

Chapter 14

Multi-System, Generalised and Disseminated Infections

ADENOVIRUS INFECTIONS: acute respiratory disease (bronchitis, croup, febrile catarrh, rhinitis, sinusitis, laryngotracheitis, tracheobronchitis, pertussis-like syndrome in children < 36 mo, 'influenza-like illness', pharyngitis/sore throat, acute exudative tonsillitis, acute laryngitis, pneumonia, pneumonitis, otitis media, pharyngoconjunctival fever), acute diarrhoea and/or vomiting, intussusception in children, pancreatitis, acute hemorrhagic cystitis in immunosuppressed, non-pyogenic meningitis and meningoencephalitis, maculopapular rash, roseola-like illness, rhabdomyolysis, carditis, myocarditis and pericarditis, mesenteric lymphadenitis, hepatitis, arthritis, follicular conjunctivitis, keratoconjunctivitis, acute hemorrhagic conjunctivitis; disseminated with hepatic necrosis in AIDS, severe combined immunodeficiency, other immunodeficiency; important pathogen in adult bone marrow transplant patients (respiratory infection, urinary tract infection, disseminated disease with hepatitis or conjunctivitis); transmission by droplets, contact; incubation period 2-10 d

Diagnosis: complement fixation test, hemagglutination inhibition antibody technique, neutralisation antibody titre; mild increase in white cell count in 60% of cases; virus isolation in tissue culture from throat and/or conjunctival swabs or pharyngeal washing, feces, CSF (lung tissue post mortem)

Treatment: i.v. ribavirin

Prophylaxis: live, attenuated oral vaccine (experimental)

CYTOMEGALIC INCLUSION DISEASE: worldwide; occurs in noncompromised older children and adults as mononucleosis syndrome (fever, malaise, sore throat, headache, increased levels on liver function tests, atypical lymphocytosis, antibiotic rash common; exudative pharyngitis, splenomegaly, cervical lymphadenopathy, nonspecific rash, anemia less common; icteric hepatitis rare; antinuclear antibodies, rheumatoid factor, cold agglutinins) and in immunocompromised patients (AIDS and after suppressive therapy preceding organ transplantation and after treatment with chemotherapy, steroids or other immunosuppressive agents in other conditions) and as bloodborne disease; encephalitis, myelitis, peripheral neuropathy, polyradiculopathy, chorioretinitis, Guillain-Barré syndrome, intestinal ulceration, pancreatitis, myocarditis, pneumonia, thrombocytopenia purpura, gastrointestinal bleed (particularly in bone marrow transplant recipients 1-3 mo post transplantation); transmission respiratory, blood transfusions (especially cardiac surgery and neonates who require several units of blood); incubation period 1-3 mo

Agent: *human cytomegalovirus*

Diagnosis: fever, leucopenia, hepatomegaly, splenomegaly, arthralgia; 'glandular fever type atypical mononuclears' in peripheral blood smear; culture of 5 mL of first morning's sample of urine (most dependable source), heparinised blood during acute phase, throat swabs (may be successful weeks or months after acute illness has subsided) using human diploid cell culture; serology by complement fixation test, IgM indirect fluorescent antibody titre test, ELISA (IgG, IgM and IgM capture)

Nonimmunocompromised: IgG seroconversion, presence of IgM antibody specific for *human cytomegalovirus*, urine culture (may reflect remote infection), blood culture

Immunocompromised: demonstration of viral antigen or DNA/RNA in diseased tissue (lung, esophagus, colon), IgG seroconversion (rarely occurs)

Kidney and Liver Transplant Recipients: viral culture by shell vial procedure

Treatment: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria $\leq 2+$ and creatinine clearance ≥ 55 mL/min) then as above every 2 w

Prophylaxis

Hematopoietic Stem Cell Transplantation: use of blood products from seronegative donors; ganciclovir 5 mg/kg i.v. every 12 h for 5-7 d, then 5-6 mg/kg i.v. daily for 5 d/w from engraftment until day 100

Human cytomegalovirus Seropositive HIV Patient with CD4 Cell Count < 50/ μ L: valganciclovir 900 mg orally daily

REOVIRUS INFECTIONS: epidemic viral diarrhoea, non-pyogenic meningitis, acute respiratory illness (pharyngitis, rhinitis), neonatal hepatitis, maculopapular rash

Diagnosis: tissue culture and inoculation of suckling mouse with material from feces and throat swab

Treatment: non-specific

HUMAN HERPESVIRUS 3 INFECTIONS: varicella (chickenpox; vesicular rash; case-fatality rate 9/100,000, with 80% in adults), zoster (shingles), abortion, encephalitis, Guillain-Barré syndrome, non-pyogenic meningitis, pneumonia (including diffuse interstitial) with exanthem, pneumonitis, retinochoroiditis, anterior uveitis, nonpurulent conjunctivitis, iridocyclitis, iritis, keratoconjunctivitis, arthritis, hepatitis (adult, perinatal and prenatal), mouth lesions, myocarditis and pericarditis, oophoritis, prenatal generalised disease, 1/3 of ischemic strokes in children, Ramsay Hunt syndrome (reactivation of latent virus in geniculate ganglion in immunocompromised patients, causing vesicles over pinna and external auditory meatus, facial nerve palsy, tinnitus, vertigo and deafness); uncommonly, gastrointestinal visceral motor manifestations; transmission by respiratory droplets, crusts from lesions; chickenpox 0.4% of new episodes of illness in UK, herpes zoster 0.4%; herpes zoster affects 10-20% of general population throughout lifetime; chickenpox latent period 8-12 d, incubation period 13-17 d, infectious period 10-11 d, interepidemic period 2-4 y

Diagnosis: Tzanck smear; complement fixation test, ELISA, fluorescent antibody staining, radioimmunoassay; tissue culture of scrapings from skin lesions, vesicle fluid, sputum (lung, liver, spleen post mortem)

Test for Susceptibility: fluorescent antibody to membrane antigen test

Treatment:

Varicella (Chicken Pox):

Immunocompromised, Normal Patient with Pneumonitis or Encephalitis: aciclovir 10 mg/kg i.v. every 8 h for 7-10 d

Immunocompetent Children (< 12 y):

Primary Cases: symptomatic treatment with acetaminophen and antipruritics

Secondary Cases: aciclovir 20 mg/kg orally 4 times a day for 5 d, starting within 24 h of rash onset

Adolescents and Young Adults: aciclovir 800 mg orally 4-5 times daily for 5-10 d, starting therapy within 24 h of rash onset

Pregnant Women: aciclovir 10 mg/kg i.v. every 8 h

AIDS: famciclovir 500 mg orally 8 hourly for 7-14 d, valaciclovir 1 g orally 8 hourly for 7-14 d, aciclovir 800 mg orally 5 times daily or 10 mg/kg i.v. 8 hourly for 1-2 w (adjust dose for renal function)

Zoster (Shingles; Ophthalmic Zoster, Immunocompromised Patient, Any Patient Seen Within 72 h of Onset of Vesicles): famciclovir 250 mg orally 8 hourly for 7 d (500 mg orally 8 hourly for 10 d in immunocompromised), valaciclovir 1 g orally 8 hourly for 7 d, aciclovir 20 mg/kg to 800 mg orally 5 times daily for 7 d (preferred in children and pregnancy)

Prophylaxis: varicella-zoster immune globulin; supplies limited; administration limited to patient with leukemia, lymphoma, congenital or acquired immunodeficiency, < 24 mo after hematopoietic stem cell transplant or on immunosuppressive therapy or with chronic graft-versus-host disease, with exposure to chickenpox or herpes zoster patient who was household contact, playmate contact of a fairly close nature or hospital contact in adjacent bed, with negative or unknown prior history of chickenpox (except patients who have bone marrow transplantation), and aged < 15 y or adult with good evidence of not having been infected previously, or neonate whose mother had onset of chickenpox within a period of 5 d before and 2 d after delivery; in either case, must be < 96 h after exposure; dose 1 vial/10 kg body weight up to maximum 5 vials; no evidence of beneficial effect against established infection or fetal infection (ie., exposure of women in early pregnancy); immunodeficient patients, especially children, with a negative or unknown history of chickenpox, should be tested for serum antibody to *simplexvirus 3*, thus avoiding unnecessary varicella-zoster immunoglobulin in the future; isolation of cases; live attenuated varicella vaccine gives protection rate of 44-100% and should be given to all susceptible health care workers, household contacts and family members ≥ 12 mo and not pregnant or immunocompromised

SIMPLEXVIRUS INFECTIONS: non-purulent conjunctivitis, iritis, keratoconjunctivitis, anterior uveitis, retinochoroiditis, encephalitis, non-pyogenic meningitis, meningoencephalitis, hepatitis (adult, neonatal and prenatal), localised skin lesions, papulovesicular rash (neonatal), acute herpetic gingivostomatitis, esophagitis, genital herpes, balanitis, nonpurulent cervicitis, urethritis, proctitis, vaginitis, dysuria without frequency, urinary infection, perinatal and prenatal genital disease, arthritis, rhabdomyolysis, acute exudative tonsillitis, pneumonia (neonatal and diffuse interstitial in T cell deficiency) with exanthem, disseminated infection associated with atopic eczema in children

Diagnosis: culture by MRC-5 shell vial centrifugation enhancement and direct immunoperoxidase staining of material from vesicle fluid, throat swab, CSF, corneal scraping, brain post mortem; electron microscopy; indirect fluorescent antibody test for IgM; ELISA (types 1 and 2); complement fixation test, neutralisation antibody titre

Treatment: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famciclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Prophylaxis (Bone Marrow Transplantation): aciclovir 200 mg 6 hourly from 8 d before to 35 d after bone marrow transplantation

RUBELLA (GERMAN MEASLES): 376 notified cases in Australia in 1999 (steady decrease from 4590 cases in 1995), 271 in USA (58,000 in 1969; 86% in adults in 1999); 0.1% of new episodes of illness in UK; epidemic, worldwide; attack rate 5%; respiratory transmission; incubation period 2-3 w, latent period 7-14 d, infectious period 11-12 d, interepidemic period 2-7 y; up to 90% of infants born to mothers infected during first 11 w of gestation develop congenital rubella syndrome but the risk falls rapidly from this point

Agent: *human rubella virus*

Diagnosis: 20-50% asymptomatic; incubation period 12-23 d; infectious period 7 d before to 5-7 d after rash onset; infants infected in utero can shed for 1 y or more; conjunctivitis ±, pharyngitis ±, rhinitis ±, exanthem (generalised maculopapular or erythematous rash) ±, postauricular, suboccipital and cervical lymphadenopathy, low grade fever (> 37.2°); arthralgia and polyarthritides in ≤ 70% of adults and adolescent females; thrombocytopenia feature in children; thrombocytopenic purpura, encephalitis, neuritis and orchitis; EIA capture for IgM (false positives with acute Epstein-Barr virus infection, recent *human cytomegalovirus* infection, *Parvovirus* infection), significant rise in serum rubella IgG, tissue culture of throat swab, nasal swab, urine, blood, cerebrospinal fluid (lung, kidney, bone marrow, spleen, brain, lymph node post mortem), reverse transcriptase PCR

Treatment: non-specific

Prophylaxis: highly effective live vaccine (95% efficacy), encephalitis 0.04/M doses, lifetime immunity, highly cost effective; contraindicated in ≤ 12 mo old, pregnant, patients with neomycin allergy and immunocompromised

MUMPS: acute viral disease of childhood; worldwide; endemic in urban areas; ≈ 180 notified cases/y in Australia (≈ 40% in Victoria); case-fatality rate 2/10,000; encephalitis (1:6000 cases; 0.5-2.3% death rate), non-pyogenic meningitis, meningoencephalitis, hydrocephalus, deafness (may be sudden, unilateral and permanent), demyelinating disorders, transverse myelitis, Guillain-Barré syndrome, cerebellar ataxia, pancreatitis, mastitis, myocarditis, oophoritis, orchitis, parotitis, salivary adenitis, neuroretinitis, arthritis; 70% salivary gland (60% parotid, 10% submandibular, 5% submaxillary), 10% CNS (5% symptomatic, 0.02% encephalitis), 1% gonadal in prepubertal, 25% epididymoorchitis and 5% oophoritis in postpubertal; respiratory transmission; incubation period 12-26 d, latent period 12-18 d, infectious period 4-8 d, interepidemic period 2-6 y

Agent: *mumps virus*

Diagnosis: complement fixation test, immunofluorescent antibody test for IgG and IgM, ELISA (IgM), hemadsorption, passive hemagglutination, hemagglutination inhibition antibody technique, neutralisation antibody titre (not routine); culture of blood, saliva, throat swab, secretions from Hansen's duct, CSF, urine (brain, salivary glands post mortem) in monkey or human kidney, chick embryo amnion

Treatment: none effective

Prophylaxis: highly effective (83%) live vaccine; all persons ≥ 12 mo not pregnant or immunocompromised

MONKEYPOX: tropical rainforests of West and Central Africa; sporadic zoonosis in man, occasionally fatal, especially in children; secondary attack rate < 4%

Agent: *monkeypox virus*

Diagnosis: electron microscopy

Treatment: non-specific

Prophylaxis: vaccination with smallpox vaccine for laboratory workers involved with virus

HEMORRHAGIC FEVERS

Agents: black measles, hemorrhagic smallpox, hepatitis A, hepatitis B, hepatitis C, chikungunya fever, Sindbis fever, yellow fever, dengue, Crimean-Congo fever, Omsk fever, Kyasanur Forest disease, West Nile fever, Rift Valley fever, Lassa fever, Argentinian hemorrhagic fever (*Junin arenavirus*), Bolivian hemorrhagic fever (*Machupo virus*), Venezuelan haemorrhagic fever (*guanarito virus*), hemorrhagic fever with renal syndrome, *Marburgvirus*, *Ebola-like viruses*, *Russian spring-summer encephalitis virus*, epidemic typhus fever, tick-bite fever, Rocky Mountain spotted fever, Q fever, *Neisseria meningitidis* septicemia, streptococcal septicemia, staphylococcal septicemia, septicemic plague, *Plasmodium falciparum* (haemoglobinuric falciparum malaria, blackwater fever, bilious haematuric fever, haematuric bilious fever, haematuric fever, haemoglobinuric bilious fever, haemoglobinuric fever, haemoglobinuric malaria, haemoglobinuric malarial fever, melanuric fever, malarial

haematuria, malarial haemoglobinuria, West African fever), *Typanosoma brucei rhodesiense*; specific agent not demonstrated in large series of cases

Diagnosis: incubation period < 21 d; fever, myalgia and malaise progressing to multiple organ involvement with evidence of vascular damage and hemorrhage; progressive renal failure, rising blood urea, proteinuria, fluid and electrolyte imbalance, sometimes thrombocytopenia (all viral hemorrhagic fevers); specific clinical presentation and epidemiological features may provide clues; repeated blood films for malaria parasites, trypanosomes and spirochaetes; PCR; ELISA for viral antigen; culture of blood, urine and throat swab; fluorescent antibody; serology

Arenaviral Haemorrhagic Fevers: S America, principally Argentina and Bolivia; acute febrile illness with petechiae on skin and palate (*Junin arenavirus*: vesicles on palate); isolation of virus from throat washings or from blood; also serology

Arthropod-Borne Viral Haemorrhagic Fevers: mainly tropical (not found in Australia); usually serology

Haemoglobinuric Falciparum Malaria: sudden onset of chills and irregular fever, nausea, hemoglobinuria, tender and enlarged liver, jaundice, palpable spleen, very dark urine, kidney failure, severe anemia; death in severe cases; due to combination of low level parasitemia, high antibody level and idiosyncratic, probably drug induced, intravascular hemolysis after exposure to amino-alcohol quinolones

Treatment: supportive +:

Argentinian Fever: postconvalescent plasma

Rickettsia: tetracycline, chloramphenicol

Neisseria meningitidis, Streptococci: penicillin

Plague: gentamicin 4-7.5 mg/kg/d i.v., doxycycline 4 mg/kg to 200 mg i.v. then 2 mg/kg to 100 mg i.v. twice daily (not < 8 y), ciprofloxacin 15 mg/kg to 400 mg i.v. twice daily, chloramphenicol 25 mg/kg i.v. 4 times a day

Malaria: sulphadoxine-pyrimethamine, artemisinin, atovaquone-proguanil

Typanosoma brucei rhodesiense: i.v. suramin 1 w, then i.v. melarsoprol

Prophylaxis:

Plague Postexposure: doxycycline 2 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Neisseria meningitidis: ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children)

MEASLES (MORBILLI): of worldwide occurrence but coming rapidly under control in temperate countries; virtually eliminated in USA; ≈ 230 notified cases/y in Australia (steady decrease from 4825 cases in 1994); incidence 256/100,000 in Africa; 0.3% of new episodes of illness in UK; global case-fatality rate 2% (67% pneumonia, 33% encephalitis); > 1.5 M deaths/y worldwide; cross-sex transmission gives increased mortality; latent period 6-9 d, incubation period 11-14 d, infectious period 6-7 d, interepidemic period 2-4 y

