleosis Burkitt's and other lymphomas Nasopharyngeal carcinoma Oral hairy leucoplakia (AIDS patients) Other lymphomas, post-transplant lymphoproliferative disorder (p. 225)
Human herpesvirus 6 and 7 (HHV-6, HHV-7)	Exanthem subitum Disease in immunocompromised patients
Human herpesvirus 8 (HHV-8) (p. 248)	Kaposi's sarcoma, primary effusion lymphoma, multicentric Castleman's disease

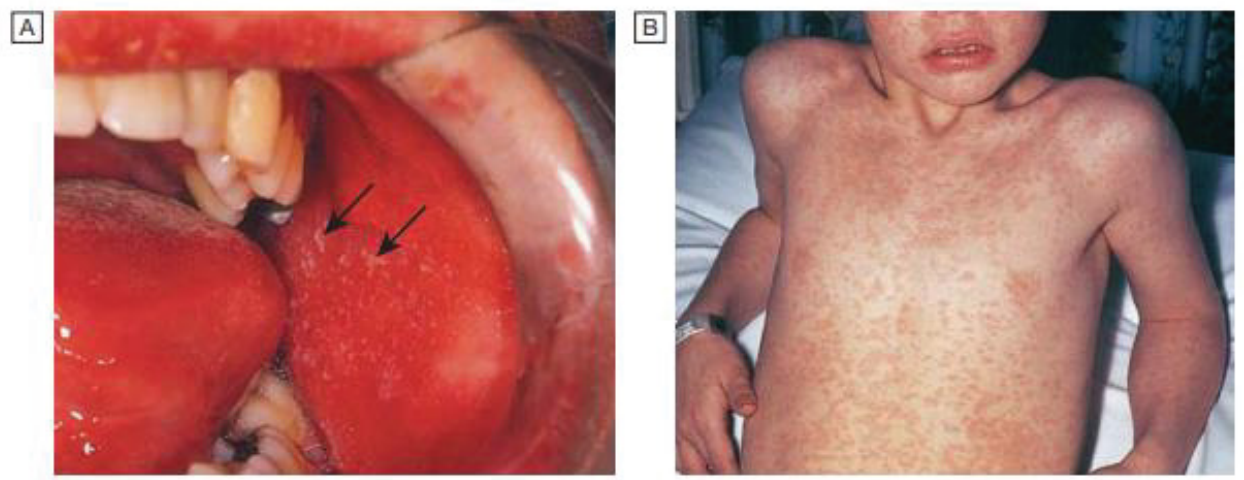


Fig. 11.8 Measles. A Koplik's spots (arrows) seen on buccal mucosa in the early stages of clinical measles. B Typical measles rash.

11.30 Therapy for herpes simplex and varicella zoster virus infection

Disease state	Treatment options
Primary genital HSV	Famciclovir 250 mg 3 times daily for 7–10 days Valaciclovir 1 g twice daily for 7–10 days Oral aciclovir 200 mg 5 times daily or 400 mg 3 times daily for 7–10 days
Severe and preventing oral intake	Aciclovir 5 mg/kg 3 times daily IV until patient can tolerate oral therapy
Recurrent genital HSV-1 or 2	Oral aciclovir 200 mg 5 times daily or 400 mg 3 times daily for 5 days Famciclovir 125 mg twice daily for 5 days Valaciclovir 500 mg twice daily for 3–5 days or 2 g twice daily for 1 day. Shorter durations increasingly favoured
Primary or recurrent oral HSV	Usually no treatment If required, usually short duration, e.g. valaciclovir 2 g twice daily for 1 day
Mucocutaneous HSV infection in immunocompromised host	Aciclovir 5 mg/kg 3 times daily IV for 7–10 days Oral aciclovir 400 mg 4 times daily for 7–10 days Famciclovir 500 mg 3 times daily for 7–10 days Valaciclovir 1 g twice daily for 7–10 days
Chickenpox in adult or child	Oral aciclovir 800 mg 5 times daily for 5 days Famciclovir 500 mg 3 times daily for 5 days Valaciclovir 1 g 3 times daily for 5 days
Immunocompromised host/pregnant woman	Aciclovir 5 mg/kg 3 times daily IV until patient is improving, then complete therapy with oral therapy until all lesions are crusting over
Shingles	Treatment and doses as for chickenpox but duration typically 7–10 days
Visceral involvement (non-CNS) in HSV	Aciclovir IV 5 mg/kg 3 times daily for 14 days
Visceral involvement (non-CNS) in VZV	Aciclovir IV 5 mg/kg 3 times daily for 7 days
Severe complications (encephalitis, disseminated infection)	Aciclovir IV 10 mg/kg 3 times daily (up to 20 mg/kg in neonates) for 14–21 days
HSV disease suppression	Aciclovir 400 mg twice daily Famciclovir 250 mg twice daily Valaciclovir 500 mg daily

(CNS = central nervous system; HSV = herpes simplex virus; VZV = varicella zoster virus)

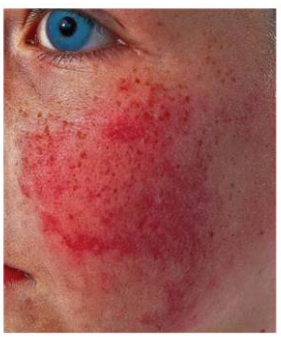


Fig. 11.9 Slapped cheek syndrome. The typical facial rash of parvovirus B19 infection.

11.31 Indications for varicella zoster immunoglobulin (VZIG) in adults

An adult should satisfy all three of the following conditions:

1. Significant contact

Contact with chickenpox (any time from 48 hrs before the rash until crusting of lesions) or zoster (exposed, disseminated or, with immunocompromised contacts, localised zoster; between development of the rash until crusting) defined as:

- Prolonged household contact, sharing a room for ≥15 mins or face-to-face contact (includes direct contact with zoster lesions)
- Hospital contact with chickenpox in another patient, health-care worker or visitor
- Intimate contact (e.g. touching) with person with shingles lesions
- Newborn whose mother develops chickenpox no more than 5 days before delivery or 2 days after delivery

2. Susceptible contact

- Individual with no history of chickenpox, ideally confirmed by negative test for VZV IgG

3. Predisposition to severe chickenpox

- Immunocompromised due to disease (e.g. acute leukaemia, HIV, other primary or secondary immunodeficiency)
- Medically immunosuppressed (e.g. following solid organ transplant; current or recent (<6 months) cytotoxic chemotherapy or radiotherapy; current or recent (<3 months) high-dose glucocorticoids; haematopoietic stem cell transplant)
- Pregnant (any stage)
- Infants: newborn whose mother has had chickenpox as above; premature infants <28 weeks

11.32 Causes of infectious mononucleosis syndrome

- Epstein–Barr virus infection
- Cytomegalovirus
- Human herpesvirus-6 or 7
- HIV-1 primary infection (p. 311)
- Toxoplasmosis

11.33 Complications of Epstein–Barr virus infection

Common

- Severe pharyngeal oedema
- Antibiotic-induced rash (80–90% with ampicillin)
- Hepatitis (80%)
- Prolonged post-viral fatigue (10%)
- Jaundice (<10%)

Uncommon

Neurological

- Cranial nerve palsies
- Polyneuritis
- Transverse myelitis
- Meningoencephalitis

Haematological

- Haemolytic anaemia
- Thrombocytopenia

Renal

- Abnormalities on urinalysis
- Interstitial nephritis

Cardiac

- Myocarditis
- ECG abnormalities
- Pericarditis

Rare

- Ruptured spleen
- Respiratory obstruction
- Agranulocytosis
- X-linked lymphoproliferative syndrome

EBV-associated malignancy

- Nasopharyngeal carcinoma
- Burkitt's lymphoma
- Hodgkin lymphoma (certain subtypes only)
- Primary CNS lymphoma
- Lymphoproliferative disease in immunocompromised

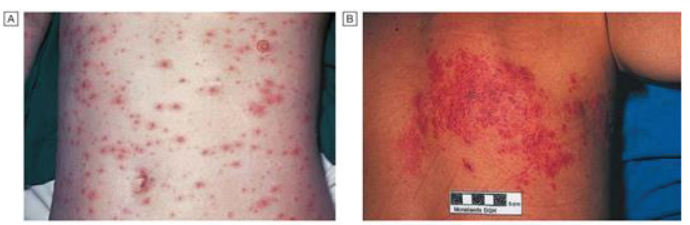


Fig. 11.10 Varicella zoster virus infection. A Chickenpox. B Shingles in a thoracic dermatome.

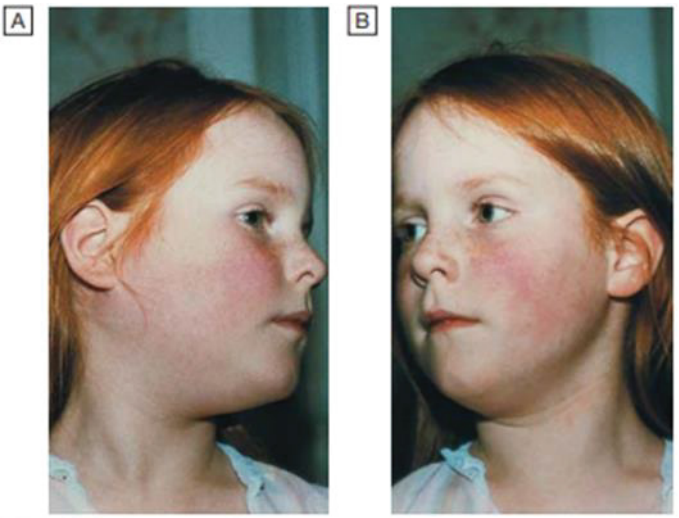


Fig. 11.11 **Typical unilateral mumps.** A Note the loss of angle of the jaw on the affected (right) side. B Comparison showing normal (left) side.

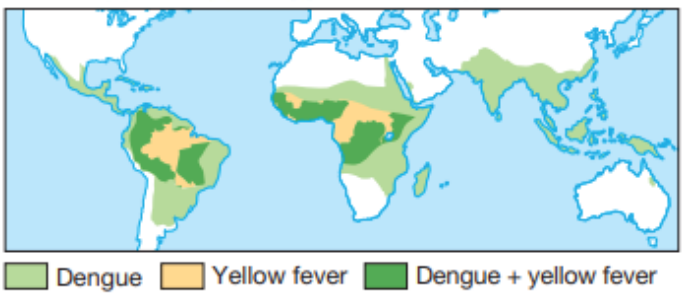


Fig. 11.13 **Endemic zones of yellow fever and dengue.**

11.34 Clinical features of dengue fever

Incubation period

- 2–7 days

Prodrome

- 2 days of malaise and headache

Acute onset

- Fever, backache, arthralgias, headache, generalised pains ('break-bone fever'), pain on eye movement, lacrimation, scleral injection, anorexia, nausea, vomiting, pharyngitis, upper respiratory tract symptoms, relative bradycardia, prostration, depression, hyperaesthesia, dysgeusia, lymphadenopathy

Fever

- Continuous or 'saddle-back', with break on 4th or 5th day and then recrudescence; usually lasts 7–8 days

Rash

- Initial flushing faint macular rash in first 1–2 days. Maculopapular, scarlet morbilliform blanching rash from days 3–5 on trunk, spreading centrifugally and sparing palms and soles; onset often with fever defervescence. May desquamate on resolution or give rise to petechiae on extensor surfaces

Convalescence

- Slow and may be associated with prolonged fatigue syndrome, arthralgia or depression

Complications

- Dengue haemorrhagic fever and disseminated intravascular coagulation
- Dengue shock syndrome
- Severe organ involvement
- Vertical transmission if infection within 5 weeks of delivery

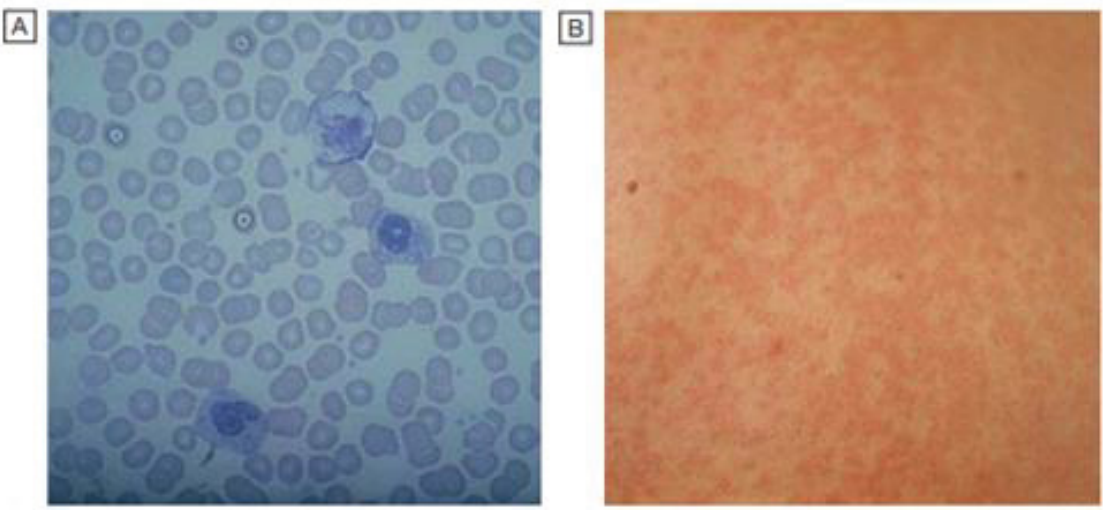


Fig. 11.12 **Features of infectious mononucleosis.** A Atypical lymphocytes in peripheral blood. B Skin reaction to ampicillin.

i 11.35 WHO case definitions of dengue, 2015

Probable dengue fever

- Exposure in an endemic area
- Fever
- Two of:
  - Nausea/vomiting
  - Rash
  - Aches/pains
  - Positive tourniquet test
  - Leucopenia
  - Any warning sign

Laboratory confirmation important

Needs regular medical observation and instruction in the warning signs

If there are no warning signs, need for hospitalisation is influenced by age, comorbidities, pregnancy and social factors

Dengue with warning signs

- Probable dengue plus one of:
  - Abdominal pain or tenderness
  - Persistent vomiting
  - Signs of fluid accumulation, e.g. pleural effusion or ascites
  - Mucosal bleed
  - Hepatomegaly >2 cm
  - Rapid increase in haematocrit with fall in platelet count

Needs medical intervention, e.g. intravenous fluid

Severe dengue

- Severe plasma leakage leading to:
  - Shock (dengue shock syndrome)
  - Fluid accumulation with respiratory distress
- Severe haemorrhagic manifestations, e.g. gastrointestinal haemorrhage
- Severe organ involvement (atypical features):
  - Liver AST or ALT ≥1000 U/L
  - CNS: impaired consciousness, meningoencephalitis, seizures
  - Cardiomyopathy, conduction defects, arrhythmias
  - Other organs, e.g. acute kidney injury, pancreatitis, acute lung injury, disseminated intravascular coagulopathy, rhabdomyolysis

Needs emergency medical treatment and specialist care with intensive care input

(ALT = alanine aminotransferase; AST = aspartate aminotransferase)
Adapted from https://www.cdc.gov/nndss/conditions/dengue-virus-infections/case-definition/2015/

i 11.36 Viral haemorrhagic fevers

Disease	Reservoir	Transmission	Incubation period	Geography	Mortality rate	Clinical features of severe disease[1]
Lassa fever	Multimammate rats (*Mastomys natalensis*)	Urine from rat Body fluids from patients	6–21 days	West Africa	15%	Haemorrhage, shock, encephalopathy, ARDS (responds to ribavirin), deafness in survivors
Ebola fever	Fruit bats (*Pteropodidae* family) and bush meat	Body fluids from patients Handling infected primates	2–21 days	Central Africa Outbreaks as far north as Sudan	25–90%	Haemorrhage and/or diarrhoea, hepatic failure and acute kidney injury
Marburg fever	Undefined	Body fluids from patients Handling infected primates	3–9 days	Central Africa Outbreak in Angola	25–90%	Haemorrhage, diarrhoea, encephalopathy, orchitis
Yellow fever	Monkeys	Mosquitoes	3–6 days	See Figure 11.13	~15%	Hepatic failure, acute kidney injury, haemorrhage
Dengue	Humans	*Aedes aegypti*	2–7 days	See Figure 11.13	<10%[2]	Haemorrhage, shock
Crimean–Congo haemorrhagic fever	Small vertebrates Domestic and wild animals	*Ixodes* tick Body fluids	1–3 days up to 9 days 3–6 days up to 13 days	Africa, Asia, Eastern Europe	30%	Encephalopathy, early haemorrhage, hepatic failure, acute kidney injury, ARDS
Rift Valley fever	Domestic livestock	Contact with animals, mosquito or other insect bites	2–6 days	Africa, Arabian peninsula	1%	Haemorrhage, blindness, meningoencephalitis (complications only in a minority)
Kyasanur fever	Monkeys	Ticks	3–8 days	Karnataka State, India	5–10%	Haemorrhage, pulmonary oedema, neurological features, iridokeratitis in survivors
Bolivian and Argentinian haemorrhagic fever (Junin and Machupo viruses)	Rodents (*Calomys* spp.)	Urine, aerosols Body fluids from case (rare)	5–19 days (3–6 days for parenteral)	South America	15–30%	Haemorrhage, shock, cerebellar signs (may respond to ribavirin)
Haemorrhagic fever with renal syndrome (Hantaan fever)	Rodents	Aerosols from faeces	5–42 days (typically 14 days)	Northern Asia, northern Europe, Balkans	5%	Acute kidney injury, cerebrovascular accidents, pulmonary oedema, shock (hepatic failure and haemorrhagic features only in some variants)

[1]All potentially have circulatory failure. [2]Mortality of uncomplicated and haemorrhagic dengue fever, respectively.
(ARDS = acute respiratory distress syndrome)

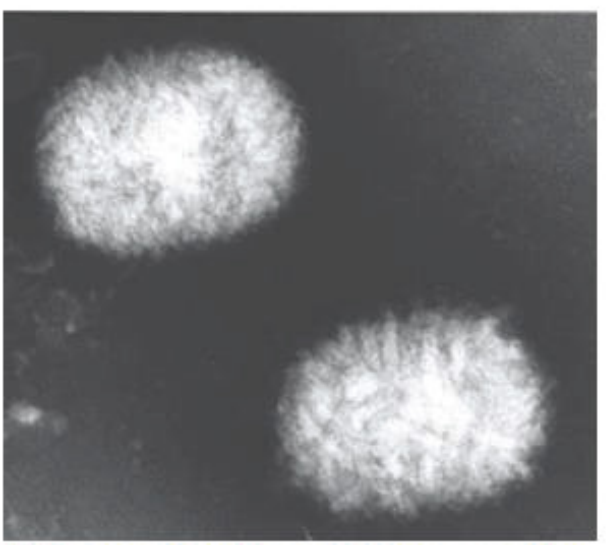


Fig. 11.15 Electron micrograph of molluscum contagiosum, a poxvirus. *Courtesy of Prof. Goura Kudesia, Northern General Hospital, Sheffield.*

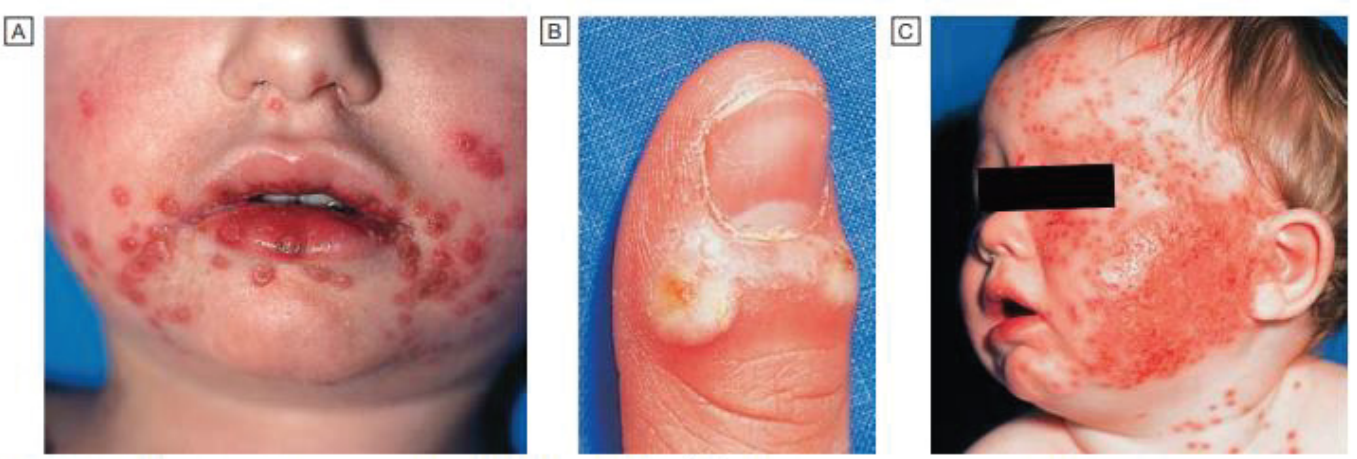


Fig. 11.14 Cutaneous manifestations of herpes simplex virus 1 (HSV-1). A Acute HSV-1. There were also vesicles in the mouth – herpetic stomatitis. B Herpetic whitlow. C Eczema herpeticum. HSV-1 infection spreads rapidly in eczematous skin.

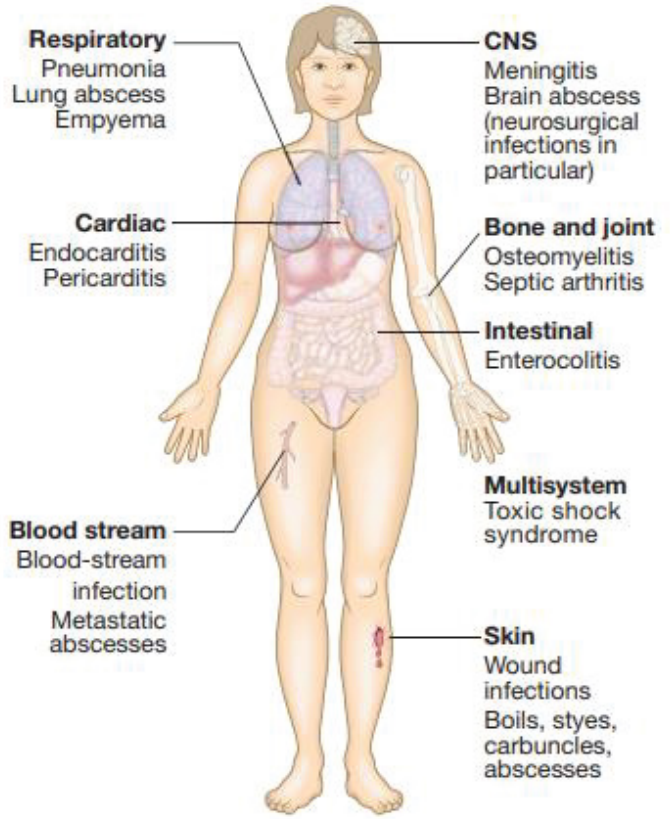


Fig. 11.16 Infections caused by *Staphylococcus aureus*.

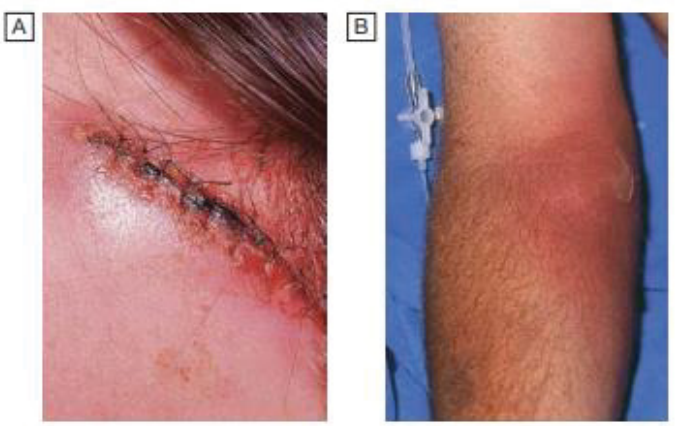


Fig. 11.17 Manifestations of skin infection with *Staphylococcus aureus*. A Wound infection. B Cannula-related infection.

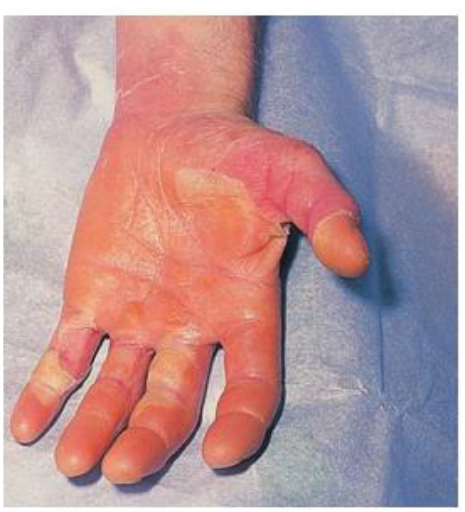


Fig. 11.18 Full-thickness desquamation after staphylococcal toxic shock syndrome.

11.37 How to assess an intravenous cannula using the Visual Infusion Phlebitis (VIP) score

Clinical features	Score	Assessment and management
IV site appears healthy	0	**No signs of phlebitis** Observe cannula
One of the following is evident: Slight pain near IV site Slight redness near IV site	1	**Possible first signs of phlebitis** Observe cannula
Two of the following are evident: Pain near IV site Erythema Swelling	2	**Early stage of phlebitis** Resite cannula
ALL of the following are evident and extensive: Pain along path of cannula Erythema Induration	3	**Medium stage of phlebitis** Resite cannula Consider treatment
ALL of the following are evident and extensive: Pain along path of cannula Erythema Induration Palpable venous cord	4	**Advanced stage of phlebitis or start of thrombophlebitis** Resite cannula Consider treatment
ALL of the following are evident: Pain along path of cannula Erythema Induration Palpable venous cord Pyrexia	5	**Advanced stage of thrombophlebitis** Initiate treatment Resite cannula

Adapted from Jackson A. Nursing Times 1997; 94:68–71.

11.38 Streptococcal and related infections

β-haemolytic group A (*Strep. pyogenes*)

- Skin and soft tissue infection (including erysipelas, impetigo, necrotising fasciitis)
- Streptococcal toxic shock syndrome
- Puerperal sepsis
- Scarlet fever
- Glomerulonephritis
- Rheumatic fever
- Bone and joint infection
- Tonsillitis

β-haemolytic group B (*Strep. agalactiae*)

- Neonatal infections, including meningitis
- Female pelvic infections
- Cellulitis

β-haemolytic group C (various zoonotic streptococci)

- Cellulitis
- Endocarditis
- Pharyngitis
- Septic arthritis

α-, β- or non-haemolytic group D (*Enterococcus faecalis, E. faecium*)

- Endocarditis
- Intra-abdominal infections
- Urinary tract infection

α- or non-haemolytic group D (*Strep. gallolyticus* subsp. *gallolyticus*/*S. bovis* biotype I)

- Bacteraemia/endocarditis associated with large bowel malignancy

β-haemolytic group G streptococci

- Cellulitis
- Endocarditis
- Liver abscess
- Septic arthritis

α-haemolytic optochin-resistant (viridans streptococci – *Strep. mitis, Strep. sanguis, Strep. mutans, Strep. salivarius*)

- Sepsis in immunosuppressed
- Endocarditis

α-haemolytic optochin-sensitive (*Strep. pneumoniae*)

- Pneumonia
- Meningitis
- Endocarditis
- Otitis media
- Sepsis
- Spontaneous bacterial peritonitis
- Sinusitis

Variable haemolysis (*Strep. milleri* group – *Strep. anginosus, Strep. intermedius, Strep. constellatus*)

- Endocarditis
- Intra-abdominal infections
- Urinary tract infection

Anaerobic streptococci (*Peptostreptococcus* spp.)

- Sepsis in immunosuppressed
- Endocarditis

N.B. All streptococci can cause sepsis.