Agent: measles virus

Diagnosis: initially malaise, fever, conjunctival injection ++, photophobia, hacking cough without pharyngitis, rhinitis with nasal discharge; enanthem (Koplik's spots) has characteristic appearance of tiny white dots, like grains of salt, and are best seen on the cheek near the second upper molar; the exanthem (cutaneous rash) appears 2 d after the Koplik's spots, is initially macular, becomes maculopapular and multiform and may become confluent over face and trunk; complications include bronchopneumonia, otitis media, encephalitis (1 in 2000), subacute sclerosing panencephalitis, hepatitis; epidemiological; culture of throat swab or washings collected soon after rash appears (brain, lung post mortem); serology (capillary blood filter paper specimens suitable (sensitivity 100%, specificity 96%); hemagglutination inhibition (4-fold rise), complement fixation test (titre = 8 at 9 d after onset), staphylococcal protein A adsorption (specific IgM; sensitivity 71%, specificity 81%, predictive value of positive 94%; detected shortly after appearance of rash, peaks within 10 d, usually undetectable by 30 d), sucrose gradient ultracentrifugation, ELISA (IgG, IgM), fluorescent antibody staining (not routine; serum: IgG 96-97% correlation with complement fixation test or hemagglutination inhibition, IgM detected in only ≈ 30%; CSF), neutralisation antibody titre (not routine); confirmatory rather than ruling out); histology (giant multinuclear cells of Warthin-Finkedy type in submucous lymphoid tissue of appendix); neutrophilia with thrombocytopenia, pancytopenia; serum creatinine 6.8 mg/dL; white cell count 14,500 in atypical measles

Treatment: supportive; antimicrobial treatment of secondary infection

Prophylaxis: highly effective live vaccine (95-98% efficacy when given during second year of life; ≈ 100% if second dose at primary or secondary school entrance), encephalitis and encephalopathy 1/M doses, subacute sclerosing panencephalitis 0.5-1.1/M doses, lifetime immunity, highly cost effective, contraindicated in ≤ 12 mo old, pregnant,

immunocompromised, severe febrile illness (postponed), tuberculosis, caution (facilities for resuscitation) if history of marked reactions to hen's egg (generalised urticaria, swelling of mouth and throat, difficulty in breathing, hypotension, shock) or hypersensitivity to neomycin or polymyxin (vaccine is produced in chick embryo cell culture and contains trace amounts of neomycin and polymyxin), human globulin injections or other antibody-containing blood products within preceding 3 mo (deferred); passive immunity (patients with severe malnutrition in contact with measles patients): immunoglobulin 0.02 mL/kg i.m. within 5 d of contact

SMALLPOX: with measles, killed 90% of New World population 1518-1837; eliminated as natural infection by use of highly effective live vaccine; potential biowarfare agent; transmission respiratory, contact with lesions; incubation period 7-19 d (average 12 d); fatality rate variola major 5-40%, variola minor 0.1-2%

Agent: *variola major virus*, *variola minor virus*

Diagnosis: sudden onset of influenza-like symptoms (fever, malaise, headache, chills), prostration, severe back pain, anorexia and vomiting, less often abdominal pain, diarrhoea, delirium and convulsions; 2-3 d later, temperature falls and maculopapular rash appears centrifugally on face, neck and distal extremities including palms and soles and then, after a few days, on trunk and sometimes on more proximal extremities; ulcerating lesions also appear in mucous membranes of nose and mouth; skin lesions progress from macules to papules to vesicles to pustules, which, on the eighth or ninth day, form scabs which leave depressed, depigmented scabs on healing; rarely, rash accompanied by hemorrhage into mucous membranes and skin (hemorrhagic smallpox; invariably fatal) or lesions fail to form pustules but remain soft and flat (malignant smallpox; almost invariably fatal); complement fixation test, fluorescent antibody staining (not routine), hemagglutination antibody technique; tissue culture of scrapings from skin lesions, vesicle fluid, pus, blood, crust (liver, spleen, blood post mortem)

Treatment: cidofovir 5 mg/kg i.v. weekly for 2 w

Prophylaxis: vaccine up to 4 d (possibly 7 d) after exposure can prevent infection or ameliorate severity (+ vaccine immune globulin in pregnant women and patients with eczema); vaccine containing live *vaccinia virus* protects for at least 10 y; contraindicated for pregnant, persons with diseases or conditions or treatments which cause immunodeficiency or immunosuppression, with a history of eczema, atopic dermatitis or other acute, chronic or exfoliative skin conditions, with previous allergic reaction to smallpox vaccine or life-threatening allergy to polymyxin B sulphate, streptomycin sulphate, tetracycline hydrochloride or neomycin sulphate, with moderate or severe acute illness, < 12 mo old or > 18 y except in emergency, breastfeeding; complications include postvaccinal encephalitis, progressive vaccinia, eczema vaccinatum and generalised vaccinia; vaccinia immune globulin may be given with vaccine to reduce complications or as therapy for complications but is in short supply and should be reserved for most serious cases; cidofovir may be used when vaccinia immune globulin is not efficacious

YELLOW FEVER: transmitted by bite of infected mosquito; incubation period 3-6 d; sylvatic fever in tropical areas of S America (Bolivia, Brazil, Colombia, Ecuador, Peru), sylvatic and urban forms in Africa (endemic in Burkina Faso, Gambia, Ghana, Nigeria, Sudan, Zaire); 5000 cases/y worldwide; no notifications in Australia in past decade

Agent: *yellow fever virus*

Diagnosis: clinically inapparent infections common; overt attacks most common in aged; incubation period 3-6 d; acute onset and constitutional symptoms, followed by brief remission and recurrence of fever, hepatitis, albuminuria and symptoms and, in some instances, renal failure, shock and generalised hemorrhages; severe jaundice in 100%, abrupt onset of chills and fever in 96%, headache in 90%, myalgias in 75%, vomiting in 70%, palatal petechiae in 70%, black vomit in 20%, abdominal pain; raised bilirubin, proteinuria, neutropenia, anemia, thrombocytopenia, reduced levels of coagulation factors; geographic history; vaccination none or > 10 y; exposure to mosquitos; serology (specific IgM or fourfold or greater rise in titre by complement fixation test, hemagglutination inhibition antibody technique, neutralisation antibody titre); demonstration of virus, antigen or genome in tissue, blood or other body fluid; histology of liver (early ballooning and fatty infiltration of hepatocytes, followed by midzonal acidophil necrosis and 'Councilman' bodies within hepatocytes)

Treatment: tiazofurin 825 mg/m² for 10 d

Prophylaxis: immunisation administration limited to designated national centres and designated medical practitioners, contraindicated in children < 6 mo, pregnant women (may be reviewed), patients with altered immune status, patients allergic to eggs, should not be administered within 3 w of cholera vaccine

Prevention and Control: mosquito control

DENGUE: transmitted by *Aedes aegypti* mosquito bite; incubation period 3-15 d; all tropical environments, with concentration in Asia, Central and South America; ≈ 60 notified cases/y in Australia (≈ 50% in Queensland; all imported; 43% from Papua New Guinea; causes 8% of fever in returned travellers); global incidence dengue 50-100 M/y, dengue hemorrhagic fever 250,000-500,000/y (24,000 deaths/y); case-fatality rate 3-20%

Agent: *dengue virus* group

Diagnosis: severe myalgia in 100%, arthralgia in 90%, retroocular pain in 75%, nausea in 75%, maculopapular rash in 30%, headache; viral culture of serum or autopsy samples (sensitivity 30-80%), ELISA (IgM positive in 80% by fifth day) on tissue, serum or CSF, immunochromatographic card test (sensitivity 99% in primary cases, 94% in secondary, specificity 93%), reverse transcription-polymerase chain reaction, hybridisation assay (in evaluation), fourfold or greater increase in serum IgG by hemagglutination inhibition test or increase in specific IgM antibody; neutropenia and thrombocytopenia, anemia, hemoglobin 16.6 g/dL, platelet dysfunction, reduced levels of coagulation factors, disseminated intravascular coagulation, vascular injury

Dengue Hemorrhagic Fever

Grade I: fever, constitutional symptoms, positive tourniquet test (≥ 20 petechiae/cm²), hemoconcentration (rise in hematocrit of $\geq 20\%$), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$)

Grade II: Grade I + spontaneous bleeding (eg, skin, gums, gastrointestinal tract)

Grade III (Dengue Shock Syndrome): Grade II + circulatory failure, agitation, hypotension (systolic pressure < 80 mm Hg for those < 5 y or < 90 mm Hg for those ≥ 5 y) or narrowing of pulse pressure to < 20 mmHg

Grade IV (Dengue Shock Syndrome): profound shock (blood pressure = 0)

Differential Diagnosis: Chikungunya virus, Hantavirus, measles, rubella, enteroviruses, influenza, hepatitis A, meningococemia, scarlet fever, typhoid, leptospirosis, rickettsioses, malaria

Treatment: rapid volume replacement through intravenous electrolyte solutions, plasma or plasma expanders (lowers mortality from 10-20% to $\approx 3\%$)

Prevention and Control: vector control; live vaccine in development

CRIMEAN-CONGO HEMORRHAGIC FEVER (CENTRAL ASIAN HEMORRHAGIC FEVER): case-fatality rate 10-50%; Europe, Africa, Asia; source tick, nosocomial (person-to-person aerosol), during slaughter of domestic animals; incubation period 2-9 d

Agent: Nairovirus

Diagnosis: hemorrhage predominant; non-purulent conjunctivitis, hemoptysis, meningoencephalitis; disseminated intravascular coagulation in fatal cases; isolation of virus from blood; fourfold rise in antibody titre, presence and decline of IgM antibody; fibrin degradation products > 40 mg/L, platelet count $< 10,000/\mu\text{L}$, white cell count 4000-7000/ μL , reduced levels of coagulation factors, disseminated intravascular coagulation, vascular injury

Treatment: ribavirin

OMSK HEMORRHAGIC FEVER: former Soviet Union, Romania; tick source

Agent: *Omsk haemorrhagic fever virus*

Diagnosis: clinical; thrombocytopenia

Treatment: non-specific

KYASANUR FOREST DISEASE: India; tick source

Agent: *Kyasanur Forest disease virus*

Diagnosis: clinical; thrombocytopenia

Treatment: non-specific

RIFT VALLEY FEVER: usually complete recovery in 2 w but retinitis in 10%, hemorrhagic fever in 1% and encephalitis in 1%; case-fatality rate among severely ill $> 50\%$ (1% overall); Sub-Saharan Africa, Saudi Arabia, Yemen; sources several *Aedes* and *Culex* mosquitoes, slaughter of domestic animals (camels, cattle, goats, sheep)

Agent: Rift Valley fever virus

Diagnosis: anorexia, 'saddle back' fever, headache, myalgia, retroorbital pain, retinitis with characteristic cotton-wool exudates on macula in 10%, hemorrhage and jaundice (often with death from hepatic failure shock), meningoencephalitis (high death rate); thrombocytopenia, reduced levels of coagulation factors, severe liver dysfunction; serology; isolation by tissue culture or inoculation of suckling mice during acute febrile stage

Treatment: supportive; ribavirin

Prophylaxis: limiting contact with infected mosquitoes, livestock and freshly slaughtered meat

LISSA FEVER: widely distributed over W and Central Africa in Guinea, Liberia, Mali, Senegal, Sierra Leone; case-fatality rate 10%; rodent source, nosocomial transmission (person-to-person aerosol)

Agent: Lassa virus

Diagnosis: usually clinical (fever, pharyngitis, retrosternal pain, proteinuria; incubation period 6-21 d) and excluding malaria and diabetic coma, as laboratory tests dangerous; thrombocytopenia, platelet dysfunction, reduced levels of coagulation factors; isolation from blood, throat or urine; serology (fluorescent antibody staining of conjunctival scrapings)

Treatment: ribavirin 30 mg/kg i.v. loading dose, followed by 15 mg/kg i.v. 6 hourly for 4 d, then 8 mg/kg 8 hourly for 6 d

Prophylaxis: ribavirin 500 mg orally every 6 h for 7 d; experimental vaccine

ARGENTINIAN HEMORRHAGIC FEVER: Argentina; rodent source, nosocomial transmission

Agent: *Junin arenavirus*

Diagnosis: incubation period 7-16 d; thrombocytopenia, reduced levels of coagulation factors, vascular injury, disseminated intravascular coagulation in terminal shock; serology

Treatment: convalescent antisera; ribavirin

BOLIVIAN HAEMORRHAGIC FEVER: Bolivia; rodent source, nosocomial transmission

Agent: *Machupo virus*

Diagnosis: incubation period 7-16 d; thrombocytopenia; serology

Treatment: supportive

HEMORRHAGIC FEVER WITH RENAL SYNDROME (KOREAN HEMORRHAGIC FEVER): Europe, Asia, Americas, Africa; rodents, bats, birds reservoir; transmission via aerosol; person-person transmission reported; \approx 150,000 hospitalised cases/y worldwide; fatality rate 3-15%

Agent: *Hantavirus*

Diagnosis: incubation period 5-42 d; fever in 94-99%, thirst in 89%, chills in 77-92%, anorexia in 66-96%, nausea in 61-84%, pharyngeal or palatal injection in 55-70%, backache in 53-95%, insomnia in 51%, headache in 42-86%, myalgia in 38-78%, vomiting in 33-70%, epistaxis in 28%, hemorrhages in 26-72%, abdominal pain in 21-66%, constipation in 19-60%, conjunctival injection in 16-79%, dizziness and vertigo in 7-100%, petechiae in 1-99% (mainly in febrile phase); Hantavirus pulmonary infection rare but deadly infection with predominance in the Southwest of USA; creatinine increased in 96%, C-reactive protein increased in 96%, proteinuria in 94-96%, lactate dehydrogenase increased in 88%, fibrinogen increased in 85%, erythrocyte sedimentation rate increased in 84% (> 20 mm/h in 7-72%), hematuria in 73-86%, albumin decreased in 66%, polyuria in 63-97%, alanine aminotransferase increased in 60%, thrombocytopenia in 52-78%, ASAT increased in 52%, blood urea nitrogen > 20 or serum creatinine level > 2 mg/dL in 50-100%, leucocytosis in 41-92%, oliguria in 37-83%, hypotension in 22-80%, disseminated intravascular coagulation in 5%, platelet dysfunction, reduced levels of coagulation factors, prolonged prothrombin time, vascular injury; immunofluorescent antibody test, ELISA

Treatment: ribavirin 30 mg/kg i.v. then 15 mg/kg i.v. 6 hourly; fluids, vasopressors, dialysis, plasma and platelet transfusions

Prophylaxis: combined *Hantavirus/Puumala virus* vaccine

NEPHROPATHICA EPIDEMICA: mild form of hemorrhagic fever with renal syndrome occurring in Scandinavia

Agent: *Puumala virus*

Diagnosis: acute onset of symptoms in all cases, fever in 99-100%, thirst in 89%, headache in 85-90%, backache in 82-84%, nausea in 78-84%, vomiting in 70%, myalgia in 69%, abdominal pain in 67%, anorexia in 66-70%, chills in 60%, insomnia in 51%, petechiae in throat and soft palate in 36%, conjunctival injection in 18%, petechial rash in 12%, epistaxis in 10%; proteinuria in all cases, C-reactive protein raised in 96%, lactate dehydrogenase raised in 88%, bleeding time normal in 86%, erythrocyte sedimentation rate raised (> 20 mm/h) in 84-90%, thrombocytopenia in 80%, whole blood coagulation time normal in 77%, Rumpel-Leede tourniquet test normal in 77%, hematuria in 74%, blood urea nitrogen > 20 or serum creatinine level > 2 mg/dL in 70-96%, serum albumin decreased in 66%, alanine aminotransferase increased in 52%, prothrombin ratio normal in 50-60%, leucocytosis in 37%; serology; histology (hemorrhages in renal medullary interstitium in all cases, hemorrhages in renal cortex in 53%)

Treatment: as for **HEMORRHAGIC FEVER WITH RENAL SYNDROME**

MARBURG HEMORRHAGIC FEVER: Kenya and Republic of South Africa; source unknown, nosocomial transmission (person-to-person aerosol); high mortality

Agent: *Marburgvirus*

Diagnosis: incubation period 3-9 d; disseminated intravascular coagulation in fatal cases; virus specific immunofluorescence or electron microscopy of isolate (grows readily in Vero cells) from blood or serum or suspensions of heart, kidney, liver or spleen, histology and electron microscopy of autopsy specimens (liver and kidney tissue); complement fixation test less sensitive than indirect fluorescent antibody titre; IgM peaks 2-3 w after onset; IgG rises more slowly and may be found in low titres years later; leucopenia ($1400/\mu\text{L}$), relative lymphocytosis, atypical monocytes, thrombocytopenia, reduced levels of coagulation factors, disseminated intravascular coagulation; occult blood in stool, elevated serum transaminases, alkaline phosphatase, amylase and bilirubin