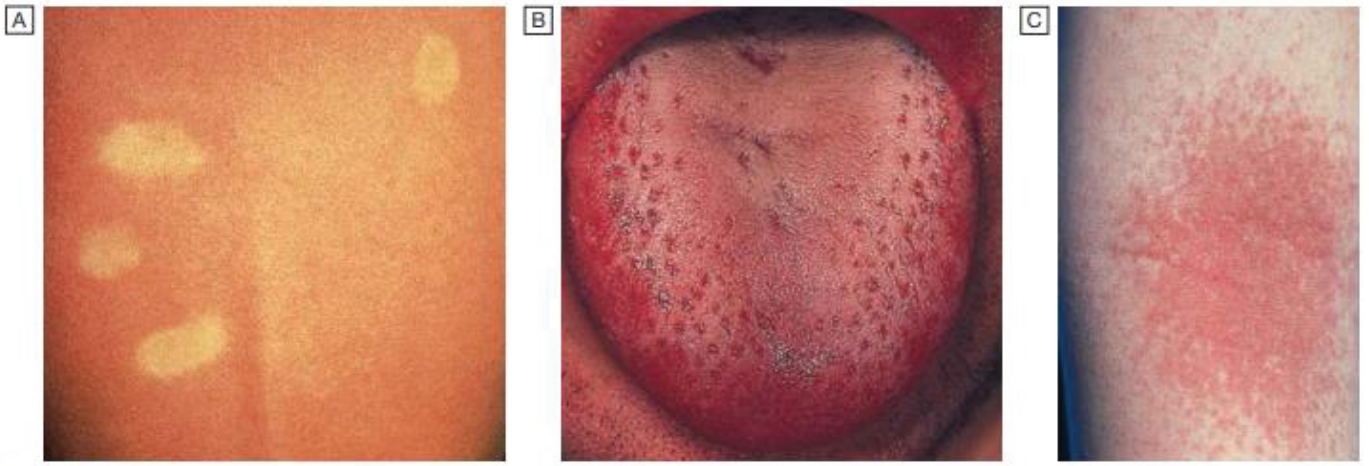


Fig. 11.19 Clinical features of scarlet fever. A Characteristic rash with blanching on pressure. B 'Strawberry tongue'. C Pastia's sign: a petechial rash in the cubital fossa.

11.39 Diagnosis and treatment of yaws, pinta and bejel

Diagnosis of early stages

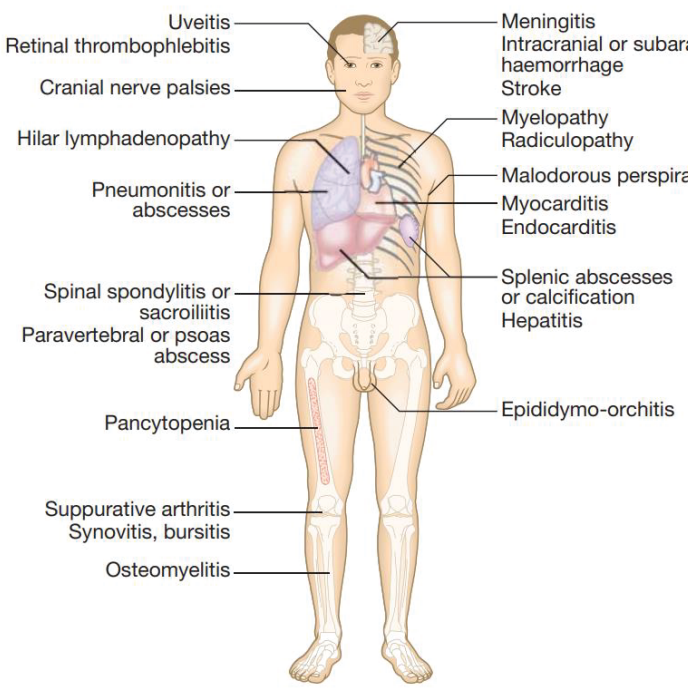
- Detection of spirochaetes in exudate of lesions by dark ground microscopy

Diagnosis of latent and early stages

- Positive serological tests, as for syphilis (see Box 13.8, p. 339)

Treatment of all stages

- Single intramuscular injection of 1.2 g long-acting penicillin, e.g. benzathine benzylpenicillin



11.40 Treatment of brucellosis

Adults with non-localised disease

- Doxycycline 100 mg twice daily orally for 6 weeks *plus* gentamicin 5 mg/kg IV once daily for 7 days

  or
- Doxycycline 100 mg twice daily *plus* rifampicin 600–900 mg orally once daily for 6 weeks

Bone disease

- Doxycycline 100 mg twice daily *plus* rifampicin 600–900 mg once daily orally for 6 weeks *plus* gentamicin 5 mg/kg IV once daily for 7 days

  or
- Ciprofloxacin 750 mg twice daily orally *plus* rifampicin 600–900 mg orally once daily for 3 months

Neurobrucellosis

- Doxycycline 100 mg twice daily *plus* rifampicin 600–900 mg orally once daily for 6 weeks *plus* ceftriaxone 2vg IV twice daily until the cerebrospinal fluid is clear (though susceptibility should be confirmed because sensitivity to third-generation cephalosporins varies among strains)

Endocarditis

- Almost always needs surgical intervention

  plus
- Doxycycline 100 mg twice daily, rifampicin 600–900 mg orally once daily and co-trimoxazole 5 mg/kg of trimethoprim component for 6 months *plus* gentamicin 5 mg/kg IV once daily for 2–4 weeks

Pregnancy

- Rifampicin 600–900 mg orally once daily and co-trimoxazole 5 mg/kg of trimethoprim component for 4 weeks, but caution in last week of pregnancy due to displacement of bilirubin from albumin by drugs and risk of kernicterus to the fetus

Fig. 11.20 Clinical features of brucellosis.

11.41 Clinical diseases caused by *Borrelia* spp.

Species	Vector	Geographical distribution
Lyme disease		
B. burgdorferi sensu stricto	Tick: *Ixodes scapularis*	Northern and eastern USA
	I. pacificus	Western USA
B. afzelii	*I. ricinus*	Europe
	I. persulcatus	Asia
B. garinii	*I. ricinus*	Europe
	I. persulcatus	Asia
Louse-borne relapsing fever		
B. recurrentis	Human louse: *Pediculus humanus corporis*	Worldwide
Tick-borne relapsing fever		
B. hermsii	Tick: *Ornithodoros hermsii*	Western North America
B. turicatae	*O. turicatae*	South-western North America and northern Mexico
B. venezuelensis	*O. rudis*	Central America and northern South America
B. hispanica	*O. erraticus*	Iberian peninsula and north-western Africa
B. crocidurae	*O. erraticus*	North Africa and Mediterranean region
B. duttonii	*O. moubata*	Central, eastern and southern Africa
B. persica	*O. tholozani*	Western China, India, Central Asia, Middle East
B. latyschewii	*O. tartakovskyi*	Tajikistan, Uzbekistan

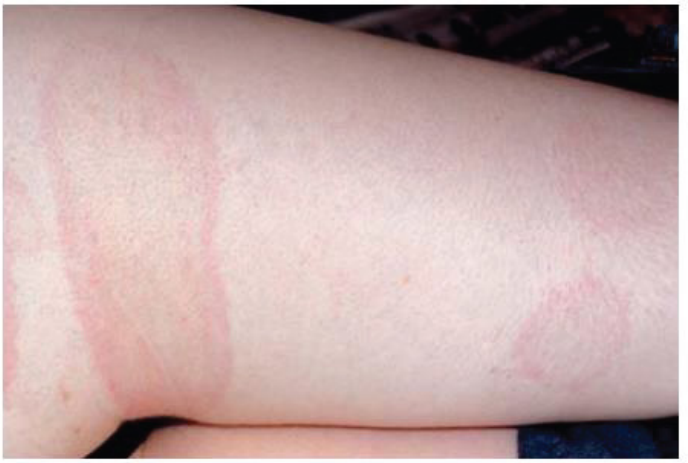


Fig. 11.21 Rash of erythema migrans in Lyme disease with metastatic secondary lesions. *Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield.*

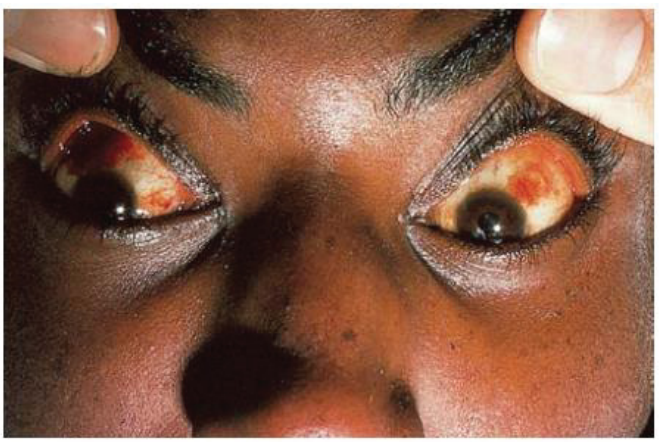


Fig. 11.22 Louse-borne relapsing fever. Injected conjunctivae.

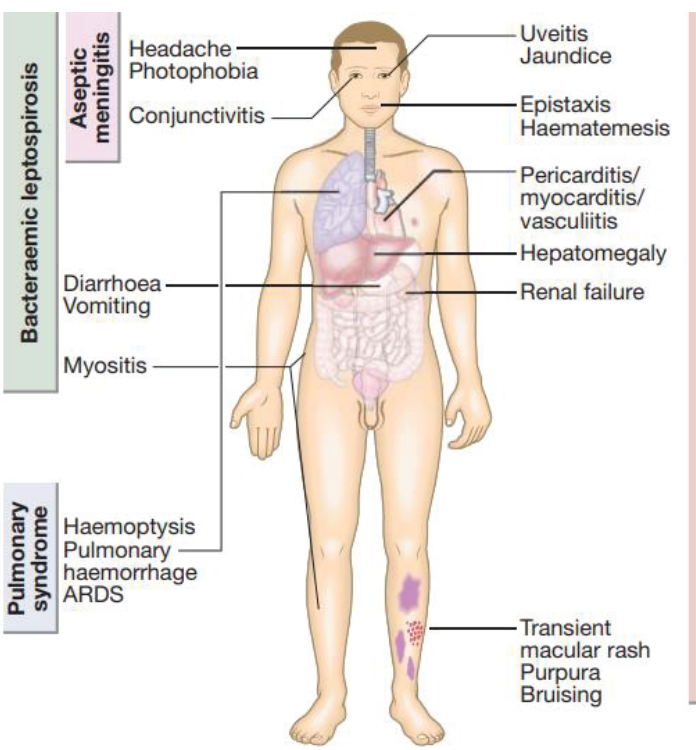


Fig. 11.23 Clinical syndromes of leptospirosis. (ARDS = acute respiratory distress syndrome)

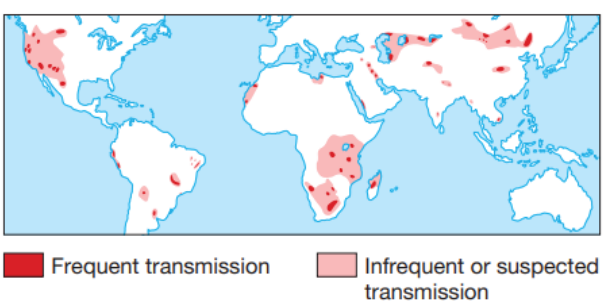


Fig. 11.24 Foci of the transmission of plague. *Reproduced by permission of the World Health Organisation.*

11.42 Clinical features of typhoid fever

First week

- Fever
- Headache
- Myalgia
- Relative bradycardia
- Constipation
- Diarrhoea and vomiting in children

End of first week

- Rose spots on trunk
- Splenomegaly
- Cough
- Abdominal distension
- Diarrhoea

End of second week

- Delirium, complications, then coma and death (if untreated)