Treatment: supportive

EBOLA HEMORRHAGIC FEVER (AFRICAN HEMORRHAGIC FEVER): case-fatality rate 50-90%; Central and E Africa, Sudan; source unknown, nosocomial transmission (person-to-person aerosol); acute febrile systemic infection

Agent: *Ebola-like viruses*

Diagnosis: incubation period 2-21 d; fever, extreme asthenia, gastroenteritis with diarrhoea, nausea and vomiting, headache, arthralgias, back pain, myalgias; bilateral conjunctival injection, maculopapular rash and pharyngitis with severe odynophagia in patients prone to hemorrhagic manifestations; antibody ELISA (IgG and/or IgM), virus isolation, immunohistochemistry of skin biopsy, reverse transcriptase polymerase chain reaction; thrombocytopenia, reduced levels of coagulation factors

Treatment: supportive

ROSS RIVER FEVER (EPIDEMIC POLYARTHRITIS): endemic in Australia (\approx 4000 notified cases/y (\approx 52% in Queensland)), New Guinea, Solomon Islands; mosquito vector

Agent: Ross River virus

Diagnosis: polyarthralgia, rash, malaise, myalgia, fever; culture of serum; ELISA (IgG and IgM)

Treatment: non-specific

BARMAH FOREST VIRUS INFECTION: widespread in Eastern states of Australia (\approx 600 cases/y, \approx 50% in Queensland)

Agent: Barmah Forest virus

Diagnosis: rash in 80-90%, fever in 60-80%, arthritis or arthralgia in 50%, headache in 40-50%, respiratory symptoms in 20%, gastrointestinal symptoms in 15%; serology

Treatment: non-specific

PHLEBOTOMUS FEVER (SANDBLY FEVER)

Agent: *Phlebovirus*

Diagnosis: serology

Treatment: supportive

Prophylaxis: ribavirin

MUCOCUTANEOUS LYMPH NODE SYNDROME (KAWASAKI DISEASE, KAWASAKI SYNDROME): acute, febrile, exanthematous infectious disease (mucocutaneous, lymph node inflammation and systemic vascular disease); worldwide but unusual, affecting mainly children; attack rate 7/100,000 in children < 5 y, 0.4/100,000 in Caucasian, and 2.7/100,000 in Oriental, children

< 8 y; case-fatality rate 1-2% (cardiac involvement); several cases found in Australia; vector ? house mites and cat fleas

Agent: ? *Ehrlichia*, ? retrovirus

Diagnosis: rash (macular, papular, polymorphous, scarlatiniform, urticarial, vesicular, erythema multiforme) in 100% of cases (erythema multiforme rash without vesicles or crusts in 90%), \geq 5 d of fever in 95%, desquamation of fingertips in 85-95%, bilateral conjunctival injection in 81-90%, dryness of lips in 80%, non-suppurative lymphadenopathy in 75-85%, indurative edema of hands or feet in 75%, desquamation of palms and soles in 73%, red oropharynx in 73%, carditis in 70%, periungual desquamation in 69%, other desquamation in 58%, redness and fissuring of lips in 66-90%, coronary artery abnormalities in 23% (cardiac arteries may be affected by widespread endarteritis, resulting in aneurism formation, thrombosis or rupture, causing death in third or fourth week; even those apparently not affected may develop highly premature coronary artery disease in later life), diarrhoea, arthralgias/arthritis, aseptic meningitis, mild jaundice, transient nail furrow 1-2 mo post-onset; electrocardiogram (transient changes associated with diffuse ischemia or myocarditis in 11% of cases, myocardial infarction in 4-8%, increased PR interval, increased ST interval, decreased R waves, flat T waves); raised erythrocyte sedimentation rate, platelet count increased days 10-25; white cell count increased in 68% (shift to left), proteinuria and increased urinary leucocytes in 46%, slight anemia in 44%, slight elevation in serum transaminases in 19%

Differential Diagnosis: infectious mononucleosis, leptospirosis, scarlet fever, serum sickness, systemic lupus erythematosus, rubella, measles, Rocky Mountain spotted fever, scalded skin syndrome, juvenile rheumatoid arthritis, staphylococcal toxic shock

Treatment: aspirin 60-100 mg/kg daily in divided doses, then 10-30 mg/kg daily for 6-8 w (reduces incidence of aneurisms) + γ -globulin 400 mg/kg/d i.v.; PGE₁ or sympathetic block + thrombolytic and anticoagulant therapies in peripheral ischemia

REYE SYNDROME: case-fatality rate 23-30%; age of onset 4 d-29 y (usually 6 mo-15 y; 95% age < 14 y), 94% Caucasian, 55% antecedent respiratory illness, 25% varicella, 10% diarrhoea; permanent neurological or psychiatric disorders in 34-61% of survivors

Agents: interaction of aspirin and other salicylates with *influenza A virus*, *influenza B virus*, *simplexvirus 3* (5-30%) and other viruses

Diagnosis: history of viral infection; encephalopathy, varying from drowsiness to deep coma (also combativeness, confusion), associated with vomiting and hepatic enlargement; no evidence of drug intoxication; no jaundice (slightly elevated or normal serum bilirubin), but ≥ 3 fold rise in serum transaminases and serum ammonia levels, and there may be hypoglycemia (only in children < 5 y) and disturbances of acid-base balance and of blood clotting (prolonged prothrombin time); CSF < 8 leucocytes/ μL ; cerebral edema without perivascular or meningeal irritation; histologically (biopsy or autopsy), liver shows microvesicular fatty metamorphosis, with fine droplets of fat scattered through cytoplasm of hepatocytes; electron microscopy shows specific mitochondrial damage which is self-limiting

Treatment: supportive

MULTISYSTEM *STREPTOCOCCUS PYOGENES* DISEASE: in children; preexisting varicella in 47%; also associated with use of nonsteroidal antiinflammatory drugs

Agent: *Streptococcus pyogenes*

Diagnosis: confusion in 62% of cases, abdominal pain in 62%, headache/irritability in 50%, vomiting in 50%, anorexia in 50%, local extremity swelling/pain in 50%, hyperesthesia in 50%; hypoalbuminemia in 100%, renal sediment abnormalities in 100%, elevated immature polymorphonuclears in 87%, hyponatremia in 87%, lymphopenia in 75%, elevated AST in 67%, thrombocytopenia in 62%, prothrombin time > 14 s in 60%, fibrin split products or fibrinogen < 500 in 60%, elevated creatinine in 50%, direct hyperbilirubinemia in 50%; blood cultures

Treatment: benzylpenicillin 150,000-200,000 U/kg i.v. daily in divided doses

LISTERIOSIS (LISTERELLOSIS, LISTEROSIS): ≈ 50 notified cases/y in Australia; ≈ 30 cases/y in USA (50% nosocomial), 56% of isolates from blood, 16% blood and CSF; bacteremia without known focus (43% of infections), cutaneous listeriosis, disseminated (typhoidal) listeriosis, food poisoning (from unpasteurised or inadequately pasteurised milk, fresh soft cheeses, ready to eat deli meats and hot dogs), genital tract listeriosis, listerial endocarditis (endocardial listeriosis), listerial meningoencephalitis (meningitis/meningoencephalitis 43% of infections; associated with malignancy; also, neonatal and postneonatal pyogenic meningitis), listerial septicemia, lymph gland infections, neonatal disseminated listeriosis, oculoglandular listeriosis, prenatal generalised disease; case-fatality rate from 0% in previously healthy patients to 80% in disseminated infection; fatal neonatal listeriosis 0.1-0.3% of births, 1-7% of perinatal deaths; risk factors pregnancy, neonatal status, hematological, gastrointestinal or pulmonary malignancy, organ transplantation, oncologic chemotherapy, steroid therapy, systemic lupus erythematosus, alcoholism, renal failure, hepatic failure, portal hypertension and ascites, increased age, splenectomy, *human immunodeficiency virus* infection

Agent: *Listeria monocytogenes*

Diagnosis: incubation period 9-48 h for gastrointestinal symptoms, 2-6 w for invasive disease; fever, muscle aches and nausea or diarrhoea; pregnant women may have mild flu-like illness (fever in 82%, chills in 82%, headache in 82%, abdominal cramps in 45%, stiff neck in 45%, vomiting in 27%, photophobia in 18%) and infection can lead to premature delivery or stillbirth

Disseminated: granulomatous lesions and focal necroses; elderly or immunocompromised may have bacteremia or meningitis

for other forms, see appropriate sections

culture of appropriate specimen on blood agar; cold enrichment at 4°C may be useful in some circumstances; blood or CSF cultures; antibody to listerolysin O may be helpful to identify outbreak retrospectively

Treatment: supportive care + i.v. ampicillin, penicillin or cotrimoxazole

ACTINOMYCOSIS: cervicofacial (lumpy jaw; most common form; usually arising as result of infection following extraction of tooth or injury to jaw), pulmonary (arises from inhalation or aspiration of infective material (eg., from cervicofacial lesions), by extension of abdominal disease or, more rarely, by metastasis of disseminated disease), abdominal (gastrointestinal actinomycosis; most common in ileorectal region but sometimes in anorectal or gastric areas; arises from intestinal flora and intestinal perforation), septicemia (usually from pulmonary), brain, bone, liver, kidney, genital (uterus, associated with intrauterine devices), disseminated; ≈ 6 cases/y in USA; endogenous (oral)

Agents: *Actinomyces israelii*, *Actinomyces naeslundii*, *Actinomyces odontolyticus*, *Actinomyces meyeri*, *Actinomyces bovis*, *Propionibacterium propionicum*, *Bifidobacterium*

Diagnosis: visualisation of macroscopic sulphur-coloured colonies in pus; Gram stain, direct immunofluorescent stain and anaerobic culture of pus, curettings, biopsy from wall of abscess; neutrophilia and raised erythrocyte sedimentation rate usual

Cervicofacial: painful swelling on jaw that enlarges and eventually forms sinuses that open onto cheek or submandibular region

Abdominal: abdominal discomfort, fever, palpable mass, production of external sinus

Pulmonary: severe pneumonia, lung abscess or empyema, with characteristic production of small, multiple abscesses and sinuses in chest wall; on occasion, actinomycotic pneumonia may simulate a pulmonary neoplasm or tuberculosis

Treatment: penicillin (mild disease: phenoxymethylpenicillin 500 mg 6 hourly (< 12 y: 25-50 mg/kg daily orally in 4 divided doses); severe disease: benzylpenicillin 10M units (children: 100 000-250 000 U/kg) daily i.v. in 4 divided doses for 6 w, then phenoxymethylpenicillin as above), tetracycline 500 mg 6 hourly orally for 6 weeks, erythromycin 500 mg 4 times daily (children: 30 mg/kg daily in 4 divided doses) orally for 6 w

Prophylaxis: good dental hygiene

ANTHRAX (CONTAGIOUS ANTHRAX, FELLMONGER'S DISEASE, TANNER'S DISEASE): an acute disease of herbivorous animals readily transmitted to man; worldwide; rare in Australia

Agent: *Bacillus anthracis*

Diagnosis: Gram positive bacilli seen on microscopy; confirmed by culture; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Treatment: see **CUTANEOUS ANTHRAX, PULMONARY ANTHRAX, GASTROINTESTINAL ANTHRAX, MENINGITIS, BACTEREMIA**

Prophylaxis: vaccine 93% effective against cutaneous form, effectiveness against other forms not known

Prevention and Control: sterilisation of infected tissue, hides, etc

NOCARDIOSIS: worldwide; 70 cases (\approx 20 deaths)/y in USA; associated with Hodgkin's disease, connective tissue disorders, diseases treated by organ transplantation and corticosteroid administration; 75% lungs (33% only; may simulate pulmonary tuberculosis; subacute chronic pneumonia, occasionally with extension to pleura, resulting in empyema (pulmonary mycetoma) and dissemination), 23% brain, meninges and spinal cord; skin and subcutaneous tissue lesions \pm osteomyelitis, kidneys, adrenals, eye, liver, lymph nodes, pericardium, myocardium (disseminated disease); lymphocutaneous (may present similarly to sporotrichosis, most commonly *Nocardia brasiliensis*); actinomycetoma (usually lower extremity secondary to trauma); septic arthritis; disseminated; epididymoorchitis (extremely rare)

Agents: *Nocardia asteroides*, *Nocardia brasiliensis*, *Nocardia brevicatena*, *Nocardia otitidiscaviarum*, *Nocardia farcinica*, *Nocardia nova*

Diagnosis: Gram (Brown-Breen or Hueker modification) and Ziehl-Neelsen (Kinyoun or Putt modification) stains and culture of sputum, thoracentesis specimen, transtracheal aspirate, bronchial brushings, lung biopsy, pus from abscess or draining sinus, biopsy from other affected sites; serology (immunodiffusion)

Treatment: cotrimoxazole 320/1600 mg orally 12 hourly (child: 6/30 mg/kg daily in 2 divided doses) for 6-12 mo; sulphadiazine 100 mg/kg orally daily in 4 divided doses (child: 75 mg/kg initially, then 160 mg/kg daily in 4-6 divided doses to 6 g daily) + sodium bicarbonate 50 mg/kg orally daily in 4 divided doses for 4-6 w, then sulphisoxazole 60 mg/kg 6 g orally daily in divided doses for 12-18 mo; minocycline 300 mg orally 12 hourly; ciprofloxacin, cefotaxime, amikacin, imipenem, linezolid; surgical excision or drainage of abscesses, empyema and other necrotic tissue

TUBERCULOSIS: progressive or chronic disease; usually begins in lung but may affect any other organ or system, eg., lymphatic, osseous, urogenital, nervous and gastrointestinal systems and skin; conditions caused include tuberculous laryngitis (laryngeal tuberculosis), lymphadenitis (tuberculosis of intrathoracic lymph nodes, tuberculous peripheral lymphangitis), meningitis, leptomeningitis, meningoencephalitis, brain abscess, myelitis, ascites, peritonitis (peritoneal tuberculosis, tuberculosis of the peritoneum), arthritis, osteitis, osteomyelitis, synovitis, tenosynovitis, kyphosis (Pott curvature), spondylitis, dactylitis, mastoiditis, pyelitis, pyelonephritis, epididymitis, oophoritis, salpingitis, erythema nodosum, adenitis, episcleritis, interstitial keratitis, keratoconjunctivitis, otitis media, Addison disease, mediastinal tuberculosis (tuberculosis of the mediastinum), nasal tuberculosis, nasopharyngeal tuberculosis (tuberculosis of the nasopharynx), pharyngeal tuberculosis, cerebral tuberculosis (tuberculosis of the brain), intestinal tuberculosis (tuberculosis of the intestine, tuberculous enteritis), rectal tuberculosis, anorectal tuberculosis, anal tuberculosis, spinal tuberculosis (David disease, Pott caries, tuberculosis of the vertebral column, tuberculous spondylitis), tuberculosis of the hilar and other lymph nodes, sinuses, ear, mouth, esophagus, liver, genitourinary system, kidney, bladder, ureter, prostate, seminal vesicle, testis, endometrium (tuberculous endometritis), skin and subcutaneous tissues, thyroid gland, adrenal glands, spleen, endocardium, myocardium, pericardium, hip and knee, meningeal tuberculoma; miliary tuberculosis is a disseminated tuberculosis that spreads via lymphatic vessels and bloodstream from any active tuberculous lesion; massive hematogenous spread of bacilli results in tubercles scattered throughout pulmonary tissue and other body tissues (rarely, skin tissue); occurs mainly in elderly and immunocompromised; old foci may be reactivated by alcoholism, anthracosis, corticosteroid therapy, cytotoxic therapy, diabetes mellitus, gastric resection, malignancy, malnutrition, old age, pulmonary infections, radiation, sarcoidosis, severe viral infections, silicosis, thoracic surgery, thoracic trauma; abscesses in liver, abdominal wall, psoas muscle,

mediastinum and peripancreatic area common in AIDS (12% of cases of tuberculosis); leading cause of death due to infectious organism worldwide (2 M deaths/y, with 8-10 M new active cases (20% in India); 1.9 billion infected worldwide; ≈ 1000 notified cases/y in Australia (≈ 26% in Victoria; most new cases in migrants from Indochina and South East Asia); 69% pulmonary, 9% lymphatic, 5% pleural, 3% multiple, 2% bone/joint, 1% meningeal, 6% other; ≈ 20,000 cases/y in USA; transmission from elephants to humans recently reported

Agents: *Mycobacterium tuberculosis* (usually acquired by inhalation), *Mycobacterium bovis* (usually acquired by ingestion; 30-40% respiratory; also genitourinary, lymphatic, skeletal and disseminated), *Mycobacterium africanum*