11.43 Complications of typhoid fever

Bowel

- Perforation
- Haemorrhage

Septic foci

- Bone and joint infection
- Meningitis
- Cholecystitis

Toxic phenomena

- Myocarditis
- Nephritis

Chronic carriage

- Persistent gallbladder carriage

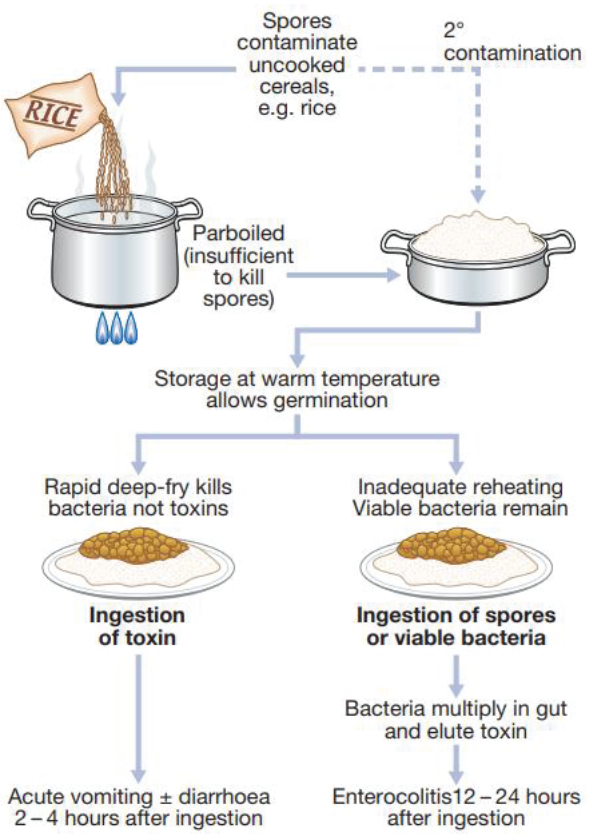


Fig. 11.25 ***Bacillus cereus*** **food poisoning.**

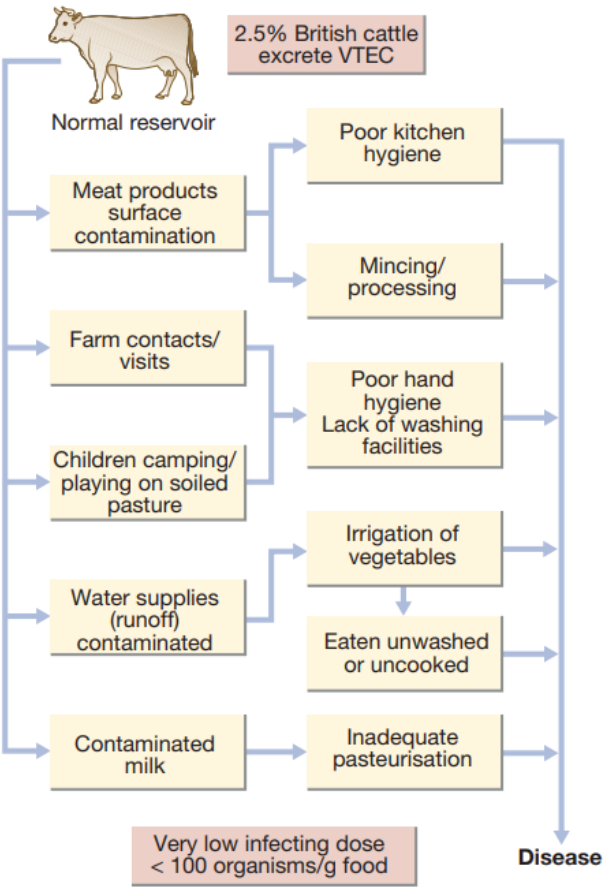


Fig. 11.26 **Verocytotoxigenic** ***Escherichia coli*** **(VTEC) infections.**

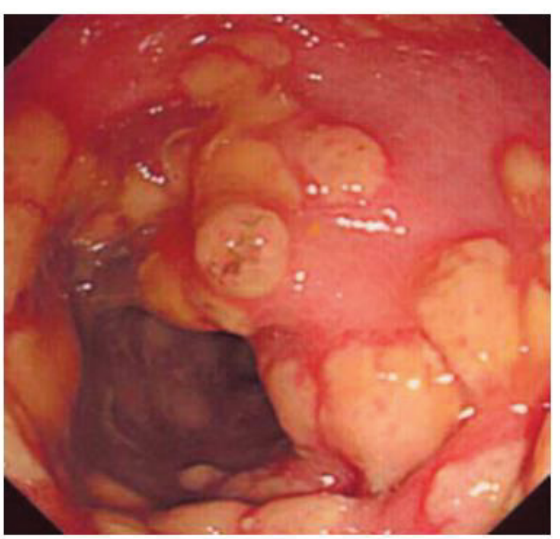


Fig. 11.27 **Clostridium difficile infection.** Colonoscopic view showing numerous adherent 'pseudomembranes' on the mucosa.

11.44 Clinical features of diphtheria

Acute infection

- Membranous tonsillitis
- *or* Nasal infection
- *or* Laryngeal infection
- *or* Skin/wound/conjunctival infection (rare)

Complications

- Laryngeal obstruction or paralysis
- Myocarditis
- Peripheral neuropathy

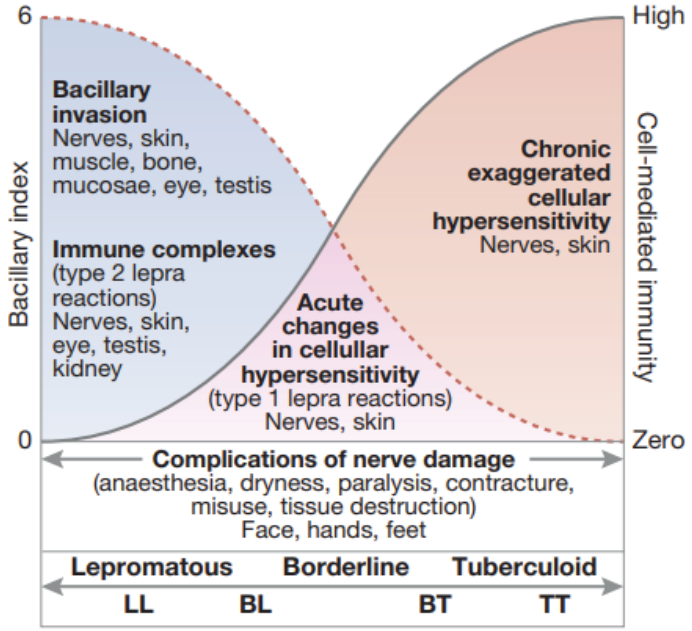


Fig. 11.28 Leprosy: mechanisms of damage and tissue affected. Mechanisms under the broken line are characteristic of disease near the lepromatous end of the spectrum, and those under the solid line are characteristic of the tuberculoid end. They overlap in the centre where, in addition, instability predisposes to type 1 lepra reactions. At the peak in the centre, neither bacillary growth nor cell-mediated immunity has the upper hand. (BL = borderline lepromatous; BT = borderline tuberculoid) *Adapted from Bryceson ADM, Pfaltzgraff RE. Leprosy, 3rd edn. Churchill Livingstone, Elsevier Ltd; 1990.*

i 11.45 Cardinal features of leprosy

- Skin lesions, typically anaesthetic at tuberculoid end of spectrum
- Thickened peripheral nerves
- Acid-fast bacilli on skin smears or biopsy

i 11.46 Clinical characteristics of the polar forms of leprosy

Clinical and tissue-specific features	Lepromatous	Tuberculoid
Skin and nerves		
Number and distribution	Widely disseminated	One or a few sites, asymmetrical
Skin lesions		
Definition:		
Clarity of margin	Poor	Good
Elevation of margin	Never	Common
Colour:		
Dark skin	Slight hypopigmentation	Marked hypopigmentation
Light skin	Slight erythema	Coppery or red
Surface	Smooth, shiny	Dry, scaly
Central healing	None	Common
Sweat and hair growth	Impaired late	Impaired early
Loss of sensation	Late	Early and marked
Nerve enlargement and damage	Late	Early and marked
Bacilli (bacterial index)	Many (5 or 6+)	Absent (0)
Natural history	Progressive	Self-healing
Other tissues	Upper respiratory mucosa, eye, testes, bones, muscle	None
Reactions	Immune complexes (type 2)	Cell-mediated (type 1)

i 11.47 Reactions in leprosy

	Lepra reaction type 1 (reversal)	Lepra reaction type 2 (erythema nodosum leprosum)
Mechanism	Cell-mediated hypersensitivity	Immune complexes
Clinical features	Painful tender nerves, loss of function Swollen skin lesions New skin lesions	Tender papules and nodules; may ulcerate Painful tender nerves, loss of function Iritis, orchitis, myositis, lymphadenitis Fever, oedema
Management	Prednisolone 40 mg, reducing over 3–6 months[1]	Moderate: prednisolone 40 mg daily Severe: thalidomide[2] or prednisolone 40–80 mg daily, reducing over 1–6 months; local if eye involved[3]

[1]Indicated for any new impairment of nerve or eye function. [2]Contraindicated in women who may become pregnant. [3]1% hydrocortisone drops or ointment and 1% atropine drops.

i 11.48 Principles of leprosy treatment

- Stop the infection with chemotherapy
- Treat reactions
- Educate the patient about leprosy
- Prevent disability
- Support the patient socially and psychologically

i 11.49 Modified WHO-recommended multidrug therapy (MDT) regimens in leprosy

Type of leprosy[1]	Monthly supervised treatment	Daily self-administered treatment	Duration of treatment[2]
Paucibacillary	Rifampicin 600 mg	Dapsone 100 mg	6 months
Multibacillary	Rifampicin 600 mg Clofazimine 300 mg	Clofazimine 50 mg Dapsone 100 mg	12 months
Paucibacillary single-lesion	Ofloxacin 400 mg Rifampicin 600 mg Minocycline 100 mg		Single dose

[1]Classification uses the bacillary index (BI) in slit-skin smears or, if BI is not available, the number of skin lesions:
- paucibacillary single-lesion leprosy (1 skin lesion)
- paucibacillary (2–5 skin lesions)
- multibacillary (>5 skin lesions).

[2]Studies from India have shown that multibacillary patients with an initial BI of >4 need longer treatment, for at least 24 months.

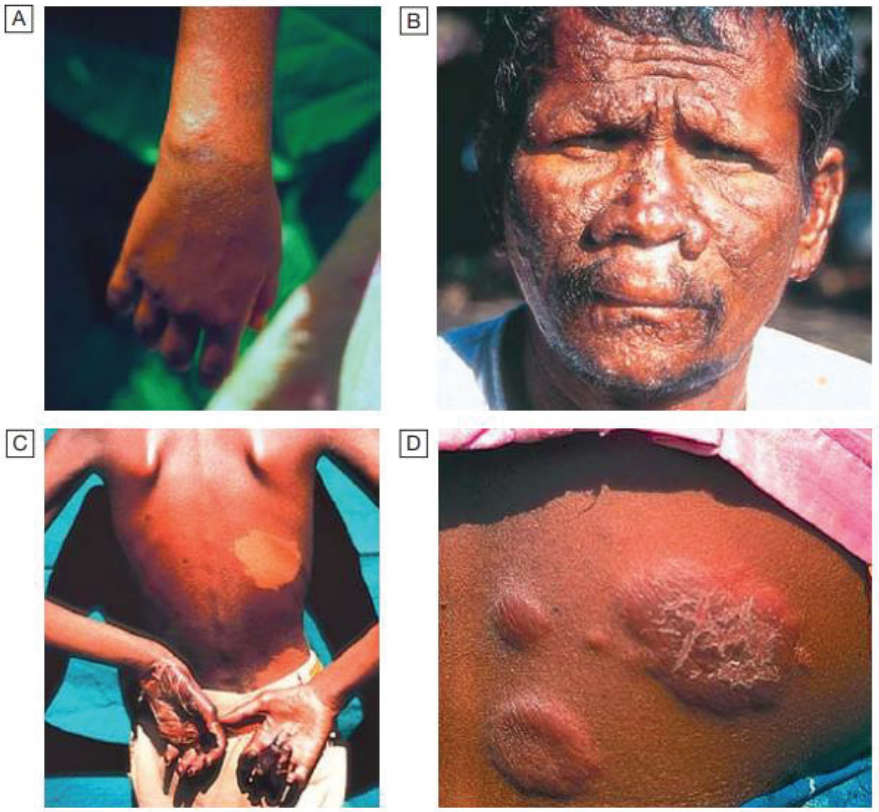


Fig. 11.29 Clinical features of leprosy. A Tuberculoid leprosy. Single lesion with a well-defined active edge and anaesthesia within the lesion. B Lepromatous leprosy. Widespread nodules and infiltration, with loss of the eyebrows. This man also has early collapse of the nose. C Borderline tuberculoid leprosy with severe nerve damage. This boy has several well-defined, hypopigmented, macular, anaesthetic lesions. He has severe nerve damage affecting both ulnar and median nerves bilaterally and has sustained severe burns to his hands. D Reversal (type 1) reactions. Erythematous, oedematous lesions.

i 11.50 Features of rickettsial infections

Disease	Organism	Reservoir	Vector	Geographical area	Rash	Gangrene	Target organs	Mortality
Spotted fever group								
Rocky Mountain spotted fever	*R. rickettsii*	Rodents, dogs, ticks	*Ixodes* tick	North, Central and South America	Morbilliform Haemorrhagic	Often	Bronchi, myocardium, brain, skin	2–12%[2]
Boutonneuse fever	*R. conorii*	Rodents, dogs, ticks	*Ixodes* tick	Mediterranean, Africa, South-west Asia, India	Maculopapular	–	Skin, meninges	2.5%[3]
Siberian tick typhus	*R. sibirica*	Rodents, birds, domestic animals, ticks	Various ticks	Siberia, Mongolia, northern China	Maculopapular	–	Skin, meninges	Rare[3]
Australian tick typhus	*R. australis*	Rodents, ticks	Ticks	Australia	Maculopapular	–	Skin, meninges	Rare[3]
Oriental spotted fever	*R. japonica*	Rodents, dogs, ticks	Ticks	Japan	Maculopapular	–	Skin, meninges	Rare[3]
African tick bite fever[1]	*R. africae*	Cattle, game, ticks	*Ixodes* tick	South Africa	Can be spotless	–	Skin, meninges	Rare[3]
Typhus group								
Scrub typhus	*Orientia tsutsugamushi*	Rodents	*Trombicula* mite	South-east Asia	Maculopapular	Unusual	Bronchi, myocardium, brain, skin	Rare[3]
Epidemic typhus	*R. prowazekii*	Humans	Louse	Worldwide	Morbilliform Haemorrhagic	Often	Brain, skin, bronchi, myocardium	Up to 40%
Endemic typhus	*R. typhi*	Rats	Flea	Worldwide	Slight	–	–	Rare[3]

[1]Eschar at bite site and local lymphadenopathy. [2]Highest in adult males. [3]Except in infants, older people and the debilitated.

i 11.51 Clinical diseases caused by *Bartonella* spp.

Reservoir	Vector	Organism	Disease
Cats	Flea	*B. henselae*	Cat scratch disease, bacillary angiomatosis, endocarditis
Undefined	Lice	*B. quintana*	Trench fever, bacillary angiomatosis, endocarditis
Undefined	Sandfly	*B. bacilliformis*	Carrion's disease: Oroya fever and verruga peruana
Undefined	Flea	*B. rochalimae*	Fever, rash, anaemia, splenomegaly

i 11.52 Chlamydial infections

Organism	Disease caused
Chlamydia trachomatis	Trachoma Lymphogranuloma venereum (see Box 13.12, p. 341) Cervicitis, urethritis, proctitis (p. 334)
Chlamydia psittaci	Psittacosis (see Box 17.36, p. 582)
Chlamydophila (Chlamydia) pneumoniae	Atypical pneumonia (see Box 17.36, p. 582) Acute/chronic sinusitis

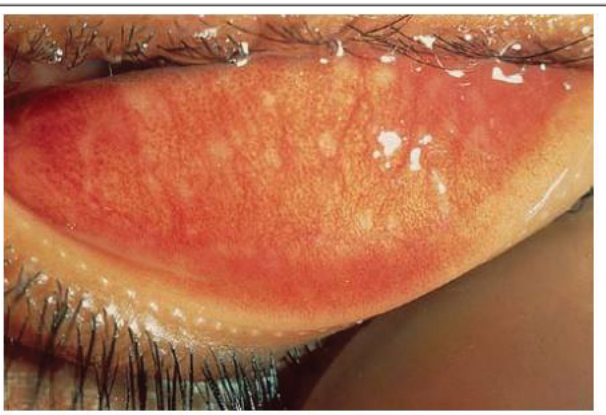


Fig. 11.30 Trachoma. Trachoma is characterised by hyperaemia and numerous pale follicles. *Courtesy of Institute of Ophthalmology, Moorfields Eye Hospital, London.*

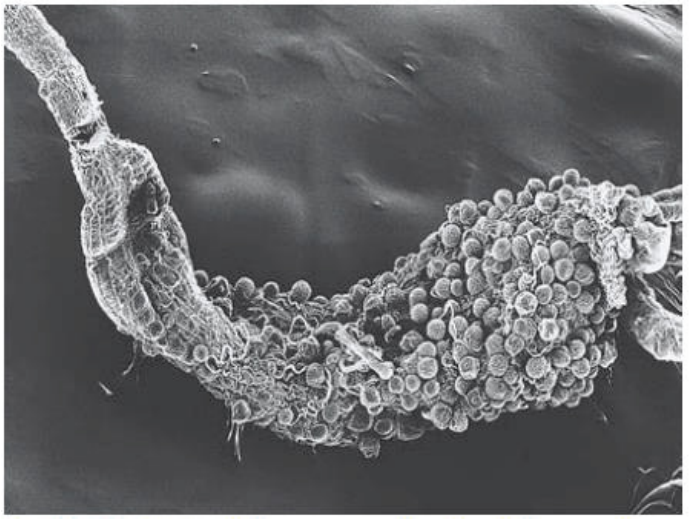


Fig. 11.32 Scanning electron micrograph of *Plasmodium falciparum* oöcysts lining an anopheline mosquito's stomach.

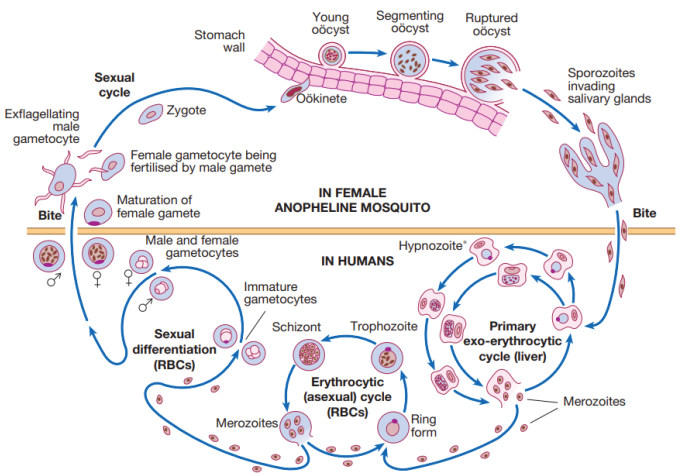


Fig. 11.33 **Malarial parasites: life cycle.** Hypnozoites(*) are present only in *Plasmodium vivax* and *P. ovale* infections. (RBC = red blood cell)

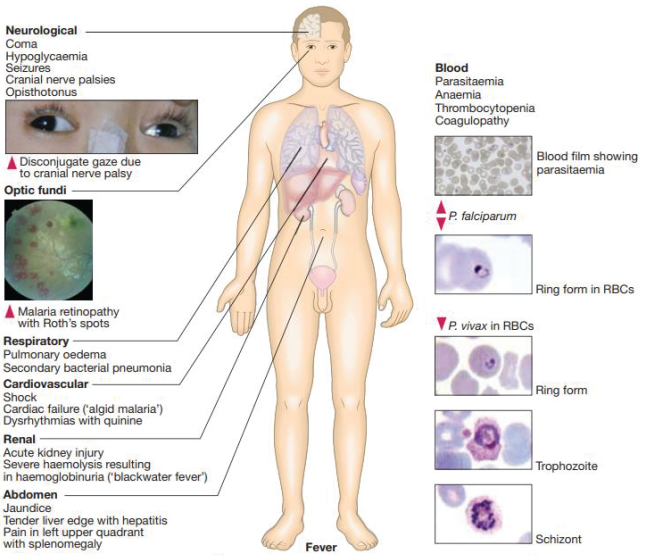


Fig. 11.34 **Features of *Plasmodium falciparum* infection.** (RBC = red blood cell) *Insets (malaria retinopathy) Courtesy of Dr Nicholas Beare, Royal Liverpool University Hospital; (blood films of* P. vivax *and* P. falciparum*) Courtesy of Dr Kamolrat Silamut, Mahidol Oxford Research Unit, Bangkok, Thailand.*

11.53 Relationships between life cycle of parasite and clinical features of malaria

Cycle/ feature	*Plasmodium vivax, P. ovale*	*P. malariae*	*P. falciparum*
Pre-patent period (minimum incubation)	8–25 days	15–30 days	8–25 days
Exo-erythrocytic cycle	Persistent as hypnozoites	Pre-erythrocytic only	Pre-erythrocytic only
Asexual cycle	48 hrs synchronous	72 hrs synchronous	<48 hrs asynchronous
Fever periodicity	Alternate days	Every third day	None
Delayed onset	Common	Rare	Rare
Relapses	Common up to 2 years	Recrudescence many years later	Recrudescence up to 1 year

11.54 Severe manifestations/complications of *falciparum* malaria and their immediate management

Coma (cerebral malaria)
- Maintain airway
- Nurse on side
- Exclude other treatable causes of coma (e.g. hypoglycaemia, bacterial meningitis)
- Avoid harmful ancillary treatments such as glucocorticoids, heparin and adrenaline (epinephrine)
- Intubate if necessary

Hyperpyrexia
- Tepid sponging, fanning, cooling blanket
- Antipyretic drug (paracetamol)

Convulsions
- Maintain airway
- Treat promptly with diazepam or paraldehyde injection

Hypoglycaemia
- Measure blood glucose
- Give 50% dextrose injection followed by 10% dextrose infusion (glucagon may be ineffective)

Severe anaemia (packed cell volume <15%)
- Transfuse fresh whole blood or packed cells if pathogen screening of donor blood is available

Acute pulmonary oedema
- Nurse at 45°, give oxygen, venesect 250 mL of blood, give diuretic, stop intravenous fluids
- Intubate and add PEEP/CPAP (p. 202) in life-threatening hypoxaemia
- Haemofilter

Acute kidney injury
- Exclude pre-renal causes
- Fluid resuscitation if appropriate
- Peritoneal dialysis (haemofiltration or haemodialysis if available)

Spontaneous bleeding and coagulopathy
- Transfuse screened fresh whole blood (cryoprecipitate/fresh frozen plasma and platelets if available)
- Vitamin K injection

Metabolic acidosis
- Exclude or treat hypoglycaemia, hypovolaemia and Gram-negative sepsis
- Fluid resuscitation
- Give oxygen

Shock ('algid malaria')
- Suspect Gram-negative sepsis
- Take blood cultures
- Give parenteral antimicrobials
- Correct haemodynamic disturbances

Aspiration pneumonia
- Give parenteral antimicrobial drugs
- Change position
- Physiotherapy
- Give oxygen

Hyperparasitaemia
- Consider exchange transfusion (e.g. >10% of circulating erythrocytes parasitised in non-immune patient with severe disease)

Specific therapy
- Intravenous artesunate
- Mefloquine should be avoided due to increased risk of post-malaria neurological syndrome

(CPAP = continuous positive airway pressure; PEEP = positive end-expiratory pressure)

From WHO. Severe falciparum malaria. In: Severe and complicated malaria, 3rd edn. Trans Roy Soc Trop Med Hyg 2000; 94 (suppl. 1):S1–41.

11.55 Malaria treatment

Mild malaria

Preferred therapy

- Co-artemether (CoArtem or Riamet); contains artemether and lumefantrine (4 tablets orally at 0, 8, 24, 36, 48 and 60 hrs)

Alternative therapy

- Quinine (600 mg of quinine salt 3 times daily orally for 5–7 days), together with or followed by doxycycline (200 mg once daily orally for 7 days)

  Use clindamycin not doxycycline if the patient is a pregnant woman or young child

  or
- Atovaquone–proguanil (Malarone, 4 tablets orally once daily for 3 days)

Pregnancy

- Co-artemether but avoid in early pregnancy.
- If not using co-artemether, use quinine plus clindamycin (450 mg 3 times daily orally for 7 days)

Other regimens

- Artesunate (200 mg orally daily for 3 days) and mefloquine (1 g orally on day 2 and 500 mg orally on day 3)

Severe malaria

Preferred therapy

- Artesunate 2.4 mg/kg IV at 0, 12 and 24 hrs and then once daily for 7 days. Once the patient is able to recommence oral intake, switch to 2 mg/kg orally once daily, to complete a total cumulative dose of 17–18 mg/kg

Alternative therapy

- Quinine, loading dose 20 mg/kg IV over 4 hrs, up to a maximum of 1.4 g, then maintenance doses of 10 mg/kg quinine salt given as 4-hr infusions 3 times daily for the first 48 hrs then twice a day, up to a maximum of 700 mg per dose or until the patient can take drugs orally. Combine with doxycycline (or clindamycin if there are contraindications to doxycycline)
- Note the loading dose should not be given if quinine, quinidine or mefloquine has been administered in the previous 24 hrs
- Patients should be monitored by ECG while receiving quinine, with special attention to QRS duration and QT interval

Non-*falciparum* malaria

Preferred therapy

- Chloroquine: 600 mg chloroquine base orally, followed by 300 mg base in 6 hrs, then 150 mg base twice daily for 2 more days plus primaquine (30 mg orally daily (for *P. vivax*) or 15 mg orally daily (for *P. ovale*) for 14 days) after confirming G6PD-negative

Patients with mild to moderate G6PD deficiency and *P. vivax* or *P. ovale*

- Chloroquine plus primaquine 0.75 mg/kg weekly orally for 8 weeks

Chloroquine-resistant *P. vivax*

- Co-artemether as for *P. falciparum*

(G6PD = glucose-6-phosphate dehydrogenase)

11.56 Chemoprophylaxis of malaria

Antimalarial tablets	Adult prophylactic dose	Regimen
Chloroquine resistance high		
Mefloquine[2]	250 mg weekly	Started 2–3 weeks before travel and continued until 4 weeks after
or Doxycycline[3,4]	100 mg daily	Started 1 week before and continued until 4 weeks after travel
or Malarone[4]	1 tablet daily	From 1–2 days before travel until 1 week after return
Chloroquine resistance absent		
Chloroquine[5] *and* proguanil	300 mg base weekly 100–200 mg daily	Started 1 week before and continued until 4 weeks after travel

[1]Choice of regimen is determined by area to be visited, length of stay, level of malaria transmission, level of drug resistance, presence of underlying disease in the traveller and concomitant medication taken. [2]Contraindicated in the first trimester of pregnancy, lactation, cardiac conduction disorders, epilepsy, psychiatric disorders; may cause neuropsychiatric disorders. [3]Causes photosensitisation and sunburn if high-protection sunblock is not used. [4]Avoid in pregnancy. [5]British preparations of chloroquine usually contain 150 mg base, French preparations 100 mg base and American preparations 300 mg base.

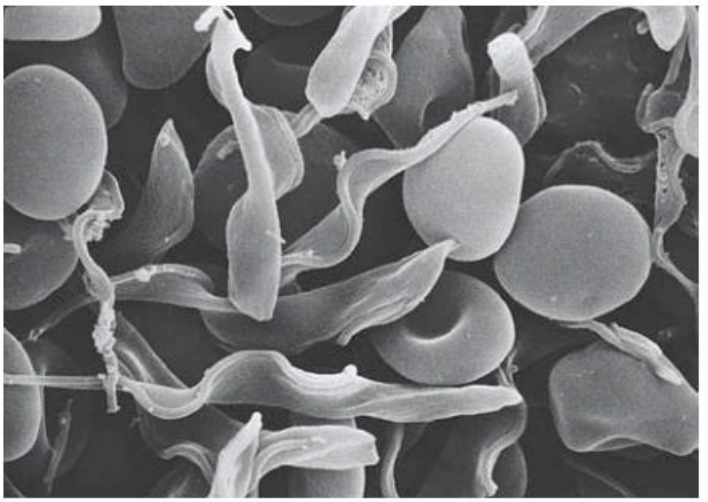


Fig. 11.35 Trypanosomiasis. Scanning electron micrograph showing trypanosomes swimming among erythrocytes.

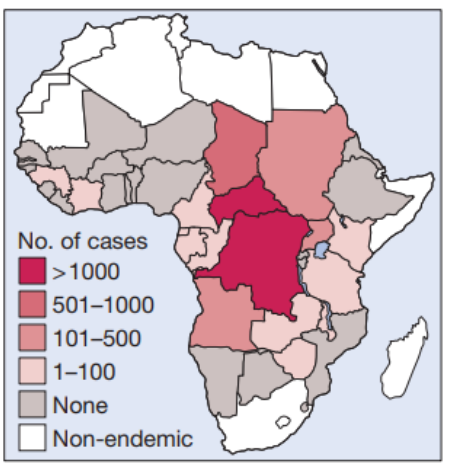


Fig. 11.36 Distribution of human African trypanosomiasis. Data are from 2009. *From Simarro PP, Diarra A, Ruiz Postigo JA, et al. The human African trypanosomiasis control and surveillance programme of the World Health Organization 2000–2009: the way forward. PLoS Negl Trop Dis 2011; 5(2):e1007.*

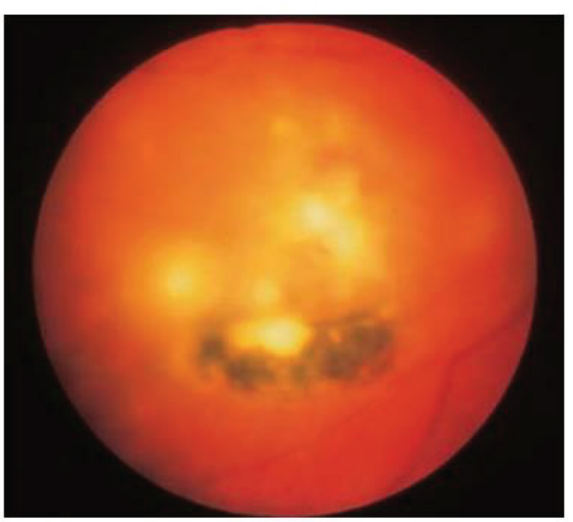


Fig. 11.38 Retinochoroiditis due to toxoplasmosis.