Diagnosis: persistent productive cough, hemoptysis, unexplained fever and night sweats, unexplained weight loss; auramine-rhodamine, Kinyoun or Ziehl-Neelsen stain and Bactec 12B (97% *M.tuberculosis* (mean 14 d) and 94% nontuberculous mycobacteria (mean 13 d) positive; 3% contamination rate), Mycobacterial Growth Indicator Tube (92% *M.tuberculosis* (mean 19 d) and 94% nontuberculous mycobacteria (mean 14 d) positive; 4% contamination) or Septicheck AFB biphasic system or routine culture (Middlebrook 7H9, 7H10, 7H11 or selective 7H11 or Lowenstein-Jensen; 95% *M.tuberculosis* (mean 29 d) and 77% nontuberculous mycobacteria (25 d) positive; 4% contamination) of appropriate specimen; tuberculin test (PPD; zone of induration read at 72 h; ≥ 5 mm positive in patients with HIV, close contacts of active TB cases, patients with chest X-ray findings of inactive tuberculosis or fibrosis, patients with organ transplants or other immunosuppression; ≥ 10 mm positive in patients with medical risk factors for TB (silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, carcinoma of head, neck or lung, weight loss of ≥ 10% of ideal body weight, gastrectomy, jejunioleal bypass), injection drug users, immigrants within last 5 y from high prevalence countries, residents and employees of prisons, nursing homes and other long term facilities for elderly, hospitals and other health care facilities, residential facilities for patients with AIDS and homeless shelters, mycobacteriology laboratory personnel, children ≤ 4 y or infants, children and adolescents exposed to adults at high risk; ≥ 15 mm positive in persons with no risk factors for TB; 'true' negative if patient never infected with *Mycobacterium tuberculosis* or if isoniazid prophylaxis begun within 3 mo of skin test conversion; can be 'false' negative (10-25% of active tuberculosis) in small children, early in infection, in acute miliary tuberculosis, tuberculous pleurisy and tuberculous meningitis, if the patient also has *human immunodeficiency virus* infection, measles, mumps, chickenpox, scarlet fever, influenza, typhoid fever, brucellosis, typhus, leprosy, pertussis, South American blastomycosis, chronic lymphocytic leukemia, lymphoma, Hodgkin's disease, sarcoidosis, amyloidosis, uremia, chronic renal failure, severe protein depletion or has received live virus vaccine (measles, mumps, polio) or is on immunosuppressive therapy, in late pregnancy and puerperium, old age and occasionally middle age, if patient has been receiving UV light therapy or sunbathing, in stress states such as surgery, burns, mental illness, graft versus host reactions, and in individuals of low sensitivity or if infected with atypical mycobacteria, also if incorrect dilution of tuberculin, incorrect diluent, improper storage (inactivated by sunlight, heat), adsorbed to container (partially controlled by addition of Tween 80), chemical denaturation, bacterial contamination, injection of too little antigen, delay in administration after drawing of preparation into syringe, injection too deep, incorrect route, improper reading (unsupervised reader, conscious or unconscious bias, error in reading); interferon gamma test; PCR (sensitivity 90%, specificity 99.6%); DNA probe identification; gene amplification and hybridisation or RFLP; ELISPOT; serum angiotensin converting enzyme decrease; rheumatoid factor may be present; 4% of cases diagnosed postmortem

Miliary Tuberculosis: fever in 89-90%, anemia in 78%, sweats in 86%, weight loss in 66%, cough in 55%, weakness in 53%, dyspnoea in 50%, tachypnoea in 47-50%; reticulonodular miliary chest radiograph in 68%; sputum culture positive in 76%, gastric aspirate in 75%, urine in 59%, bronchial washings in 54%

Treatment: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isoniazid and rifampicin (to 6 mo); vitamin A and zinc may augment efficacy

Latent Infection (Prophylaxis): rule out active tuberculosis and do not give if previous treatment for TB or previous isoniazid, previous isoniazid adverse reaction or acute or unstable liver disease; otherwise, should be given to recent tuberculin converters; children and adolescents with strongly positive tuberculin reactions; tuberculin positive juvenile close contact; old untreated tuberculosis or radiologically healed pulmonary lesion, tuberculin positive or anergy in patients about to be treated with steroid drugs or by immunosuppressive or chemotoxic therapy or radiotherapy; patients with chronic lung disease such as silicosis; patients with tuberculin skin test > 5 mm who have not had BCG or with positive TB-specific interferon gamma release assay and with cancer or other debilitating disease or with diabetes or chronic renal

failure (especially if < 35 y) or who have had a gastrectomy, having long-term corticosteroid therapy or other immunosuppressive therapy (prior to commencement), with history of tuberculosis and with leukemia, Hodgkin's disease or other chronic malignancies, with silicosis and with *human immunodeficiency virus* infection; isoniazid 10 mg/kg to 300 mg orally daily

[+ pyridoxine 25 mg (breastfed baby: 5 mg) orally with each dose] for 6-9 mo; vitamin D 2.5 mg single oral dose

Contacts of Isoniazid Resistant, Rifampicin Susceptible TB: rifampicin 10 mg/kg to 600 mg orally daily + pyrazinamide 15-20 mg/kg to 2 g daily for 2 mo

Patients Who Cannot Tolerate Pyrazinamide: rifampicin 10 mg/kg to 600 mg daily for 4 mo

Prophylaxis:

Vaccination: live vaccine (BCG) efficacy 50% total, 66% meningitis, 71% death from TB; ulceration and lymphadenitis in 1-10%, osteomyelitis 1/M vaccinees; duration of immunity unknown, cost effective; recommended for Aboriginal and Torres Strait Islander neonates in regions of high incidence, neonates born to patients with leprosy (cross-protection), children under 5 y who will be travelling to live in countries of high TB prevalence for long periods, neonates who will be living in a household which includes immigrants or visitors recently arrived from countries of high prevalence or who have returned to visit homes of relatives in countries of high prevalence, children and adolescents aged < 16 y who continue to be exposed to a patient with TB and child or adolescent cannot be given isoniazid or where the person with active disease has organisms resistant to both rifampicin and isoniazid; may also be given to healthcare workers in frequent contact with patients with tuberculosis, especially multi-drug resistant tuberculosis; should not be given to patients with current or previous tuberculosis, with a current febrile illness, with skin conditions such as eczema or dermatitis, who have had a previous live vaccination within the past 4 w, with a history of a positive reaction to a Mantoux test, who are HIV positive or are in a high risk group for HIV and have not been tested, or receiving immunosuppressive medication such as corticosteroids or cancer chemotherapy or with other conditions likely to suppress immunity

Infants of Mothers with Active Pulmonary Tuberculosis: isolation for 7-10 d and treatment of cases
MYCOBACTERIOSIS DUE TO *MYCOBACTERIUM KANSASII*: uncommon; clinically indistinguishable from pulmonary tuberculosis (great majority of patients underlying pulmonary factors, 70% nonpulmonary disposing factors), cervical adenitis in children, arthritic and renal lesions reported, disseminated infection (lung, reticuloendothelial system, bone, joint, skin) in severely immunocompromised patients, frequently with pulmonary predispositions

Diagnosis: Ziehl-Neelsen stain and culture of sputum, lymph gland, bone marrow, spleen biopsy; severe anemia, gross leucopenia (to 500/ μ L), gross thrombocytopenia; bone marrow severe hypoplasia of hematopoietic cells

Differential Diagnosis: lymphoma, leukemia (blood smear, bone marrow examination)

Treatment: isoniazid 10 mg/kg to 300 mg orally daily + rifampicin 10 mg/kg to 600 mg orally twice daily + ethambutol 15 mg/kg orally (not < 6 y) daily for 18 mo and 12 mo negative cultures

DISSEMINATED MYCOBACTERIOSIS IN AIDS

Agents: *Mycobacterium avium-intracellulare*, also *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, *Mycobacterium gordonae*, *Mycobacterium fortuitum*, *Mycobacterium chelonae*, *Mycobacterium xenopi*, *Mycobacterium szulgai*, *Mycobacterium smegmatis*, *Mycobacterium scrofulaceum*, *Mycobacterium malmoense*, *Mycobacterium flavescens*, *Mycobacterium asiaticum*, *Mycobacterium bovis*, *Mycobacterium haemophilum*, *Mycobacterium genavense*

Diagnosis: fever in 87% of cases, night sweats in 78%; anemia (< 8.5 g hemoglobin/dL) in 85%, elevated serum alkaline phosphatase in 53%; Ziehl-Neelsen stain and culture of lung biopsy (100% positive), spleen biopsy (100% positive), brain biopsy (100% positive), duodenal contents (100% positive), blood (63-86% positive; use Isolator lysis centrifugation concentrate inoculated into a Bactec 7H12 culture vial and onto Wallenstein medium or Bactec 13A broth system), sputum (56% positive), bronchial washing (50% positive), liver biopsy (43-67% positive), stool (42-100% positive); postmortem histology of lung, lymph node, spleen, bone marrow, brain, adrenals, liver, intestine (all 100% positive)

Treatment (*Mycobacterium avium*):

Initial Regimen: ethambutol 15 mg/kg orally daily (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or azithromycin 10 mg/kg to 500 mg orally daily + rifampicin 10 mg/kg to 600 mg orally daily or rifabutin 5 mg/kg to 300 mg orally daily

Salvage Regimen: amikacin 10 mg/kg daily \pm ciprofloxacin 750 mg bid

Prophylaxis (CD4 < 50/ μ L): azithromycin 1.2 g orally weekly, clarithromycin 500 mg twice a day, rifabutin 300 mg orally daily

DISSEMINATED MYCOBACTERIOSIS IN NON-AIDS PATIENTS: skin involvement in patients with no immune defect, kidney transplant recipients, collagen disease, chronic renal failure, 90% survival rate; widespread, multiorgan involvement, severe

illness in cell-mediated immunity deficiency, lymphoma, leukemia, survival rate 10%; intermediately severe illness and response to therapy in patients with other underlying diseases

Agents: *Mycobacterium fortuitum*, *Mycobacterium chelonae*; also *Mycobacterium gordonae*, *Mycobacterium malmøense*

Diagnosis: histology (dimorphic (acute and granulomatous) inflammation) and culture of skin lesions; blood cultures

Treatment:

***Mycobacterium fortuitum*, *Mycobacterium chelonae*:** 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

***Mycobacterium gordonae*:** isoniazid + rifampicin + pyrazinamide

***Mycobacterium malmøense*:** rifabutin + clofazimine + isoniazid

LEPROSY (HANSEN DISEASE, HANSENIASIS, LEPRA, LEPRA ARABUM, ST LAZARUS' DISEASE): usually chronic infectious disease mainly affecting skin, peripheral nerves and mucosa of upper respiratory tract; formerly worldwide, now largely confined to tropics; 600,000 cases worldwide (mainly in Brazil, India, Madagascar, Mozambique, Myanmar, Nepal); 150 cases/y in USA; 6 notified cases in Australia in 1999 (50% in Western Australia); transmission by personal contact; incubation period years

Agent: *Mycobacterium leprae* (? + cooperation of corynebacteria)

Diagnosis: combination of skin lesions and thickening of peripheral nerves very suggestive; leprosy is characterised by a wide variety of lesions; intradermal lepronin aids in assessing type; indeterminate leprosy (indeterminate Hansen disease, indeterminate hanseniasis, lepra incaracteristica, uncharacteristic leprosy, undifferentiated leprosy), the earliest form, is characterised by 1 or more ill-defined and asymptomatic hypopigmented or erythematous lesions with ill-defined borders appearing on face, scapular region, buttocks or extremities; there may be minimal sensory loss in lesions; lesions may be transient and self-healing but may evolve to lepromatous or tuberculoid type; nerve damage does not occur; in tuberculoid leprosy (paucibacillary leprosy, TT leprosy, tuberculoid Hansen disease, tuberculoid hanseniasis), there may be 1 or several well-defined erythematous or brownish red anesthetic or hypesthetic skin lesions appearing on the extremities, trunk, buttocks or face; damage to peripheral nerves is usually severe but limited to the skin lesions and the main nerve trunk related to the main skin lesions; borderline leprosy (B leprosy, BB leprosy, bi-polar leprosy, borderline group, dimorphic leprosy, dimorphous Hansen disease, dimorphous hanseniasis, dimorphous leprosy, intermediate leprosy, mixed leprosy) occupies most of the spectrum between tuberculoid leprosy and lepromatous leprosy; it is unstable and may include a wide range of manifestations of either of the 2 polar forms; nerve damage may be severe, rapidly advancing and unpredictable; it may precede cutaneous manifestations of the disease; borderline leprosy with tuberculoid features (borderline tuberculoid leprosy, BT leprosy) and borderline leprosy with lepromatous features (borderline lepromatous leprosy, BL leprosy) may be distinguished; lepromatous leprosy (diffuse leprosy, elephantiasis graccorum, hanseniasis virchowiana, lepra tuberosa, lepromatous Hansen disease, LL leprosy, multibacillary leprosy, nodular Hansen disease, nodular hanseniasis, nodular leprosy, virchowian hanseniasis) is a progressive form in which skin lesions are bilateral symmetrical, numerous, diffuse, erythematous and ill-defined macules; later, papules, nodules and diffuse infiltrations appear; at a later stage, eyebrows and eyelashes may be lost; involvement of nasal mucosa may lead to crusting, obstructed breathing and epistaxis; collapse of the nose is characteristic of advanced cases; ocular involvement leads to iritis and keratitis; diffuse lepromatous leprosy (diffuse lepromatosis, diffuse leprosy, Lucio leprosy) is a variety in which there is diffuse infiltration of skin but no macules or nodules; eyebrows may be lost and generalised paresthesiae may occur, with bouts of pyrexia; polygonal ulceration of skin occurs, especially near elbows and knees; if reactions develop, patients exhibit necrotising vasculitis (Lucio phenomenon; erythema necroticans, necrotising vasculitis of leprosy) rather than erythema nodosum leprosum; essentially limited to Central America and, especially, certain States in Mexico; neural leprosy = involvement of peripheral nerves in the absence of detectable skin lesions; reactions are acute inflammatory states occurring in any type of leprosy except early or indeterminate and precipitated by a change in the hormonal state (eg., during pregnancy or parturition), pyrexia (however caused), viral infection and smallpox vaccination; reversal reaction (upgrading reaction), occurs in borderline leprosy; preexisting lesions in skin and peripheral nerves become acutely painful, erythematous and inflamed; new lesions may occur; fever usually absent; increase in cell-mediated immunity; erythema nodosum leprosum (ENL, type 2 reaction) occurs in multibacillary (especially lepromatous) leprosy; crops of red, tender nodules and 'pink patches' appear on trunk, face and exterior surfaces of limbs; usually accompanied by fever and systemic signs, eg., general malaise and pains in large muscle masses, arthralgia (perhaps with effusion into joints), lymphadenopathy, iridocyclitis, neuropathy, orchitis and nephritis; modified Ziehl-Neelsen stain of scrapings from mucosal ulcers or fluid from nodules obtained by scrape-incision method, biopsy of macule, muscle or nerve (bacilli are not found, or are extremely scanty, in indeterminate leprosy, usually very scanty in tuberculoid, easily found in borderline, rather low in borderline tuberculoid, numerous in lesions but absent from apparently normal skin and usually absent from nasal mucosa in borderline lepromatous, and found in large numbers in

lesions, apparently normal skin, peripheral nerves, mucosa of the upper respiratory tract, reticuloendothelial system, eyes, testes and bone marrow in lepromatous); histological examination of a lesion; ELISA (antibody); causes moderate anemia, increased serum globulins, reduced serum albumin, raised erythrocyte sedimentation rate, increased serum angiotensin converting enzyme

Neural Leprosy: histopathology usually consistent with tuberculoid or borderline tuberculoid disease

Lucio Phenomenon: histopathologically a necrotising vasculitis with extravasation of erythrocytes and fibroid degeneration of blood vessel walls

Differential Diagnosis: fungal infections, yaws, vitiligo, leishmaniasis, mycoides fungoides, lupus, syphilis, disseminated tuberculosis; tuberculoid leprosy may be histologically indistinguishable from sarcoidosis unless there are changes (lymphocytic and histiocytic infiltration) in the cutaneous nerve fibrils

Treatment: zinc in all cases

Paucibacillary Leprosy: dapsone 1-2 mg/kg to maximum 100 mg self-administered once daily for 6 mo + rifampicin supervised 600 mg orally once a month for 6 mo; follow closely for relapse and restart if necessary

Multibacillary Leprosy: as above + clofazimine supervised 300 mg orally once monthly + 50 mg orally self-administered daily; continue complete regimen for at least 2 y and until negative for organisms; if clofazimine totally unacceptable due to skin discolouration, substitute ethionamide/prothionamide 250-375 mg orally daily self-administered

Prevention and Control: treatment of active cases

BRUCELLOSIS (FEBRIS UNDULANS, MIMIC DISEASE, UNDULANT FEVER): usually a generalised disease but may give rise to numerous localised complications; occasionally, some of these localised conditions may arise independently of systemic disease (eg., pneumonia resulting from inhalation of infected aerosols); these local conditions include bronchitis, pneumonia, meningitis, encephalitis, arthritis, osteomyelitis, osteochondritis, orchitis, cholecystitis and endocarditis; worldwide; transmission by contact with infected animals, ingestion of raw milk, goat cheese made from unpasteurised milk, contaminated meats; natural reservoir in domestic animals such as cattle, goats, sheep and swine; in Australia, cattle herds are free of *Brucella abortus*, *Brucella canis* and *Brucella melitensis* are not found, and *Brucella suis* is found only in wild pigs; \approx 50 notified cases/y in Australia (\approx 94% in Queensland); incubation period 1 w to several mo; duration of illness: acute < 60 d, subacute 60 d-1 y, chronic, > 1 y; fatality rate <1% but can cause significant illness for months to years

Agents: *Brucella abortus*, *Brucella canis*, *Brucella melitensis*, *Brucella suis*

Diagnosis: incubation period 5-60 d (usually 1-2 mo); 2/3 of cases chronic or undulating disease with wavelike relapses of weakness, headache, constipation, insomnia, generalised aches and fever; 1/3 of cases acute symptomatic illness with severe malaise in 92%, moderate or high fever (38.3-40°C) in 91-96%, fatigue and weakness in 88%, myalgia in 69%, weight loss in 63%, chills in 40-82%, drenching sweats in 39-99%, osteoarticular complications in 37%, headache (usually severe) in 23-79%, musculoskeletal symptoms (especially tenderness over spine) in 22-66%, arthralgia in 19%, gastrointestinal symptoms (diarrhoea, bloody stools, vomiting during acute phase) in 17-30%, hepatosplenomegaly in 17-47%, cough in 17%, sacroiliitis in 8-15%, pneumonia in 8%, lymphadenopathy in 7-21%, rash in 4%, malodorous perspiration and dysgeusia common; may present with localised symptoms such as ischemic limb, mediastinal mass, dementia; 5% of cases have microscopic hematuria; prostration, delirium, coma and death can occur within days or weeks; in recovering patients, relapses (anorexia, diarrhoea, constipation, colitis in 75%, weight loss, myalgias and arthralgias in 25-50%, bone and joint disease involving weight-bearing and sacroiliac joints in 20-60%, papular, maculopapular, erythema nodosum-like or purpuric eruptions in < 5%, endocarditis (rare but most common cause of death) can occur for weeks and gradually diminish in severity until patient recovers; generalised lymphadenopathy and hepatosplenomegaly; granulomas in liver, spleen, bone marrow, lymph nodes, brain, skin and kidneys; mild leucopenia, thrombocytopenia

Acute and Subacute: bone marrow culture (positive in 92%), blood cultures (positive in 54-90%), serology, direct immunofluorescence after incubation in nutrient broth; standard tube agglutination (labour intensive; agglutinins to *Brucella abortus* antigen detect all cases due to *Brucella abortus*, as well as 2/3 of infections with *Brucella melitensis* and *Brucella suis*; significant titres (> 160) appear late in second week; cross-reactions occur with *Proteus* OX-19 antigen, *Yersinia*, *Vibrio*, *Francisella*, measures IgM mainly but also IgG; becomes low or negative later)

Chronic: 2-mercaptoethanol test (measures IgG), antihuman globulin (Coomb's) test (measures non-agglutinating IgG and some IgA), complement fixation test (measures IgG), ELISA (IgA, IgG, IgM), fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Treatment:

< 8 y: cotrimoxazole 4/20-6/30 mg/kg orally 12 hourly for 6 w + rifampicin 15 mg/kg orally once daily for 6 w (relapse rate 2%) or gentamicin 7.5 mg/kg i.v. daily for 2 w (adjust dose for renal function)

> 8 y: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 6 w (not pregnant or breastfeeding) + rifampicin 15 mg/kg to 600 mg orally once daily for 6 w (relapse rate 8%) or gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose for 2 w (adjust dose for renal function); ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally 4 times a day for 30 d

Prophylaxis: live vaccine (veterinary use); pasteurisation of milk products

GLANDERS: an uncommon disease of horses and other equines, on rare occasions transmitted to man; may be acute, affecting mainly the nose, or chronic, causing cutaneous, pulmonary or gastrointestinal nodular lesions

Agent: *Burkholderia mallei*

Diagnosis: incubation period 1-21 d; Gram stain and culture of swab of discharge from necrotic foci in skin or from enlarged regional lymph nodes (also blood, sputum, nasopharyngeal discharge); complement fixation test, agglutinations; contact with horses or mules

Treatment and Prophylaxis: as for MELIOIDOSIS

MELIOIDOSIS (PSEUDOCHOLERA, STANTON DISEASE, WHITMORE DISEASE, WHITMORE FEVER): SE Asia and Northern Australia, also Africa, N America; acute septicemic (57% of cases; 45% disseminated, 12% nondisseminated; associated with diabetes mellitus and hematological diseases; often associated with patchy pneumonitis), acute localised and suppurative (42% of cases; cellulitis, subcutaneous abscess, infected wound, septic arthritis of knee, ankle and elbow joints, osteomyelitis, liver abscess, splenic abscess, pyelonephritis, prostatitis or prostatic abscess, lymphadenitis or lymphatic abscess, pericarditis, pericardial effusion common; erythema gangrenosum, hemorrhagic bleb, cutaneous pustules, pyomyositis, urticaria, mastitis, subperiosteal abscess, cholangitis, pancreatic abscess, epididymoorchitis, perinephric abscess, scrotal abscess, endocarditis, endarteritis, meningitis, encephalitis, intracisternal abscess, ophthalmitis (corneal ulcer), parotid abscess rare), acute or chronic pulmonary (pneumonitis, lung abscess, pleural effusion, empyema common; miliary, granuloma rare; chronic resembles tuberculosis and is marked by granulomatous abscess formation), chronic suppurative (chronic granuloma)

Agent: *Burkholderia pseudomallei*

Diagnosis: incubation period 1-21 d; manifestations vary from asymptomatic to rapidly overwhelming septicemia (case-fatality rate 85-95%), prolonged fever without localising signs, localised infections (either acutely suppurative or chronic and granulomatous), septicemia of abrupt onset with metastatic lesions in skin, muscle, bone and joints; culture of pus swab from ulcers and abscesses, sputum, urine, blood; indirect hemagglutination antibody titre (< 1:80, unlikely; 1:80-1:320, suggestive; > 1:320, very likely)

Treatment: ceftazidime 50 mg/kg to 2 g i.v. 6 hourly or meropenem 25 mg/kg to 1 g i.v. 8 hourly or imipenem 25 mg/kg to 1 g i.v. 6 hourly for at least 14 d (4-8 w in deep-seated infections, osteomyelitis, septic arthritis), then cotrimoxazole 8 + 40 mg/kg to 320 + 1600 mg orally 12 hourly + folic acid 0.1 mg/kg to 5 mg orally daily ± doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y) for at least further 3 mo

Prophylaxis (Postexposure): cotrimoxazole 8 + 40 mg/kg to 320 + 1600 mg orally 12 hourly, doxycycline 100 mg orally 12 hourly (adults only)

NON-PNEUMONIC LEGIONNAIRE'S DISEASE (FORM CHARACTERISED BY MALAISE, MYALGIA AND HEADACHE KNOWN AS PONTIAC FEVER): a self-limited febrile disease

Agents: species of genera *Fluoribacter*, *Legionella* and *Tatlockia*

Diagnosis: malaise, myalgia, headache, encephalopathy (and possibly other neurological syndromes) and gastrointestinal upset, mainly diarrhoea; serology

Treatment: erythromycin

PLAGUE (BLACK DEATH, GREAT MORTALITY, ORIENTAL PLAGUE, PEST, PESTIS): ≈ 1800 cases/y (240 deaths) worldwide; great deal of central and eastern Africa—Tanzania ≈ 900 cases (70 deaths), Zaire ≈ 320 cases (85 deaths)/y, Madagascar ≈ 260 cases (60 deaths)/y, Asia total ≈ 960 cases (50 deaths)/y, Vietnam ≈ 600 cases (25 deaths)/y, Burma ≈ 280 cases (4 deaths)/y, recent outbreak in India, Americas total ≈ 520 cases (30 deaths)/y, Western USA, ≈ 40 cases (7 deaths)/y, Peru ≈ 260 cases (20 deaths)/y; last notification in Australia in 1923; killed 40% of population of Constantinople in 541 and 542, 44 M in Europe in latter half of fourteenth century, 12 M in India 1896-1936; bubonic plague (glandular plague, malignant polyadenitis, pestis bubonica, pestis fulminans, pestis major, polyadenitis maligna, St Roch disease, Tarabagan disease; most frequent form; characterised by inflammation and enlargement of lymphatic glands, especially in groin (pestis inguinalis) and axilla; hemorrhage may occur (black plague, hemorrhagic plague); cervical form associated with meningitis and pneumonia; mortality in untreated 50-60%), primary pneumonic plague (pulmonary plague; arises from inhalation, usually rapidly fatal; secondary plague pneumonia is complication of plague elsewhere in body through hematogenous spread, variable in severity), pharyngeal plague (anginal plague, tonsillar plague; result of exposure to larger infectious droplets or ingestion of infected tissues), septicemic plague (pesticemia, pestis siderans; primary septicemic

plague; relatively infrequent, no involvement of lymphatics and no buboes); bubosepticemic plague (secondary septicemic plague; more frequent, result of delay in treatment of bubonic plague); transmission by infected rodents and fleas (*Xenopsylla cheopis*), pus from lesions, sputum; zootic plague resulting from transmission from an animal; may be sylvatic (rodents living in wooded areas), campestral (rodents living in plains) or domestic (peridomestic, agrestial; in 'domestic' rodents and domestic cats), demic (mostly from transmission from other humans)

Agent: *Yersinia pestis*

Diagnosis: incubation period 1-6 d; prostration in 75% of cases, chills in 40-61%, headache in 40-55%, abdominal pain in 39% of septicemic and 8% of bubonic, malaise in 38-44%, vomiting in 33-50%, confusion in 30%, nausea in 29-44%, cough in 25%, diarrhoea in 23-39%, chest pain in 15%, fever, lymphadenitis (bubo), meningitis; geographic history; contact with rodents; Gram stain, fluorescent antibody stain and culture of lymph node and bubo aspirates, sputum; blood cultures; also sputum, CSF and urine; identify isolates by fluorescent antibody and bacteriophage; fourfold or greater change in serum antibody titre to *Yersinia pestis* F1 antigen (serum passive hemagglutination; ELISA (sensitivity 100%)); rapid monoclonal antibody test (sensitivity 100%, specificity 100%, positive predictive value 91%, negative predictive value 87%) white cell count 9000-17,400/ μ L with marked shift to left, 79% neutrophils, 13% bands, 5% monocytes, 3% lymphocytes; gross haematuria, 4+ proteinuria, many granular and red blood cell casts, pyuria, bacteriuria

Treatment: gentamicin 4-7.5 mg/kg/d i.v., doxycycline 4 mg/kg to 200 mg i.v. then 2 mg/kg to 100 mg i.v. twice daily (not < 8 y), ciprofloxacin 15 mg/kg to 400 mg i.v. twice daily, chloramphenicol 25 mg/kg i.v. 4 times a day

Prophylaxis (Postexposure): doxycycline 2 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

PSEUDOTUBERCULOSIS (RODENT PSEUDOTUBERCULOSIS): 3 forms: systemic pseudotuberculosis, pseudotuberculous enterocolitis, pseudotuberculous mesenteric lymphadenitis

Agent: *Yersinia pseudotuberculosis*

Diagnosis: culture of appropriate specimen

Treatment: gentamicin, cefotaxime, doxycycline, ciprofloxacin

TULAREMIA (ALKALI DISEASE, DEER-FLY DISEASE, FRANCIS DISEASE, OHARA DISEASE, PAHVANT VALLEY FEVER, PAHVANT VALLEY PLAGUE, RABBIT FEVER, YATO-BIGO, YATO-BYO): Europe, Japan, USA, former Soviet Union; incidence 0.1/100,000 in USA; 75-85% ulceroglandular (fever, development of a cutaneous ulcer at the site of infection, with regional, and sometimes general, lymphadenopathy), 5-15% typhoidal (generalised tularemia; severe systemic form with septicemia, arising by dissemination via bloodstream from a primary lesion; fever, prostration, weight loss), 1-2% oculoglandular (ophthalmic tularemia; portal of entry is the eye; fever, regional lymphadenopathy, purulent conjunctivitis, swollen eyelids), < 1% oropharyngeal (fever, adenopathy, inflammation of the mouth or pharynx, sometimes resembling tonsillitis), tracheobronchitis (primary from inhalation of contaminated material or secondary from dissemination via bloodstream), bronchopneumonia and lobar pneumonia, gastrointestinal (abdominal tularemia, ingestion tularemia; gastrointestinal lesions, often severe); death in 18%; transmission by contact with infected animal (eg., rabbit), ticks (*Dermacentor variabilis* and *Amblyomma americanum* in southern and eastern USA, *Dermacentor andersoni* in southern and western USA), deerfly, rarely cat bite

Agent: *Francisella tularensis*

Diagnosis: residence in, or visit to, endemic area; exposure to ticks, rabbits or other animals; incubation period 1-57 d (average 4 d); fever in all, cutaneous ulcer in 64%, painful adenopathy in 55%, cough in 45%, diarrhoea in 18%, headache, malaise, pneumonia, pleural effusion and patchy infiltrates on chest X-ray; culture of nodules, pustules, ulcers, lymph node aspirate, blood, pleural exudate or sputum on glucose-cysteine agar; fluorescent antigen staining of exudates; microagglutination, tube agglutination, ELISA (sensitivity 96%, specificity 98%); animal inoculation; erythrocyte sedimentation rate 40 mm/h; white cell count 11,400/ μ L, 60% segmented neutrophils, 16% band forms, 13% lymphocytes, 2% atypical lymphocytes, 5% monocytes

Treatment: gentamicin 4-7.5 mg/kg i.v. daily for 10 d, doxycycline (< 45 kg, 2.2 mg/kg i.v. twice daily for 14-21 d; \geq 45 kg, 100 mg i.v. twice a day), chloramphenicol 15 mg/kg i.v. 4 times a day for 14-21 d, ciprofloxacin 15 mg/kg i.v. twice a day for 10 d

Prophylaxis (Postexposure): doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Prevention and Control: avoid contact; regularly detick dogs with 6% malathion powder

RAT BITE FEVER: usually transmitted by bite of rats and certain other animals but, in the case of streptobacillosis, transmission via contaminated milk has occurred and the disease has been reported in the absence of bites following contact with live or dead rats or dogs

Agents: *Streptobacillus moniliformis* (epidemic arthritis erythema, Haverhill fever, streptobacillary fever; distinctly uncommon disease of N and S America; single case reported from Australia; complications uncommon but severe; case-fatality rate \approx 13%), '*Spirillum minus*' (Sodoka; complications very rare; case-fatality rate \approx 6%)

Diagnosis: dark ground, Gram stain, culture and guinea pig inoculation of pus from bite site, metastatic abscess or infected joint, lymph gland aspirate, blood; serology; marked neutrophilia

'*Spirillum minus*': Gram negative, spiral; incubation period > 10 d; local skin reaction at site of bite; regional lymphadenopathy; chills; arthritis and leucocytosis rare; isolation of organism by animal inoculation; no specific serology; false positive serologic test for syphilis in > 50% of cases

Streptobacillus moniliformis: microaerophilic, Gram negative, pleomorphic; incubation period < 10 d; no local skin reaction at site of bite; lymphadenopathy and chills rare; polyarthritis and leucocytosis present; palmar and plantar rash; isolation of organism in artificial medium; serology; false positive test for syphilis in < 25% of cases

Treatment: aqueous procaine penicillin 600,000 U i.m. twice daily (child: 25,000-50,000 U/kg daily in 2 divided doses) for 7-10 d; phenoxymethylpenicillin 500 mg orally 6 hourly (< 12 y: 25-50 mg/kg orally daily in 4 divided doses) for 7-10 d, tetracycline 500 mg orally 6 hourly for 7-10 d, erythromycin 500 mg orally 6 hourly (child: 30-50 mg/kg daily in 4 divided doses) for 7-10 d

Differential Diagnosis: acute viral exanthems, rickettsial infections, drug reactions, septic arthritis, leptospirosis, collagen-vascular diseases, secondary syphilis, neisserial infections, influenza, infective endocarditis, acute rheumatic fever, malaria, relapsing fever, lymphoma/leukemia

DISSEMINATED GONOCOCCAL DISEASE: a generalised gonococcal disease arising as a result of hematogenous spread, usually from a urogenital tract or pharyngeal disease; during septicemic phase, manifested by cutaneous (especially palmar and plantar) lesions that develop necrotic centres (gonococcal keratosis, gonococcal dermatitis, gonococcal dermatosis, keratoderma blenorrhagica, keratosis blenorrhagica); occurs most frequently in women; may be manifested by any of numerous clinical conditions, including gonococcal endocarditis, gonococcal myocarditis, gonococcal pericarditis, gonococcal meningitis, gonococcal brain abscess, gonococcal peritonitis and gonococcal pneumonia; frequently gives rise to arthritis and occasionally to septicemic adrenal hemorrhage syndrome