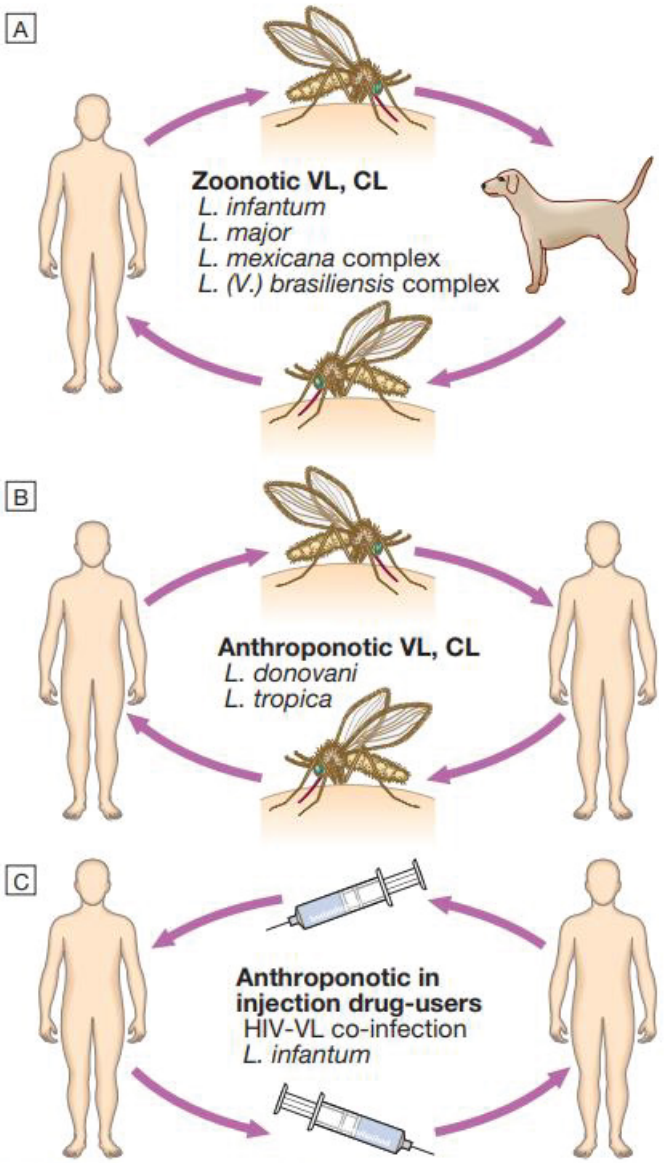


Fig. 11.39 Transmission of leishmaniasis. A Zoonotic transmission. B Anthroponotic transmission. C Anthroponotic transmission in the injection drug-user. (CL = cutaneous leishmaniasis; VL = visceral leishmaniasis)

Fig. 11.41 World distribution of visceral leishmaniasis.

i 11.57 Types of Old World cutaneous leishmaniasis

Leishmania spp.	Host	Clinical features
L. tropica	Dogs	Slow evolution, less severe
L. major	Gerbils, desert rodents	Rapid necrosis, wet sores
L. aethiopica	Hyraxes	Solitary facial lesions with satellites

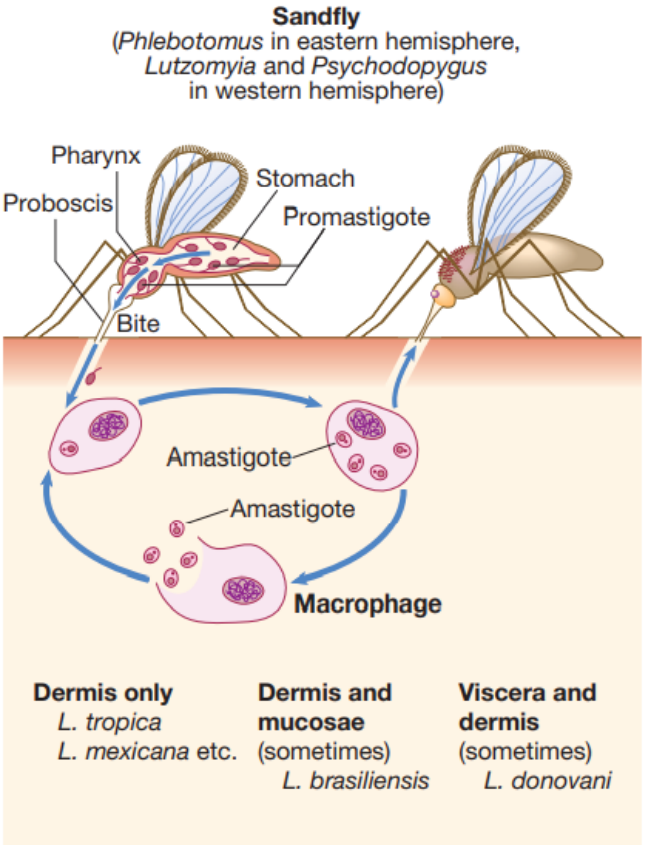


Fig. 11.40 Life cycle of *Leishmania*. *From Knight R. Parasitic disease in man. Churchill Livingstone, Elsevier Ltd; 1982.*

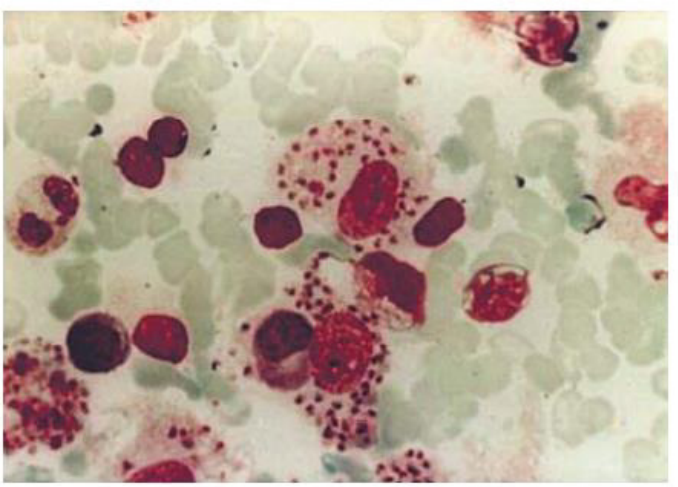
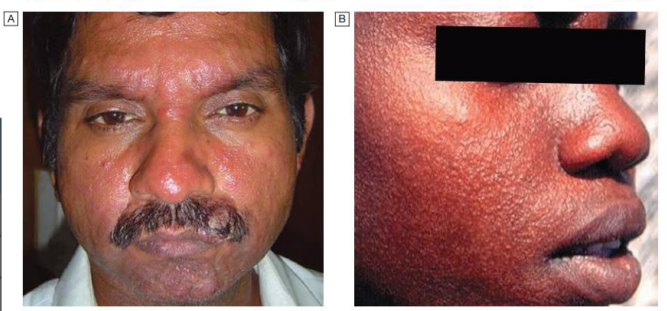


Fig. 11.42 Splenic smear showing numerous intracellular, and a few extracellular, amastigotes. *Courtesy of Dr S. Sundar and Dr H.W. Murray.*



11.43 Post-kala-azar dermal leishmaniasis. A In India, with macules, papules, nodules and plaques. B In Sudan, with micronodular rash. *rom Sundar S, Kumar K, Chakravarty J, et al. Cure of antimony-unresponsive Indian post-kala-azar dermal leishmaniasis with oral miltefosine. Trans R Trop Med Hyg 2006; 100(7):698–700. B, Courtesy of Dr E.E. Zijlstra.*

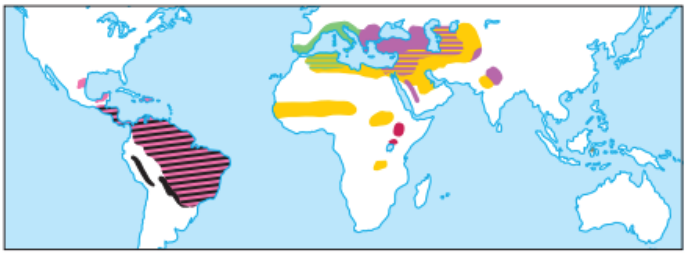


Fig. 11.44 World distribution of cutaneous leishmaniasis.

11.58 Classes of helminth that parasitise humans

Nematodes or roundworms

- Intestinal human nematodes: *Ancylostoma duodenale, Necator americanus, Strongyloides stercoralis, Ascaris lumbricoides, Enterobius vermicularis, Trichuris trichiura*
- Tissue-dwelling human nematodes: *Wuchereria bancrofti, Brugia malayi, Loa loa, Onchocerca volvulus, Dracunculus medinensis, Mansonella perstans, Dirofilaria immitis*
- Zoonotic nematodes: *Trichinella spiralis*

Trematodes or flukes

- Blood flukes: *Schistosoma haematobium, S. mansoni, S. japonicum, S. mekongi, S. intercalatum*
- Lung flukes: *Paragonimus* spp.
- Hepatobiliary flukes: *Clonorchis sinensis, Fasciola hepatica, Opisthorchis felineus*
- Intestinal flukes: *Fasciolopsis buski*

Cestodes or tapeworms

- Intestinal tapeworms: *Taenia saginata, T. solium, Diphyllobothrium latum, Hymenolepis nana*
- Tissue-dwelling cysts or worms: *Taenia solium, Echinococcus granulosus*

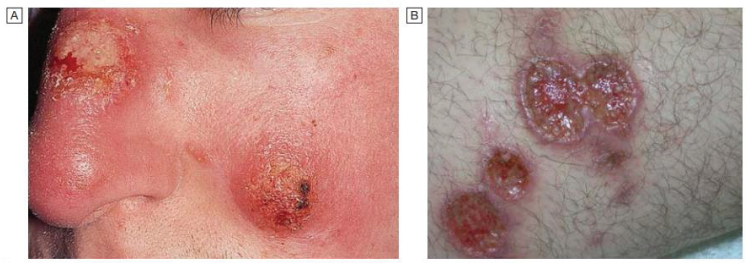


Fig. 11.45 Cutaneous leishmaniasis. A Papule. B Ulcer. *B, Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield.*

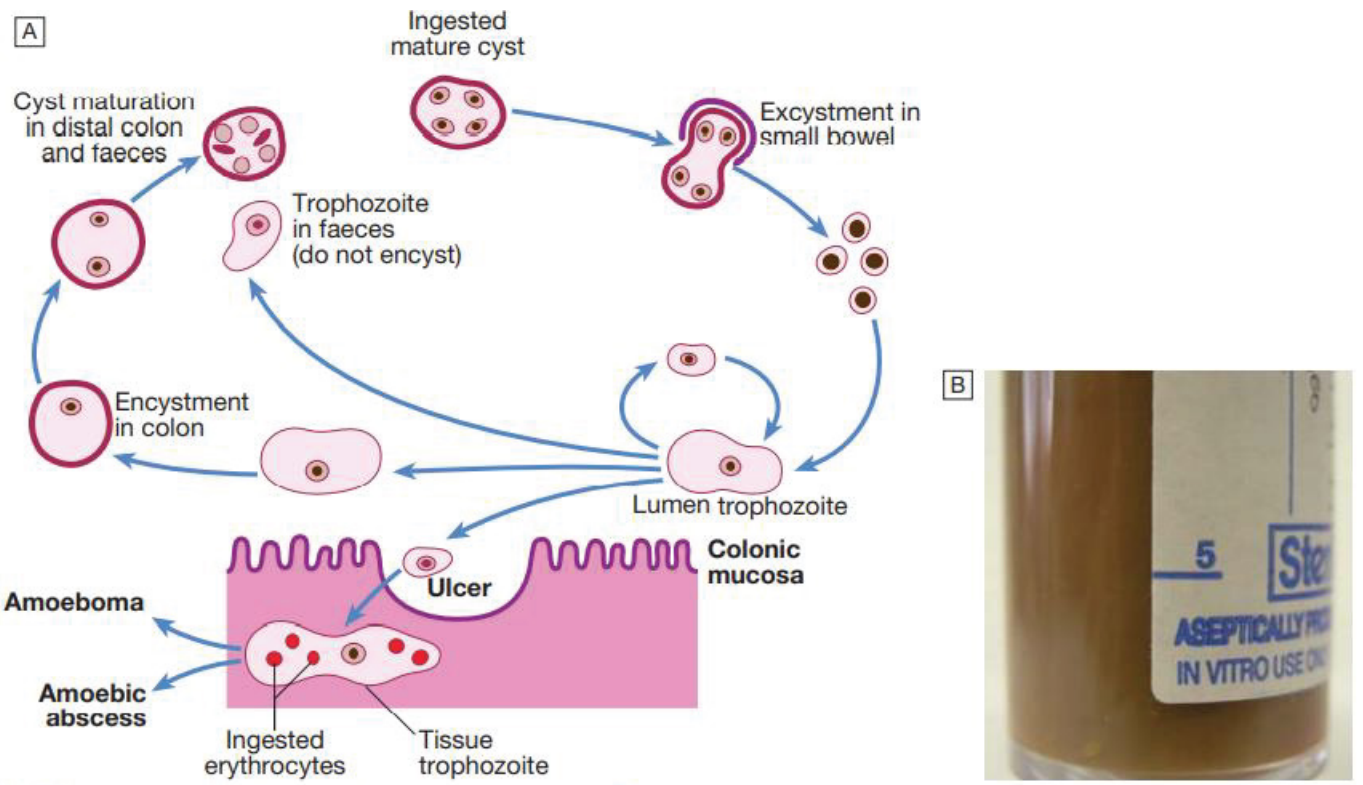


Fig. 11.46 Amoebiasis. A The life cycle of *Entamoeba histolytica*. B The chocolate-brown appearance of aspirated material from an amoebic liver abscess. *A, From Knight R. Parasitic disease in man. Churchill Livingstone, Elsevier Ltd; 1982. B, Courtesy of Dr Ravi Gowda, Royal Hallamshire Hospital, Sheffield.*

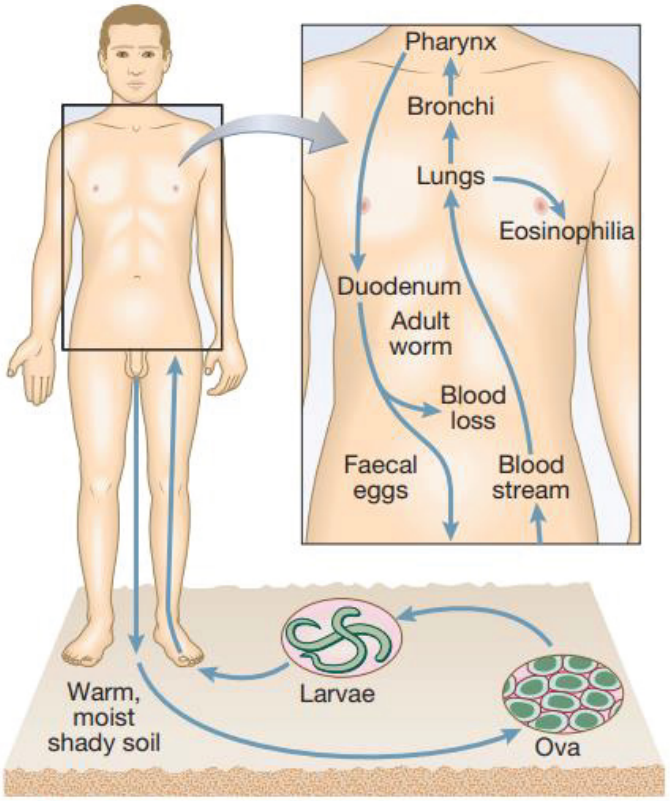


Fig. 11.47 Ancylostomiasis. Life cycle of *Ancylostoma*.