Agent: *Neisseria gonorrhoeae*

Diagnosis: blood cultures; culture of other specimens as appropriate

Treatment: benzylpenicillin 10 MU i.v. daily until patient improves, followed by 500 mg 6 hourly to complete at least 7 d of treatment; amoxycillin 3 g orally once as a single dose + probenecid 1 g orally once as a single dose, followed by amoxycillin 500 mg orally 6 hourly for at least 7 d; ceftriaxone 1 g i.v. daily for 7 days; tetracycline 500 mg orally 6 hourly for at least 7 d; cefoxitin 1 g i.v. 6 hourly for at least 7 d; cefotaxime 500 mg i.v. 6 hourly for at least 7 d; erythromycin 500 mg orally 6 hourly for a minimum of 7 d; ceftriaxone 1 g for 24 - 48 h, then ciprofloxacin for 7 d

DISSEMINATED MENINGOCOCCAL DISEASE: generalised disease arising as a result of hematogenous spread of *Neisseria meningitidis*, manifested by severe toxemia and intravascular coagulation, usually with hemorrhagic signs varying from small petechiae to widespread extravasation of blood; meningitis usually absent; occasionally gives rise to numerous clinical conditions, including meningococcal carditis, meningococcal endocarditis, meningococcal myocarditis, meningococcal pericarditis, meningococcal arthritis and meningococcal conjunctivitis; most common cause of septicemic adrenal hemorrhage syndrome

Agent: *Neisseria meningitidis*

Diagnosis: incubation period < 21 d; blood cultures

Treatment: as for **DISSEMINATED GONOCOCCAL DISEASE**; activated protein C

Prophylaxis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

RICKETTSIOSES: cause 2% of fever in returned travellers to Australia

Agents: *Rickettsia rickettsii* (spotted fever, American spotted fever, black fever, Brazilian spotted fever, Bullis fever, Choix fever, Colombian tick fever, eastern-type Rocky Mountain spotted fever, exanthematous typhus of Sao Paulo, Lone Star fever, Mexican spotted fever, New World spotted fever, pinta fever, Rocky Mountain spotted fever, Sao Paulo fever, Sao Paulo typhus, Texas tick fever, Tobia fever (Colombia), western-type Rocky Mountain spotted fever; Western Hemisphere; 3 cases/million in USA (23/million in North Carolina); wood tick (*Dermacentor andersoni*) vector in northeastern USA, dog tick (*Dermacentor variabilis*) in eastern and southern USA, and 'Lone Star' tick (*Amblyoma americana*) in southeastern USA; vertebrate host rodents, dogs, rabbits, opossum), *Rickettsia conorii* (spotted fever, African tick fever, Boutonneuse fever,

Conor and Bruch disease, eruptive Mediterranean fever, fièvre boutonneuse, India tick typhus, Kenya tick typhus, Marseilles fever, Mediterranean exanthematous fever, Mediterranean tick fever, Omer disease, South African tick bite fever; Mediterranean, Black Sea and Caspian Sea littorals, Middle East, India, Africa; tick (*Rhicephalus sanguineus*) vector; vertebrate host rodents, dogs), *Rickettsia akari* (rickettsialpox, Kew Garden fever, Kew Garden spotted fever, vesicular rickettsialpox; N America, former Soviet Union, Southern Africa, Korea, Mediterranean; mites vector; vertebrate host mice, rat), *Rickettsia sibirica* (spotted fever, North Asian tick fever, Siberian tick typhus; Armenia, Central Asia, Siberia, Mongolia, Central Europe; tick vector; vertebrate host rodents), *Rickettsia australis* (North Queensland tick typhus, Queensland coastal fever, Queensland fever, Queensland tick typhus; eastern coast of Australia east of the Great Dividing Range; tick (*Ixodes holocyclus*) vector; vertebrate host marsupials), *Rickettsia honei* (Flinders Island spotted fever; Flinders Island (Bass Strait) and Schuten Island (east coast of Tasmania); *Aponomma hydrosauri* (reptile tick) vector), '*Rickettsia pijperi*' (tick bite fever; S Africa), *Rickettsia prowazekii* (typhus fever (blasting typhus, camp fever, classical endemic typhus, classic typhus, epidemic typhus, European typhus, exanthematous typhus, famine fever, Fleckfieber, flecktyphus, gaol fever, Hildebrand disease, hospital fever, jail fever, louse-borne typhus, louse typhus, primary epidemic typhus, ship fever, typhus, typhus exanthematicus, war fever) and benign typhus (Brill disease, Brill-Zinsser disease, recrudescence fever, recrudescence fever, recrudescence louse-borne typhus, recrudescence typhus, sporadic typhus, typhus sidera) for form appearing years after complete recovery; human body louse (*Pediculus humanus corporis*) vector; vertebrate host man, squirrels; epidemic disease, late recrudescence; 'sylvatic typhus' in eastern USA probably transmitted by squirrel fleas; not seen in Australia since gold rush and convict times), *Rickettsia typhi* (typhus fever, benign typhus, Congolian red fever, endemic typhus, fièvre nautique, flea-borne tarbardillo, flea-borne typhus, latent typhus, Manchurian fever, Manchurian typhus, Mexican typhus, Moscow typhus, murine typhus fever, rat-borne typhus, rat typhus, red fever of the Congo, ship typhus, shop typhus (Malaysia), Toulon typhus, typhus marinus, urban tropical typhus; worldwide, with outbreaks reported from Australia, China, Greece, Israel, Kuwait, Thailand; < 100 cases/y in USA; vector flea (classically, rat flea *Xanopsylla cheopsis*, but free-ranging cats, dogs, opossums and their fleas assuming increasing importance) and rat louse; vertebrate host wild rats, field mice), *Rickettsia africae* (African tick bite fever; main cause of rickettsiosis in travellers to sub-Saharan Africa; transmitted by *Ambylomma* tick), *Orientia tsutsugamushi* (typhus fever, akamushi disease, akamushi fever, Burma eruptive fever, chigger-borne rickettsiosis, China fever, flood fever, inundation fever, island disease, island fever, island typhus, Japanese flood fever, Japanese river fever, kedani disease, kedani fever, Malayan fever, mite-borne typhus, mite typhus, rural typhus, scrub fever, scrub typhus, shashitsu, shima-mushi disease, shimu-mushi, Shishito, Sumatran typhus, tsutsugamushi, tsutsugamushi disease, tsutsugamushi fever, yochubyo; Asia, Indian subcontinent, tropical northern Australia, Pacific Islands, Indonesia; trombiculid mites (*Leptotrombidium deliense* in Australia) vector; vertebrate host native rodents, bandicoots), *Rickettsia sibirica* (Siberian tick typhus; central Asia; tick vector; rodents, dog reservoir), *Coxiella burnetii* (Q fever, Australian Q fever, Australian typhus, Balkan grippe, Derrick-Burnet disease, Nine Mile fever, quadrilateral fever; worldwide; vector tick (unnecessary); vertebrate host sheep, cattle, goats; respiratory pathogen, infection by aerosol from vertebrate carrier; ≈ 700 notified cases/y in Australia (≈ 40% in Queensland)), *Ehrlichia sennetsu* (Hyuga fever), *Rickettsia felis* (transmitted by cat fleas; causes murine typhus-like syndrome); **EHRlichiosis** see Chapter 10.

Diagnosis: incubation period 7-14 d; acute onset, fever, true rigours, rash (except in Q fever; macular, maculopapular or petechial, starting on extremities and extending to trunk, with regular occurrence on palms and soles in Rocky Mountain spotted fever; vesicular or vesiculopapular (may be sparse or diffuse) in rickettsialpox; macular or maculopapular, starting on trunk and extending to extremities in typhus fever), headache, arthralgias, myalgias, conjunctivitis; primary lesion in Boutonneuse fever, Siberian tick typhus, Queensland tick fever, scrub typhus; adenopathy in scrub typhus; murine typhus mild disease; tachypnoea in 97% of cases of typhus fever, fever in 85%, conjunctival suffusion in 53%, raised erythrocyte sedimentation rate in 57%, increased lactate dehydrogenase in 82%, aspartate aminotransferase increased in 63%, severe involvement of CNS, myocardium and kidneys not unusual; spotted fever due to *Rickettsia sibirica* resembles that due to *Rickettsia rickettsii* but is less severe; usually leucopenia with rickettsialpox; often pneumonitis in tsutsugamushi (relapses and second attacks common); on rare occasions, Q fever may become latent and reappear as chronic condition, usually complicated by chronic hepatitis, thrombocytopenia and endocarditis (latter invariably fatal if untreated); manifestations of *Ehrlichia sennetsu* infection vary from low grade fever with mild headache and slight back pain to persistent high fever, anorexia, lethargy, lymphadenopathy and prominent hematological abnormalities; geographic, epidemiological; indirect microimmunofluorescence; ELISA (antibody); growth in tissue culture (VERO or L929); Weil-Felix (Boutonneuse fever, Rocky Mountain spotted fever, tick bite fever, tick typhus: OX19⁺, OX2⁺, tenth to fourteenth day; epidemic typhus, murine typhus: OX19⁺, OX2[±]; scrub typhus: OXK⁺; Brill's disease: usually negative; Q fever, rickettsialpox: negative; specificity not absolute; many false positive and false negative reactions occur; cross-reactions with typhoid, *Proteus* urinary tract infection,

leptospirosis, severe liver disease), complement fixation test (tenth to fourteenth day), microscopic agglutination; animal inoculation; lysis-centrifugation blood cultures

Boutonneuse Fever: microimmunofluorescence, latex agglutination of serum; immunofluorescence of skin lesion biopsy; Western blot; isolation of *Rickettsia conorii* from blood culture with shell vial cell culture; abnormal serum γ -glutamyl transferase in 60% of cases, abnormal SGOT in 55%, abnormal SGPT in 54%

Q Fever: incubation period < 21 d; farm worker, slaughtering or dressing animals, exposure to parturient cats; histology of liver (multiple non-caseating granulomas); complement fixation test (phase 1 negative in first 3-4 w, phase 2 $\geq 4X$ increased in acute; phases 1 and 2 titre ≥ 160 in chronic), immunofluorescent antibody and ELISA tests (IgG significantly increased in acute, titre ≥ 1280 in chronic; IgA titre ≥ 1280 in chronic; IgM positive in acute, negative or low in chronic)

Rocky Mountain Spotted Fever: incubation period 2 w; fever, spotted rash, headache, myalgia, abdominal pain; pulmonary complication (pharyngitis, pleural effusion, pleurisy; pleural effusion, diffuse infiltrates and pulmonary edema on chest X-ray) occurs; IgM, IgG, serology

'*Rickettsia africae*': 95% inoculation eschar (54% multiple), 88% fever, 63% influenza-like syndrome, 63% myalgias, 46% rash (usually maculopapular or vesicular, rarely purpuric), 43% regional lymphadenopathy; microimmunofluorescence assay + Western blot + cross-adsorption assay (sensitivity 56%; each test positive predictive value and specificity 100%)

Treatment:

Q Fever:

Acute: doxycycline 2 mg/kg to 100 mg orally 12 hourly for 14 d (not < 8 y, pregnant or breastfeeding), chloramphenicol 12.5 mg/kg to 500 mg i.v. 6 hourly for 14 d

Chronic: doxycycline or chloramphenicol + rifampicin or hydroxychloroquine for 2 y

Endocarditis: see ENDOCARDITIS

Australian Spotted Fever, Tick Typhus, Scrub Typhus, Rocky Mountain Spotted Fever, Epidemic Typhus, Endemic Typhus: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 7-10 d (not < 8 y), chloramphenicol 12.5 mg/kg to 500 mg i.v. 6 hourly for 7-10 d (until afebrile for 2-3 d)

Others: tetracycline or doxycycline as above

Prophylaxis: doxycycline 200 mg orally weekly; use of protective clothing and tick repellent containing N,N-diethyl-m-toluamide in tick areas

Rocky Mountain Spotted Fever: incomplete natural immunity; vaccine available (yearly booster, exposed persons)

Rickettsialpox: complete natural immunity; no vaccine available

Epidemic Typhus: natural immunity gives complete protection against infection but recrudescence illness in some individuals common; vaccine available (epidemics)

Endemic Typhus: natural immunity gives protection against both endemic and epidemic typhus; vaccine available but not recommended

Scrub Typhus: natural immunity gives complete protection for strain of organism but second infection with another strain occurs; no vaccine available

Q Fever: complete natural immunity; vaccine available for laboratory workers, animal processors

TRENCH FEVER (FEBRIS QUINTANA, 5-DAY FEVER, HIS-WERNER DISEASE, IKAWA FEVER, MEUSE FEVER, QUINTAN FEVER, SALONICA FEVER, SALONIKI FEVER, SHANK FEVER, SHIN-BONE FEVER, TIBIALGIC FEVER, VAN DER SHEER FEVER, VOLHYNIA FEVER, WERNER-HIS DISEASE, WOLHYNIAN FEVER): Europe, Africa, S and Central America, Russia; louse vector; vertebrate host man; extracellular growth

Agent: *Bartonella quintana*

Diagnosis: primary inoculation site, discrete macular rash, sweating and splenomegaly common; serology; smear and culture; PCR

Treatment: erythromycin, doxycycline, tetracycline, minocycline, rifampicin, ciprofloxacin

Prophylaxis: doxycycline 200 mg orally weekly; use of protective clothing and tick repellent containing N,N-diethyl-m-toluamide in tick areas; incomplete natural immunity; no vaccine available

YAWS (BOBA, BOUBI, BREA DISEASE, BUBA, CHARLOUIS DISEASE, COKO (FIJI), DUBE, FRAMBOESIA TROPICA, PARANGI (SRI LANKA), PURRU (MALAYSIA), TONGA, TROPICAL YAWS): acute and chronic; transmission by indirect or direct nonvenereal contact

Agent: *Treponema pallidum subsp pertenu*

Diagnosis: preclinical incubation period of 3-5 w; initial yaws (initial framboesia, primary framboesia, primary yaws) begins as a papule and becomes either papillomatous (chancre of yaws, chancre pianique, mother yaw, primary framboesioma) or ulceropapillomatous (initial framboesial ulcer, ulcère post-chancreux); cutaneous involvement in early yaws is manifested by a wide variety of lesions—plaques (yaws patches), erythematous macular yaws (erythematous macular framboesia, roséle pianique), squamous macular early yaws (depigmented framboeside, furfureaceous macular framboeside, yaws trash), macular early yaws, papillomatous early yaws (butter yaws, framboesia secundaria papillomatosa, framboesioma, pianoma, papilloma tropicum, tropical papilloma; includes palmar and plantar papillomatous early yaws (crab yaws, framboesia papillomatous palmaris/plantar, pian guigne, wet crabs, web crab yaws)), palmar and plantar squamous macular early yaws (erythematous squamous psoriform plaque of yaws, papulosquamous palmar/plantar pianides, squamous plaques of yaws, yaws of the first type of Baerman), palmar and plantar hyperkeratotic macular early yaws (hyperkeratosis and trichophytoid pianides, keratomas of yaws, keratoderma punctata of yaws, polymorphic hyperkeratosis of yaws, punctate keratosis of palms/soles, worm-eaten soles), squamous maculopapular early yaws (lichenoid pianide, pityriasisiform pianide), simple papular early yaws, umbilicate papular early yaws (hyperkeratotic papules), acuminate micropapular early yaws (follicular framboeside, folliculopapular framboeside; desquamation may cause apparent depigmentation), squamous micropapular early yaws (corymbiform framboeside, furfureaceous framboeside, keratitis-pilaris-like framboeside, lichenoid macular framboeside, papulosquamous framboeside, pityriasisiform framboeside, pain dartre); mucosal early yaws may be either maculopapular or papillomatous; osteoarthropathy (osteitis, periostitis, osteoperiostitis (frequently polydactylitis (spina ventosa pianides)), osteomyelitis, hydrarthrosis (synovitis), ganglion) in early yaws is usually nondestructive and most frequently affects shafts of long bones; latent yaws with no symptoms; late yaws characterised by destructive lesions of skin—plaques (papulo-erythematous framboeside; squamous, well demarcated lesions), nodular late yaws (gummatous framboesides, gomme pianique; cutaneous or subcutaneous nodular lesions), ulcerated nodular late yaws (tuberculo-crusted circinate ulcers of yaws, yaws ulcers; ulcerated nodular lesions which may result in keloid scarring, contractures and pigmentary changes), palmar and plantar hyperkeratotic late yaws (ghoul hand, keratosis palmaris/plantar of yaws, pintoid lesions of yaws, yaws hyperkeratosis with trichophytoid characteristics, yaws keratoderma; polymorphic, ill-defined hyperkeratotic lesions of palms or soles, with tendency to leave scars and pigmentary changes (leukomelanoderma)), mucous membrane and bone—osteitis, periostitis, osteoperiostitis, arthritis, hydrarthrosis (synovitis), ganglion, juxta-articular nodules of late yaws (Lutz-Jeanselme nodules; fibromatous tumour like masses arising beneath skin in vicinity of joints), goundou (hyperkeratotic osteitis of nasal processes of maxilla, frequent in Africa, not seen in some areas), gangosa (ogo, rhinopharyngitis mutilans; ulcerative destructive lesion of nose and hard palate which may cause severe disfiguration); serology