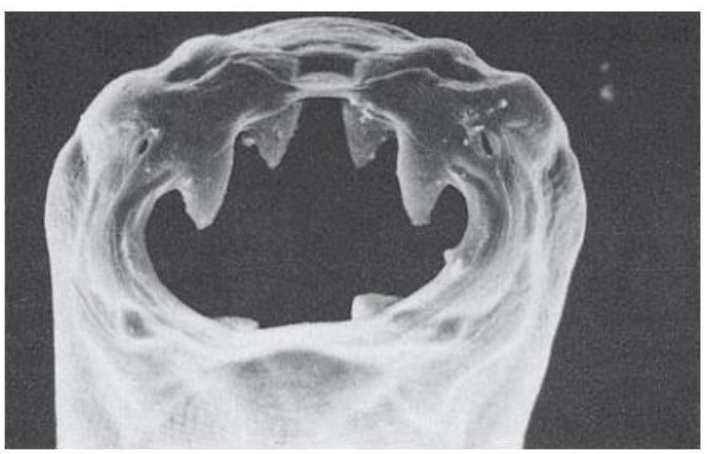


Fig. 11.48 *Ancylostoma duodenale*. Electron micrograph showing the ventral teeth. *From Gibbons LM. SEM guide to the morphology of nematode parasites of vertebrates. Farnham Royal, Slough: Commonwealth Agricultural Bureau International; 1986.*

i 11.59 Clinical features of strongyloidiasis

Penetration of skin by infective larvae

- Itchy rash

Presence of worms in gut

- Abdominal pain, diarrhoea, steatorrhoea, weight loss

Allergic phenomena

- Urticarial plaques and papules, wheezing, arthralgia

Autoinfection

- Transient itchy, linear, urticarial weals across abdomen and buttocks (larva currens)

Systemic (super-)infection

- Diarrhoea, pneumonia, meningoencephalitis, death

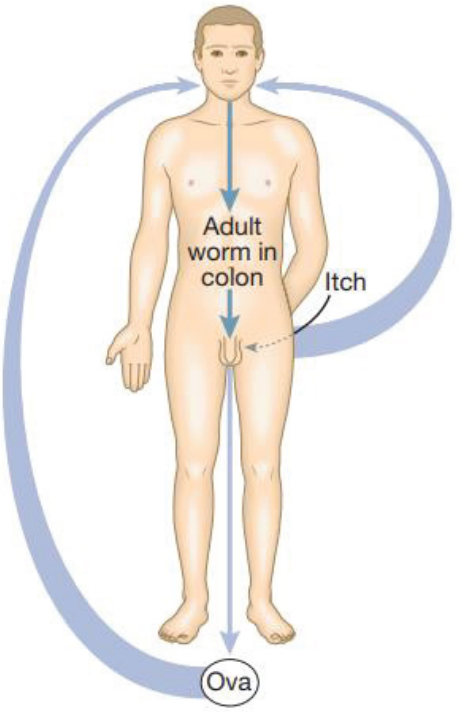


Fig. 11.49 Threadworm. Life cycle of *Enterobius vermicularis*.

i 11.60 Pathogenicity of filarial infections depending on site and stage of worms

Worm species	Adult worm	Microfilariae
Wuchereria bancrofti* and *Brugia malayi	Lymphatic vessels^{+++}	Blood^{-} Pulmonary capillaries^{++}
Loa loa	Subcutaneous^{+}	Blood^{+}
Onchocerca volvulus	Subcutaneous^{+}	Skin^{+++} Eye^{+++}
Mansonella perstans	Retroperitoneal^{-}	Blood^{-}
Mansonella streptocerca	Skin^{+}	Skin^{++}

(+++ severe; ++ moderate; + mild; – rarely pathogenic)

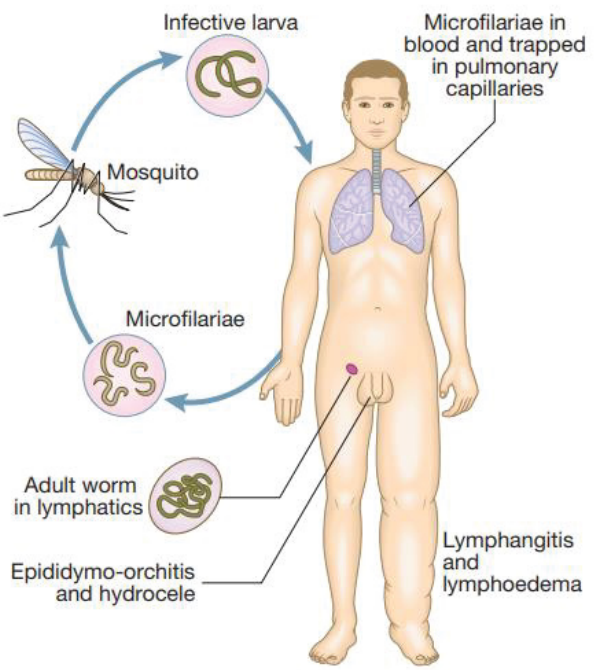


Fig. 11.50 *Wuchereria bancrofti* and *Brugia malayi*. Life cycle of organisms and pathogenesis of lymphatic filariasis.

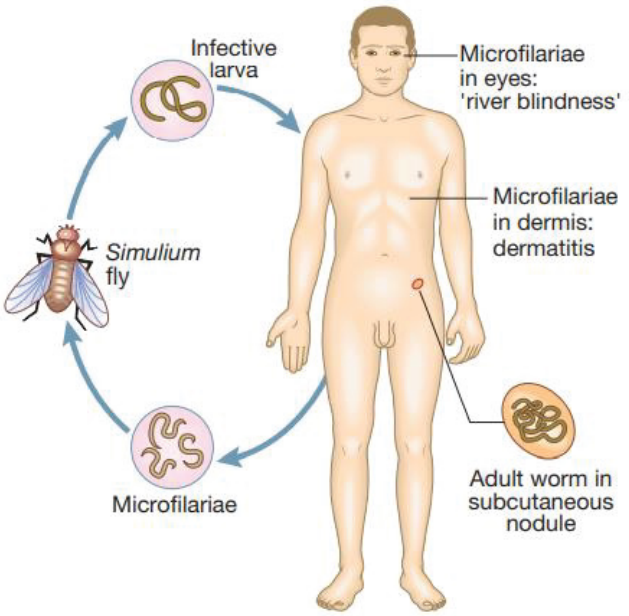


Fig. 11.51 ***Onchocerca volvulus.*** Life cycle of organism and pathogenesis of onchocerciasis.

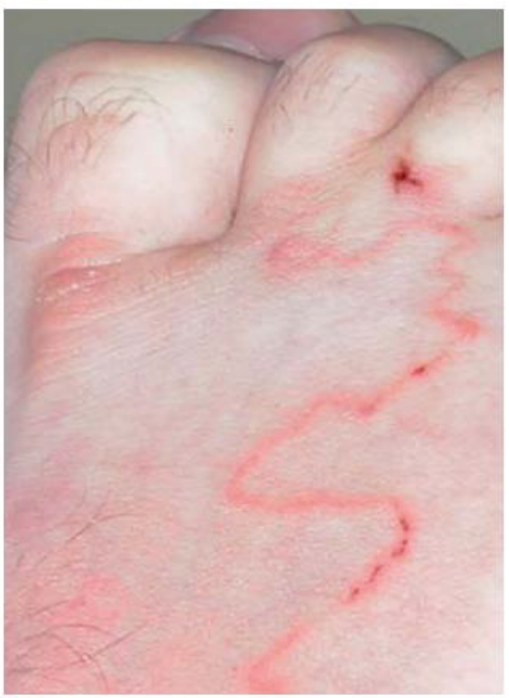


Fig. 11.52 Cutaneous larva migrans. *Courtesy of Dr Ravi Gowda, Roy Hallamshire Hospital, Sheffield.*

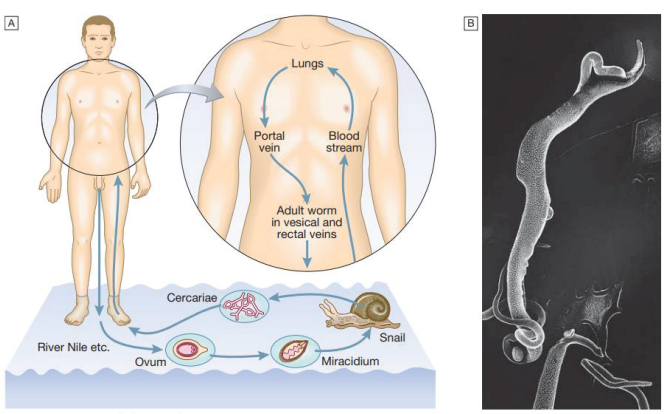
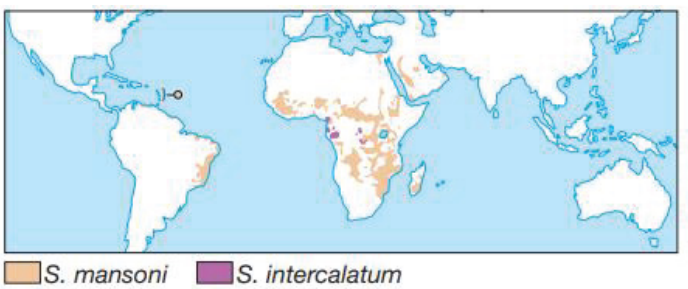


Fig. 11.53 ***Schistosoma.*** A Life cycle. B Scanning electron micrograph of adult schistosome worms, showing the larger male worm embracing the thinner female.

i 11.61 Pathogenesis of schistosomiasis

Time	*Schistosoma haematobium*	*S. mansoni* and *S. japonicum*
Cercarial penetration		
Days	Papular dermatitis at site of penetration	As for *S. haematobium*
Larval migration and maturation		
Weeks	Pneumonitis, myositis, hepatitis, fever, 'serum sickness', eosinophilia, seroconversion	As for *S. haematobium*
Early egg deposition		
Months	Cystitis, haematuria	Colitis, granulomatous hepatitis, acute portal hypertension
	Ectopic granulomatous lesions: skin, CNS etc.	As for *S. haematobium*
	Immune complex glomerulonephritis	
Late egg deposition		
Years	Fibrosis and calcification of ureters, bladder: bacterial infection, calculi, hydronephrosis, carcinoma	Colonic polyposis and strictures, periportal fibrosis, portal hypertension
	Pulmonary granulomas and pulmonary hypertension	As for *S. haematobium*



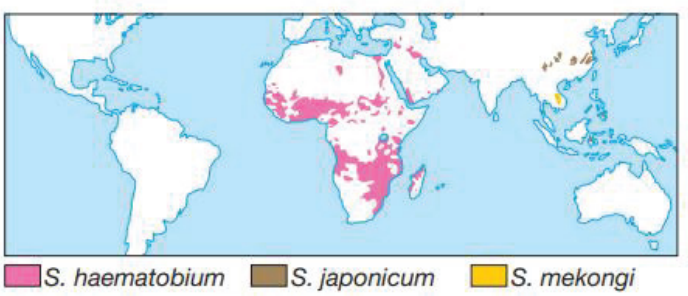


Fig. 11.54 Geographical distribution of schistosomiasis. *From Cook GC, ed. Manson's tropical diseases, 20th edn. Saunders, Elsevier Inc.; 1995.*

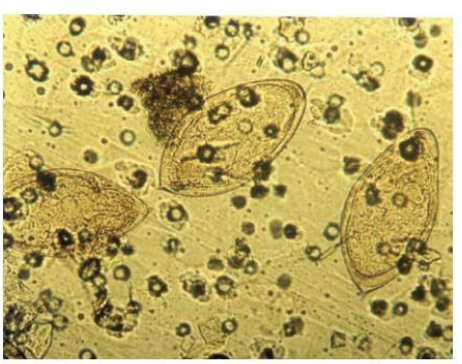


Fig. 11.55 Ova of *Schistosoma haematobium* in urine. Note the terminal spike.

i 11.62 Diseases caused by flukes in the bile duct

	Clonorchiasis	Opisthorchiasis	Fascioliasis
Parasite	*Clonorchis sinensis*	*Opisthorchis felineus*	*Fasciola hepatica*
Other mammalian hosts	Dogs, cats, pigs	Dogs, cats, foxes, pigs	Sheep, cattle
Mode of spread	Ova in faeces, water	As for *C. sinensis*	Ova in faeces on to wet pasture
1st intermediate host	Snails	Snails	Snails
2nd intermediate host	Freshwater fish	Freshwater fish	Encysts on vegetation
Geographical distribution	Far East, especially South China	Far East, especially North-east Thailand	Cosmopolitan, including UK
Pathology	*Escherichia coli* cholangitis, abscesses, biliary carcinoma	As for *C. sinensis*	Toxaemia, cholangitis, eosinophilia
Symptoms	Often symptom-free, recurrent jaundice	As for *C. sinensis*	Unexplained fever, tender liver, may be ectopic, e.g. subcutaneous fluke
Diagnosis	Ova in stool or duodenal aspirate	As for *C. sinensis*	As for *C. sinensis*, also serology
Prevention	Cook fish	Cook fish	Avoid contaminated watercress
Treatment	Praziquantel 25 mg/kg 3 times daily for 2 days	As for *C. sinensis* but for 1 day only	Triclabendazole 10 mg/kg single dose; repeat treatment may be required*

*In the UK, available from the Hospital for Tropical Diseases, London.