Treatment: penicillin

LEPTOSPIROSIS (AKIYAMI B, AUTUMNAL FEVER, AUTUMN FEVER, CANE-CUTTER'S DISEASE, CANE-FIELD FEVER, FELDFIEBER B, FIELD FEVER, HASAMI FEVER, JAPANESE SEVEN-DAY FEVER, LEPTOSPIROSIS FEBRILIS, MUD FEVER, NANUKAYAMI, PEA-PICKER'S DISEASE, SCHLAMMFIEBER, SLIME FEVER, SPIROCHAETASIS, SWAMP FEVER, SWINEHERD'S FEVER, WATER FEVER): ≈ 300 notified cases/y in Australia (≈ 70% in Queensland; incidence 1.9/100,000; 11% prevalence in banana growers); wherever domestic animals are kept, particularly pigs; survival enhanced by alkaline pH of animal urine, ground water and soil (days to weeks under optimal conditions); concentrated in summer and early autumn; most cases during childhood through middle age because of increased hazards resulting from recreational and occupational activities; transmission by food or water contaminated with animal (eg., rat) urine; incubation period 4-19 d

Agent: *Leptospira interrogans*

Diagnosis: incubation period < 21 d; asymptomatic to severe (with jaundice, anemia, hemorrhage and renal failure; epidemic spirochaetal jaundice, hemorrhagic jaundice, icterogenic spirochaetosis, icterohemorrhagic jaundice, Indonesian Weil disease, infectious spirochaetal jaundice, Landouzy disease, leptospiral hemorrhagic icterus, leptospiral jaundice, leptospirosis icterohemorrhagica, Mathieu disease, ricefield fever, spirochaetosis icterohemorrhagica, spirohematosis icterohemorrhagica, Vasilev disease, Weil icterus, Weil syndrome); typically a biphasic disease, the first phase being an acute febrile illness with leptospiremia and a wide variety of manifestations and the second (urine) phase being less febrile with different manifestations; fever in 75-90% of cases, headache in 66%, severe myalgias in 40-55% (pain on raising extended leg positive predictive value of 67%), stiff neck in 40%, arthralgia in 38%, CSF pleocytosis in 35%, jaundice in 35%, CSF protein increased in 30%, nausea and/or vomiting in 30%, rigours in 19%, rash in 15%, chills in 10%, conjunctivitis or conjunctival hemorrhage in 9%; pulmonary hemorrhage may occur; sudden onset; phase examination and culture of blood (first week of infection), urine (second and third weeks of infection); serology (complement fixation test detects antibodies to group antigen, 4-fold rise in titre diagnostic, titres > 160 in abattoir workers and veterinarians, negative result does not exclude infection; microscopic agglutination test distinguishes antibody to range of serovars; ELISA sensitivity 100%, specificity 93-

100%; Lepto dri-dot test for IgM gives comparable results to ELISA and is faster, more economical and does not require sophisticated equipment or skilled personnel); culture and inoculation of young hamster or guinea-pig with CSF or blood; normochromic anemia with marked neutrophilia; raised erythrocyte sedimentation rate; hematuria in 25%, protein ± casts in urine in 20%, oliguria in 15%; history of exposure to animals (30% dogs, 10% cattle/swine, 8% rodent, 5% wildlife (skunks, raccoons, foxes, opossums, armadillos; horses), occupational (construction, farm, veterinary, abattoir) or recreational (swimming in contaminated water, hunting) exposure (incubation period usually 7-14 d)

Serovar canicola: influenza-like illness followed by meningitis

Serovar hardjo: usually a less severe disease with influenza-like symptoms, slight meningitis, slight renal failure

Serovar icterohaemorrhagiae: jaundice, renal failure, meningitis

Differential Diagnosis: meningitis (initial diagnosis in 30% of cases), hepatitis (initial diagnosis in 15%), encephalitis (initial diagnosis in 10%), fever of unknown origin (initial diagnosis in 9%), pneumonia (initial diagnosis in 2%), influenza (initial diagnosis in 2%)

Treatment: administer within first 4 d of illness; doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 5-7 d (not < 8 y, pregnant or breastfeeding), benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly for 5-7 d, ceftriaxone 25 mg/kg to 1 g i.v. daily for 5-7 d, cefotaxime 25 mg/kg to 1 g 6 hourly for 5-7 d

Prevention and Control: good sanitation

RELAPSING FEVER (BILIOUS TYPHOID FEVER, FEBRIS RECURRENTIS, POLYLEPTIC FEVER, RECURRENT FEVER, SPIRILLUM FEVER, TYPHUS RECURRENS): general term for a systemic borreliosis in man, characterised by alternating febrile and nonfebrile periods, each of the febrile periods ending in crisis

Agents: louse-borne: *Borrelia recurrentis* (carapata, carapata disease, epidemic relapsing fever, European relapsing fever, famine fever, louse-borne relapsing fever, Obermeier relapsing fever, vagabond fever); tick-borne: *Borrelia crocidurae*, *Borrelia duttonii* (D fever, Dutton fever, Dutton relapsing fever, Novy relapsing fever), *Borrelia hermsii*, *Borrelia hispanica*, *Borrelia parkeri*, *Borrelia persica* (miameh disease, miameh relapsing fever, miana disease), *Borrelia turicatae*, several other species

Diagnosis: disease usually begins with rigours and fever, nausea, vomiting, photophobia, arthralgia and myalgia, followed by marked pulmonary signs, hepatosplenomegaly, jaundice and hemorrhagic diathesis; organisms seen in Giemsa or Wright-stained peripheral blood smears or in dark ground microscopy of blood at time of rising temperature in 70% of cases; urinalysis normal to trace of protein, red blood cells, casts; hematocrit 40%, hemoglobin decreased, white cell count 10,000/ μ L, 71% neutrophils (6% bands), 22% lymphocytes, 8% monocytes; ESR 67 mm/h; serum creatinine and alkaline phosphatase normal, serum bilirubin 3.1 mg/dL, SGOT 55 U/mL, SGPT 67 U/mL; CSF protein 95 mg/dL, glucose 75 mg/dL, 950 cells/ μ L, organism seen in 10%; Weil-Felix: OX-19 negative, OX-2 negative, OX-K \geq 1:40 in 90% of louse-borne and 30% of tick-borne; complement fixation test for *Borrelia* positive in 50%; positive animal inoculation in 85% of cases

Louse-borne: splenomegaly in 75% of cases, hepatomegaly in 66%, jaundice in 35%, respiratory symptoms in 35%, CNS involvement in 30%, rash in 9%

Tick-borne: splenomegaly in 40%, rash in 25%, hepatomegaly in 15%, respiratory symptoms in 15%, CNS involvement in 9%, jaundice in 7%

Differential Diagnosis: malaria and dengue (febrile periods shorter), leptospirosis (conjunctival suffusion), rat-bite fever (bite history, inflammatory reaction at site of bite), Rocky Mountain spotted fever (rash typically different—first on limbs, involves palms and soles)

Treatment:

Louse-borne: aqueous procaine penicillin 600,000 U (child: 25,000-50,000 U/kg) i.m. at once and repeated after 12-24 h, tetracycline 500 mg orally as a single dose, erythromycin 500 mg orally as a single dose (infants and young children: 25-50 mg/kg daily in divided doses for 4-5 d), chloramphenicol 500 mg orally 6 hourly for 5 d (child > 2 w: 50 mg/kg daily orally in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg daily in 4 divided doses), doxycycline

Tick-borne: tetracycline 500 mg orally 6 hourly for 5-10 d, doxycycline 100 mg orally 12 hourly for 5-10 d
Treatment may be complicated by a severe Herxheimer reaction.

Prophylaxis (Within 48 h of Tick Bite): tetracycline 1 g/d for 3-5 d

Prevention and Control: lice and tick control

LYME DISEASE (LYME ARTHRITIS): multi-system, immune-mediated, inflammatory disorder that may last several years; erythema chronicum migrans (exanthema; in 26%), followed (in 10%) by disease of central and peripheral nervous system (aseptic meningitis, encephalitis, cranial and spinal neuropathies, especially unilateral or bilateral Bell's palsy, Garin-

Bujadoux-Bunwarti syndrome of meningoencephalitis, cranial neuritis and radiculoneuritis) and (in 6-8%) of heart (atrioventricular conduction defects, myocarditis, pericarditis), by acromodermatitis chronica atrophicans and by solitary or diffuse lymphadenosis benigna cutis, followed (in 50%) by arthritis; hepatitis, nephritis, uveitis, myositis, pulmonary complication (cough, acute respiratory distress, respiratory failure) also occur; recorded from Algeria, Belgium, England, Federal Republic of Germany, France, Italy, Northern Ireland, Scotland, Sweden, USA (95% of vector borne illness; \approx 16,000 cases/y), few cases in Australia; vector *Ixodes ricinus* in Europe, *Ixodes scapularis* in NE, E and midwest USA and *Ixodes pacificus* in western USA, also *Amblyoma americana* and *Dermacentor variabilis*, ? *Ixodes holocyclus* in Australia; principal mammalian host deer; 24-53% of healthy dogs from enzootic areas show serological evidence of infection; ticks acquire infection from rodents (white-footed mice and eastern chipmunks); transplacental transmission documented in child with congenital heart defect; incubation period 1 w stage 1, 5-6 w stage 2

Agent: *Borrelia burgdorferi* group (*Borrelia afzelii* associated with erythema migrans and acrodermatitis chronica atrophicans, *Borrelia burgdorferi* and genospecies *Borrelia garinii* associated with extracutaneous symptoms)

Diagnosis: single erythema migrans 3-30 d after tick bite, with myalgia, arthralgia, fever, headache, fatigue, regional lymphadenopathy; at 1-12 w after tick bite, erythema migrans may become multiple, with neck pain, meningitis, cranial neuritis (facial palsy), radiculoneuritis, carditis (variable heart block), eye involvement; arthritis and/or chronic CNS involvement may develop after \approx 2 mo; may have pulmonary edema, cardiomegaly on chest X-ray; quantitative PCR using skin biopsy (sensitivity 81%), borreliacidal antibody test (sensitivity 79%, specificity 100%), acute + convalescent phase serology (sensitivity 68%), nested PCR (sensitivity 64%); circulating immune complexes during erythema chronicum migrans; patients with increased IgM and cryoglobulins containing IgM at risk of developing arthritis; cryoglobulins and immune complexes found in synovial fluid, but not serum, during arthritis

Treatment:

Erythema Chronicum Migrans: tetracycline 250 mg orally 6 hourly (child after completion of dentition: 40 mg/kg to 1 g orally daily) for 10-20 d; phenoxymethylpenicillin 500 mg orally 6 hourly (< 12 y: 25-50 mg/kg orally daily in 4 divided doses) for 10-20 d, erythromycin 250 mg orally 6 hourly (younger children: 30 mg/kg to 1 g orally daily in divided doses) for 10-20 d, doxycycline 1-2 mg/kg to 100 mg twice a day, amoxicillin 50 mg/kg/d to 1500 mg/d in 3 divided doses, cefuroxime axetil 10-15 mg/kg to 500 mg twice a day, clarithromycin 500 mg twice a day, azithromycin 500 mg on day 1 and then 250 mg 4 times a day

Arthritis: doxycycline 100 mg orally 12 hourly for 3-4 w, amoxicillin 500 mg orally 8 hourly (child: 40 mg/kg orally daily in 3 divided doses) for 4 w, ceftriaxone 2 g (child: 50-80 mg/kg) i.v. daily for 14-21 d, benzylpenicillin 20-24 MU (child: 250,000-400,000 U/kg) i.v. daily in divided doses for 21 d, benzathine penicillin 2.4 MU i.m. weekly for 3 w

Bell's Palsy, Mild Cardiac Disease: doxycycline 100 mg orally 12 hourly for 4 w, amoxicillin 250-500 mg orally 8 hourly (child: 20-40 mg/kg orally daily in 3 divided doses) for 4 w, cefuroxime axetil 10-15 mg/kg to maximum 500 mg twice a day, macrolides

Meningoencephalitis, Heart Block: oral prednisone + ceftriaxone 2 g (child: 50-80 mg/kg) i.v. daily for 14 d or benzylpenicillin 20-24 MU (child: 250,000-400,000 U/kg) i.v. daily in divided doses or oral or i.v. doxycycline

Prophylaxis: vaccine 79-92% efficacy (not cost effective unless prevalence > 2% per season)

REITER SYNDROME (ARTHRITIC SPIROCHAETOSIS, BLENORRHAGIC ARTHRITIS, CONJUNCTIVOURETHRAL-SYNOVIAL SYNDROME, ENTEROARTICULAR SYNDROME, FIESSINGER-LEROY-REITER SYNDROME, INFECTIOUS UROARTHRTIS, NONGONOCOCCAL URETHRITIS WITH CONJUNCTIVITIS AND ARTHRITIS, OCULOURETHROARTICULAR SYNDROME, POSTDYSENTERIC RHEUMATOID, POSTDYSENTERIC SYNDROME, POSTENTERIC RHEUMATOID, REITER DISEASE, REITER TRIAD, REITER RHEUMATISM, SPIROCHAETOSIS ARTHRITICA, URETHRAL ARTHRITIS, URETHRAL RHEUMATISM, URETHROARTHRTIS, URETHROOCULOARTICULAR SYNDROME, URETHROOCULOSYNOVIAL SYNDROME, WAELSCH URETHRITIS)

Agents: unknown; has followed epidemics of diarrhoea due to *Shigella*, *Salmonella*, *Yersinia* and *Cyclospora*; gonococcal and nongonococcal urethritis (especially that due to *Chlamydia trachomatis*) is also a common antecedent, particularly in young males having HLA B27 histocompatibility antigen

Diagnosis: triad of inflammatory oligoarthritis, ocular inflammation and sterile urethritis; may be fever, ulceration of glans penis (balanitis circinata) and oral mucosa, palmar and plantar lesions (keratoderma blenorrhagica), nausea, anorexia, erythema, myocarditis, pericarditis, neuritis

Treatment: symptomatic

WHIPPLE'S DISEASE: rare (< 1000 cases worldwide reported to date) systemic infectious disease; 97% Caucasian

Agent: *Tropheryma whippelii*

Diagnosis: arthralgia (initial presentation in 67%), epigastric pain (initial presentation in 15%), lethargy, anemia and low grade fever (initial presentation in 14%), neurological symptoms (initial presentation in 4%); later, diarrhoea with fetid, watery, steatorrheic stools, malabsorption of fat, protein, carbohydrate, vitamins and minerals, and weight loss in 85%; hyperpigmentation; progresses to cardiac and neurological deficits (headaches, lethargy, visual disturbances, auditory disturbances, gait disturbances, disturbed sleep, impotence, convulsions) and occasionally eye problems (edema in papilla, retinal bleeding, uveitis, corneoretinitis, keratitis); immunohistochemical analysis or PCR of tissue; PCR of CSF, peripheral blood; multiple rounded or sickle-shaped PAS diastase resistant inclusions in lamina propria macrophages in small bowel biopsy

Differential Diagnosis: AIDS, Crohn's disease, disseminated histoplasmosis, immunocomplex disease, immunodeficiency disease, infectious arthritis (shigellosis, salmonellosis, yersinosis, *Campylobacter* infection, amoebiasis), macroglobulinemia Waldenström, *Mycobacterium avium-intracellulare* infection, neoplasia (especially non-Hodgkin's lymphoma), rheumatoid arthritis, *Corynebacterium equi* infection, sarcoidosis, ulcerative colitis, prodromal stage of measles (Warthin-Finkeldey giant cells), malakoplakia (Michaelis-Gutmann bodies staining for calcium and iron in macrophages)

Treatment: parenteral cotrimoxazole or streptomycin 1 g/d + benzylpenicillin 1.2 MU/d for 2 w, then cotrimoxazole 160/800mg for 1-2 y

SARCOIDOSIS (BENIGN LYMPHOGANULOMATOSIS, BESNIER-BOECK-SCHAUMANN DISEASE, BESNIER-BOECK-SCHAUMANN SYNDROME, BOECK DISEASE, BOECK LUPOID): generalised granulomatous disease; may affect any part of body but, most frequently, lesions are found in lymph nodes, liver, spleen, lungs, skin (Besnier-Boeck disease, Boeck sarcoid, Hutchinson-Boeck disease), eyes, tonsils and bone marrow; causes defects in cell-mediated immunity, with increased susceptibility to *Mycobacterium tuberculosis*, *Nocardia* and fungi

Agent: ? *Mycobacterium* species

Diagnosis: clinical; histology and immunohistology

Treatment: steroids

CANDIDIASIS (MONILIASIS): ≈ 240 deaths/y in USA; bronchopulmonary, cutaneous, genital, oral, urinary, endocarditis, chronic and sub-acute fever