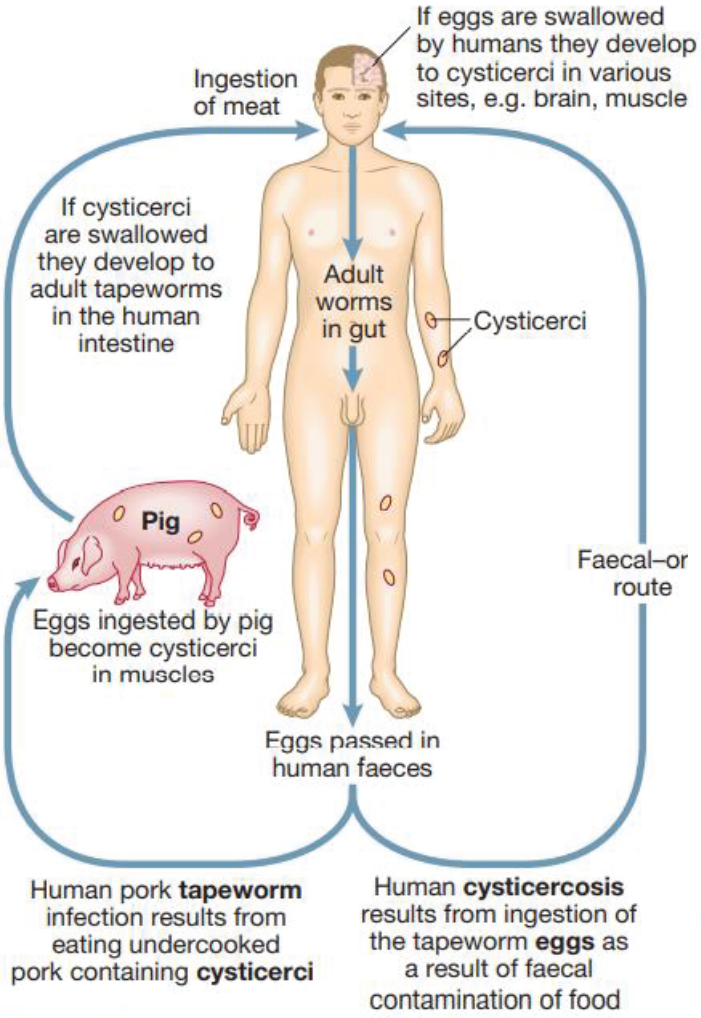


Fig. 11.56 Cysticercosis. Life cycle of *Taenia solium*.

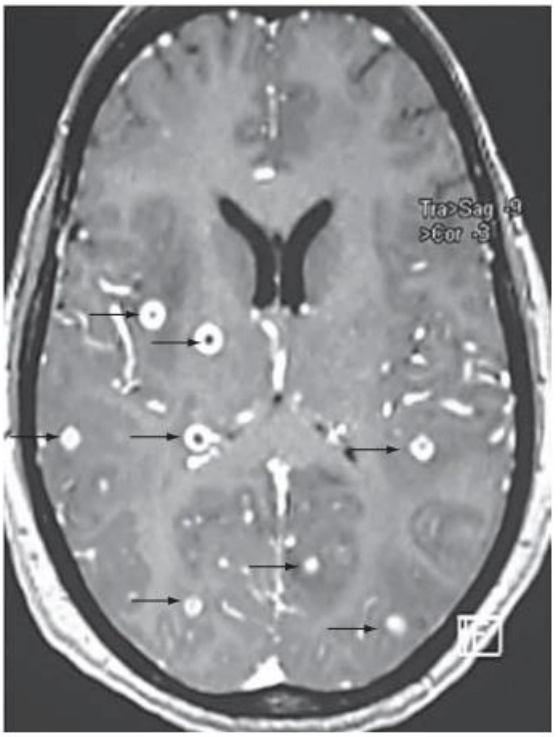


Fig. 11.57 Neurocysticercosis. T2-weighted axial image of the brain showing multiple lesions of neurocysticercosis (large arrows show the largest lesions).

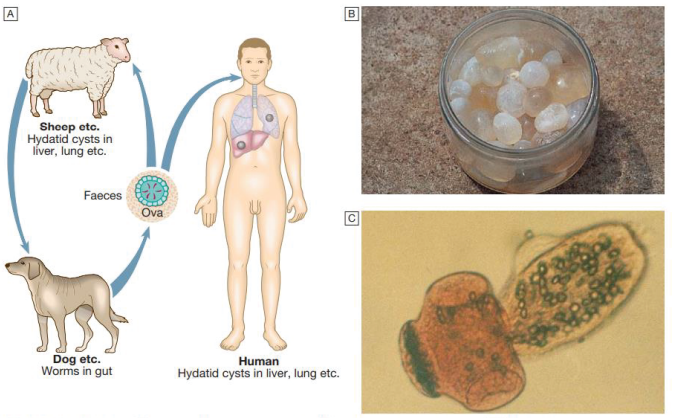


Fig. 11.58 Hydatid disease. A Life cycle of *Echinococcus granulosus*. B Daughter cysts removed at surgery. C Within the daughter cysts are the protoscolices.

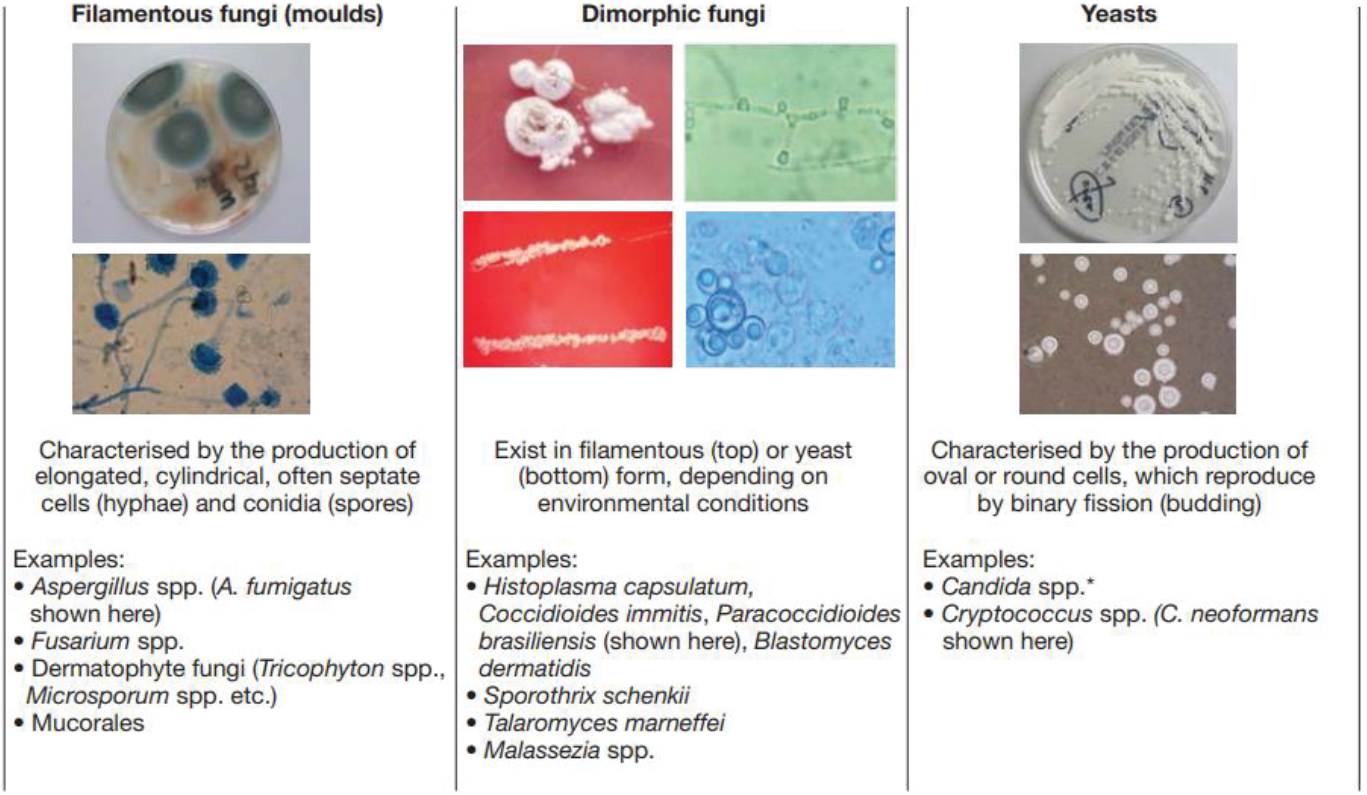


Fig. 11.59 Classification of medically important fungi. Fungal classification is based on simple morphological characteristics. *Pneumocystis jirovecii* is morphologically distinct from other fungi and does not fit into this classification. *Although *Candida albicans* exists in a number of forms, including filamentous (hyphae and pseudohyphae), it is generally encountered in its yeast form so is classified in this category. *Insets (dimorphic fungi) Courtesy of Beatriz Gomez and Angela Restrepo, CIB, Medellín, Colombia.*

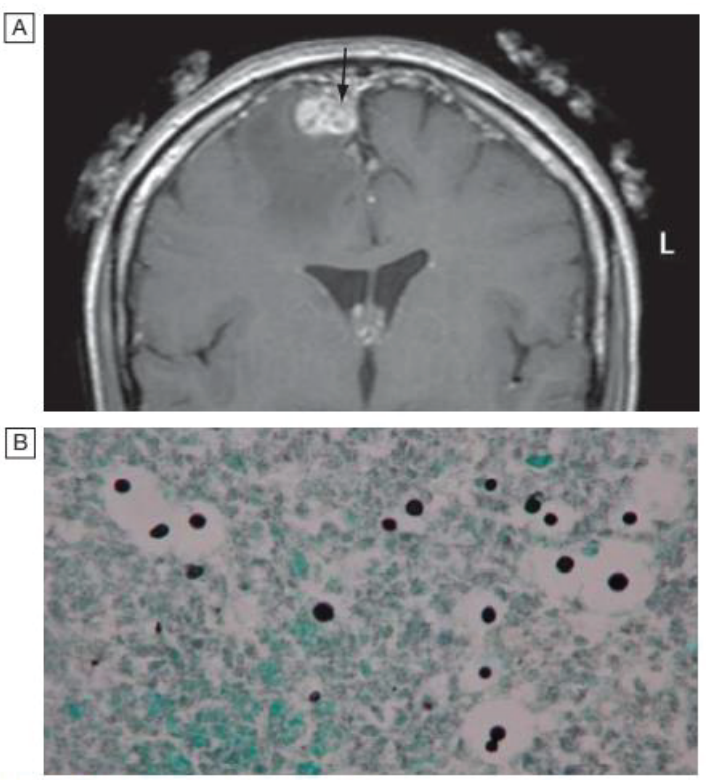


Fig. 11.60 Cryptococcal disease. A 23-year-old HIV-positive male developed headache and left-sided weakness. A MRI scan of the brain showed a space-occupying lesion (arrow) with surrounding oedema. B Histopathological examination of the lesion stained with Grocott's silver stain showed encapsulated yeasts. *Cryptococcus neoformans* was cultured.

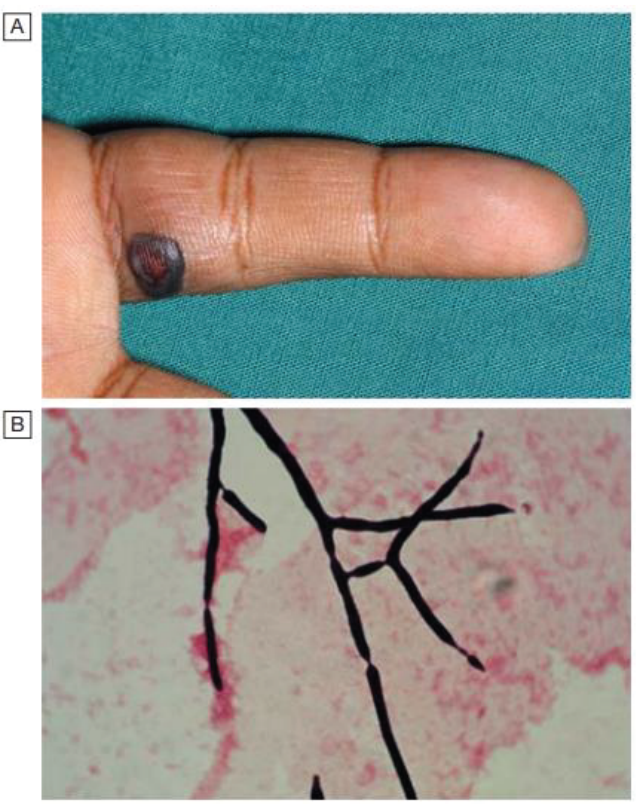


Fig. 11.61 *Fusarium* infection. A patient presented with fever and skin nodules after developing neutropenia secondary to haematopoietic stem cell transplantation and chemotherapy for relapsed leukaemia. *Fusarium solani* was cultured from skin lesions and blood cultures. A Tender, erythematous papules/nodules on upper arm. B Gram stain of *Fusarium* in blood culture medium.

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