CHRONIC MUCOCUTANEOUS CANDIDIASIS: T-cell immunodeficiency (fairly specific—*Candida* and some antigenically close fungal genera; thus different from other known immunodeficiencies; since other host defences are normal, systemic candidal infection is not a problem); candidal infection of mucous membranes, skin, hair and nails; endocrinopathy in ≈ 50% (usually several years after candidiasis; most common hypoparathyroidism, Addison's disease; cause autoantibodies); familial in ≈ 20%; other manifestations autoimmunity (eg., pernicious anemia, alopecia, depigmentation, iron-deficiency anemia); early onset chronic mucocutaneous candidiasis most severe form, hypoparathyroidism and Addison's disease very rare; late onset chronic mucocutaneous candidiasis mild, in older individuals, no endocrinopathies; familial chronic mucocutaneous candidiasis autosomal recessive, mild to moderate, endocrinopathies uncommon; juvenile familial endocrinopathy with candidiasis mild to moderate, hypoparathyroidism and/or Addison's disease usually present; other predisposing conditions diabetes mellitus, oral contraceptives, broad spectrum antimicrobials, treatment with immunosuppressive drugs, ? gastrointestinal reservoir

Agent: *Candida*

Diagnosis: micro (wet film, Gram stained film) and culture of appropriate specimen

Treatment: ketoconazole 200-400 mg orally daily, fluconazole 50-100 mg orally daily

SYSTEMIC CANDIDIASIS: associated with antibiotic administration, intravenous or intraarterial catheters or needles, corticosteroid administration (infection in brain and kidneys), use of immunosuppressive agents, neutropenia (disseminated infection), parenteral nutrition (eye may be affected), ambulatory peritoneal dialysis (peritonitis reported), heroin addiction (septicemia followed by folliculitis, bone and joint lesions, ocular abnormalities such as abscess or hypopyon), AIDS

Agent: *Candida*

Diagnosis:

Acute: cutaneous lesions, myositis, myocarditis, acute renal failure, pulmonary infiltration (often multiple), hypotension, fungemia, granulocytopenia, high mortality despite therapy

Chronic: calcified hepatic and splenic abscesses, lesions usually detectable on computerised axial tomography and magnetic resonance imaging during granulocytopenia, elevated level of serum alkaline phosphatase, low mortality urine micro (blastospores and hyphae in ≈ 1/3) and culture (≈ 80% positive), arterial blood culture (biphasic medium), sterile site culture or smear; precipitin test; agglutination titre (commercially available antigen), counterimmunoelectrophoresis (sensitivity 58%, specificity 96%), immunodiffusion (restricted availability; detects antigen and antibody)—all highly controversial tests with many false positive and negative results; antigen in urine or serum experimental; ELISA (antigen, antibody), latex agglutination, radioimmunoassay (sensitivity 71%, specificity 66%), indirect

hemagglutination (sensitivity 97%, specificity 60%), indirect immunofluorescence (sensitivity 91%, specificity 50%); increased arabinitol/creatinine ratio experimental

Treatment: ketoconazole 200-400 mg orally (< 20 kg: 50 mg; 20-40 kg: 100 mg) once daily, fluconazole 200-400 mg (child: 1-4 mg/kg) orally daily, amphotericin B under expert supervision ± flucytosine (not *Clavispora lusitanae*); removal of catheters, needles, prostheses, valves and vegetations

Secondary Prophylaxis and Maintenance: fluconazole 50-200 mg orally daily, ketoconazole 200 mg orally daily

DISSEMINATED TRICHOSPORON INFECTION: nonspecific febrile illness or pneumonia in immunosuppressed (especially neutropenic) patients (especially with acute myelogenous leukemia); lungs, liver, spleen, blood, urine, bone marrow, kidney, skin, heart, trachea, esophagus, adrenal; case-fatality rate 74%

Agent: *Trichosporon beigelii*, *Trichosporon asahii*

Diagnosis: blood cultures, culture and histology of specimens

Treatment: amphotericin B 1-1.5 mg/kg/d + flucytosine 800 mg/d; fluconazole; itraconazole for 20 mo in chronic cases

DISSEMINATED COCCIDIOIDOMYCOSIS: rare (7% of total); more common in infants, elderly, male, Filipino, African-American, native American, Hispanic, Oriental, and patients with impaired immunity (second ½ of pregnancy and postpartum, malignancy, chemotherapy, steroid use, seropositive for *human immunodeficiency virus*); skin (most common), meninges (most serious, 40% case-fatality rate), viscera (liver, spleen, prostate, adrenals), bones and joints, lymph nodes, serous membranes (peritoneum, pericardium)

Agent: *Coccidioides immitis*

Diagnosis: fever in 95%, pulmonary disease in 90%, weight loss in 60%, anemia in 50%, hepatosplenomegaly in 10-20%, meningitis in 10%, skin lesions in 5%; antibody detection often unreliable in immunocompromised host; EIA using a combination of antigens method of choice; latex agglutination (IgM) detects early acute disease, false positive results occur, positive results must be confirmed with immunodiffusion tube precipitin or immunodiffusion complement fixation test; immunodiffusion tube precipitin test (IgM) useful for diagnosis of early acute illness; immunodiffusion complement fixation test (IgG) useful for diagnosis of localised and disseminated disease, qualitative screen, may be quantitative; complement fixation test (IgG) diagnostically and prognostically valuable, titres of 1:8 diagnostic, changes in titres diagnostic, when titres of 1:2-1:8 are revealed confirmation by immunodiffusion complement fixation test necessary; coccidioidin skin test; negative skin test and serum complement fixation test titre > 1:66 indicate large likelihood; micro (30-80 µm round spherules containing 2-5 µm endospores reproducing by fission) and culture of appropriate specimen obtained directly from tissues affected or fluid from these tissues

Treatment:

Meningitis:

Induction:

Severe: i.v. amphotericin B up to 1.5 mg/kg/dose + amphotericin B + hydrocortisone intrathecally

Mild: fluconazole

Maintenance: fluconazole

Skin, Lymph Nodes: amphotericin B 1-1.5 mg/kg/d to total 1.5-2 g i.v. ± local irrigation with 10% solution or local paste and/or excision

Bones, Viscera, Genitourinary Tract, Peritonitis:

Severe or Potentially Severe Disease: amphotericin B (1-1.5 mg/kg (initial up to 50 mg) i.v. to total 1-3 g ± local irrigation and/or surgery

Mild to Moderate Stable Disease: ketoconazole 400 mg orally for 3 mo to several years, fluconazole 400 mg orally initial then 400-800 mg for 3 mo to several years, itraconazole 400 mg orally

Nondisseminated Extracutaneous Disease in Immunocompetent Host: ketoconazole

CRYPTOCOCCOSIS (EUROPEAN BLASTOMYCOSIS, TORULOSIS): sporadic, worldwide; incidence 8/M/y in Australia (from 2/M/y in Tasmania to 44/M/y in Northern Territory); associated with HIV (50%) and other immunodeficiency (21%); Hodgkin's disease, sarcoidosis, collagen disease, carcinoma, treatment with corticosteroids and immunosuppressive agents, adrenal hyperplasia, renal transplantation under treatment with azathioprine and corticosteroids); meningitis, pneumonia, pericarditis, hepatic failure, osteomyelitis, arthritis, subcutaneous and cutaneous lesions, paravertebral abscesses and cord compression, muscle weakness

Agent: 84% *Cryptococcus neoformans* var *neoformans*, 12% *Cryptococcus gattii*, 5% unknown biotype, rarely *Cryptococcus albidus*, *Cryptococcus laurentii*

Diagnosis: India ink micro preparation (positive in 33-60%), culture (usually growth in 4-7 d, may take 4-6 w or require hypertonic medium) of spinal fluid (46-100% positive), blood (lysis-centrifugation blood culture; 48-89% positive), bronchoalveolar lavage (75-100% positive), pus, sputum (50% positive), pleural fluid (50% positive), urine (17% positive), peritoneal dialysate (100% positive), bone marrow (100% positive); latex slide agglutination test (commercially available) for antigen in CSF, blood, urine (positive in 86-90%; may be positive when India ink test is negative; highly sensitive and specific for diagnosis of meningeal and disseminated forms; prozone-like effect controlled by dilution of specimen or treatment with pronase; rare false negatives with capsule-deficient *Cryptococcus neoformans* in patients with AIDS; rare false positives with *Capnocytophaga canimorsus* septicemia, patients with malignancy, *Trichosporon beigeli* disseminated infection); tube agglutination, charcoal particle agglutination, indirect fluorescent tests for antibody in serum (positive in 28%); complement fixation test; meningitis: CSF cells usually < 800/ μ L, either neutrophils or lymphocytes predominating, protein increased (rarely > 800 mg/dL), glucose decreased, chloride < 105 mEq/L

Treatment:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w \pm flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

TORULOPSIOSIS: superinfection during treatment with cytotoxic and/or immunosuppressive drugs + corticosteroids (similar to systemic candidiasis) and in diabetes mellitus, particularly with acidosis (pyelonephritis; occasionally pneumonia and/or empyema)

Agent: *Candida glabrata*

Diagnosis: direct mount and culture of urine, sputum

Treatment: amphotericin B \pm flucytosine

GEOTRICHOSIS: neutropenic leukemics; blood, urine, skin, lungs, heart, liver, spleen, lymph nodes, bone marrow, kidney

Agent: *Geotrichum candidum*

Diagnosis: micro and culture of sputum, pus from oral lesions, feces

Treatment: amphotericin B

BLASTOMYCOSIS (GILCHRIST'S DISEASE, NORTH AMERICAN BLASTOMYCOSIS): uncommon, sporadic in N and Central America, recently recorded in Spain; transmission by inhalation; 75% of patients not immunocompromised

Agent: *Ajellomyces dermatitidis*

Diagnosis: microscopy (visualisation of buds in wet preparation) and culture of scrapings from cutaneous lesions and pus from abscesses on periphery of lesion, sputum, urine, CSF; complement fixation test (usually positive only in systemic disease; sensitivity 40%, specificity 100%; predictive value positive 100%, predictive value negative 81%), immunodiffusion (sensitivity 66%, specificity 100%, predictive value positive 100%, predictive value negative 88%) and skin tests (frequently unhelpful), ELISA using purified antigen A (sandwich sensitivity 88%, specificity 100%, predictive value positive 100%, predictive value negative 98%; indirect sensitivity 80%, specificity 94%, predictive value positive 94%, predictive value negative 93%; false positives in some cases of histoplasmosis and sporotrichosis), radioimmunoassay (sensitivity 85%, specificity 100%, predictive value positive 100%, predictive value negative 92%); hypochromic anemia with neutrophilia, raised erythrocyte sedimentation rate

Treatment:

Mild Cases: itraconazole, ketoconazole 200-800 mg orally daily for up to 1 y, amphotericin B to total dose of 2 g

Severe Cases: amphotericin B under expert guidance, hydroxystilbamidine if amphotericin B fails

HISTOPLASMIOSIS: reported from 130 widely scattered countries; endemic in Ohio Valley, Mississippi Valley and Appalachian Mountains; in Australia, patients infected from a chicken coop and associated with a cave in NSW; 'cave disease' contracted by visitors to caves inhabited by bats; African form in endemic belt through central Africa; \approx 300 cases (\approx 60 deaths)/y in USA; 50-99% asymptomatic, 1-50% self-limited; pulmonary infections (tuberculosis-like disease of lungs; acute 60% of symptomatic, chronic 10%), pericarditis (10% of symptomatic), disseminated (immune defect, leukemia, Hodgkin's disease; in 75% of symptomatic patients on immunosuppression (especially steroids); < 0.5% of AIDS patients; 10% of symptomatic patients overall), arthritis and erythema nodosum (5% of symptomatic), bone marrow infections, endocarditis,

oronasopharyngeal lesions, lymph gland infections, mediastinal granulomas, meningitis (8% of cases in AIDS and ¼ of those with disseminated disease)

Agent: *Histoplasma capsulatum var capsulatum*, *Histoplasma capsulatum var duboisii* (tropical Africa; predilection for visceral involvement, higher case-fatality rate)

Diagnosis: incubation period > 21 d; fever in 95%, weight loss in 90%, anemia in 70%, pulmonary disease in 50%, hepatosplenomegaly in 25%, lymphadenopathy in 20%, skin lesions in 5-10%, meningitis in < 1%; microscopy (1-5 µm round to oval budding cells; rapid but low sensitivity and identification errors) and culture (insensitive in cases of self-limited disease, may require 2-4 w of incubation to produce growth, may require invasive procedure for obtaining specimen) of material from cutaneous and mucosal lesions, sputum, gastric washings, biopsy of oronasopharyngeal lesions, lymph glands, bone marrow; serological tests for antibody sensitive in chronic and self-limited disease, falsely negative early in infection, falsely positive in cases of other fungal disease, may remain positive for years; HP antigen detection sensitive (80-92%) in cases of disseminated disease but poor sensitivity in chronic and self-limited disease, rapid turnaround time, level of HP antigen decreases after treatment, increases with relapse); immunodiffusion (active cases 2% H positive, 10% H and M positive; 70% of all cases M positive; detection of M precipitin may be influenced by skin test), complement fixation test (commercially available; yeast antibody 90% sensitivity, nonspecific at low titres; histoplasmin antibody 80% sensitivity, more specific; skin test may interfere), latex agglutination (detects early acute disease, most chronic cases negative), radioimmunoassay detection of antigen in serum and in urine (disseminated cases 90% urine and 50% serum positive, valuable for immunodeficient patients; nondisseminated cases urine 50-75% negative, some cross-reactivity); skin test not useful diagnostically, useful epidemiologically, may confuse interpretation of serological tests by presence of booster effect; hypochromic anemia with leucopenia; in children, lymphocytosis with atypical mononuclears

Disseminated: fever in 70% of cases, weight loss in 66%, pulmonary symptoms in 50%, thrombocytopenia in 50%, anemia in 45%, splenomegaly in 40%, oral lesions in 25%, leucopenia in 25%, neurologic symptoms in 20%, leucocytosis in 10%; positive cultures from 90% of oral lesions, 70% of lymph nodes, 70% of bone marrows, 60% of sputum specimens, 55% of liver biopsies (granulomas in 70%, organism seen microscopically in 40%), 55% of blood cultures, 45% of CSF specimens and 45% of urine specimens; 1/3 of patients with negative blood cultures have positive bone marrow; none with negative bone marrow have positive blood culture; 40% of patients with positive urine culture have normal renal function

Treatment: not indicated in acute pulmonary, pericardial, rheumatologic, coin lesions, fibrous mediastinitis; indicated in disseminated, chronic pulmonary, acute respiratory distress syndrome, symptomatic mediastinal granuloma, persistent (> 1 mo) acute pulmonary

Induction:

Mild: itraconazole 400 mg/d for 3 mo, fluconazole 800 mg/d for 3 mo

Severe: amphotericin B 0.7 mg/kg/d to 50 mg/d + prednisone 60 mg daily for 2 w

Maintenance: itraconazole 200-400 mg/d for 12 w (acute pulmonary), 12-24 mo (chronic pulmonary), 6-18 mo (disseminated in non-AIDS), life (disseminated in AIDS), 6-12 mo (granulomatous mediastinitis); fluconazole 400 mg/d for life

Nondisseminated Extracutaneous Disease in Immunocompetent Host: ketoconazole 400 mg orally (child < 20 kg: 50 mg; 20-40 kg: 100 mg, > 40 kg: 200 mg) daily for 6-12 mo, cotrimoxazole 160/800 mg orally 12 hourly for 4-5 w

PARACOCCIDIOIDOMYCOSIS (KUTZ-SPLENDRE-DE ALMEIDA'S DISEASE, SOUTH AMERICAN BLASTOMYCOSIS): restricted to S America and Central America, including Mexico; may not appear till long after acquisition; mucous membrane of mouth most frequently affected area; lymph nodes affected in almost all cases; lungs affected in high proportion of cases

Agent: *Paracoccidioides brasiliensis*

Diagnosis: microscopy and culture of scrapings from affected skin (paracoccidioidal granuloma) and mucous membranes, pus from fluctuant nodules, sputum; complement fixation test (usually positive only in systemic cases); iron deficiency anemia with neutrophilia and raised erythrocyte sedimentation rate; eosinophilia sometimes

Treatment: ketoconazole 400 mg (child < 20 kg: 50 mg; 20-40 kg: 100 mg; > 40 kg: 200 mg) orally daily for 3 mo then 200 mg daily for 9-12 mo, sulphonamides, amphotericin B under expert supervision then maintenance ketoconazole as above, miconazole

SPOROTRICHOSIS: worldwide; up to 1/1000 in rural areas of Central and S America; cutaneous lymphatic (most common form; firm subcutaneous nodules), fixed cutaneous (no lymphatic involvement), localised extracutaneous (skeletal most common; pulmonary can mimic tuberculosis), disseminated (rare; immunosuppressed patients)

Agent: *Sporothrix schenckii*

Diagnosis: wet preparation micro, Gram stain (note that cigar-shaped yeast phase cells may resemble diphtheroids), methenamine silver stain, fungal culture of aspirate or purulent exudate or biopsy of cutaneous or mucosal lesion, sputum, bronchial aspirate, lung biopsy, synovium, synovial fluid; blood cultures; serology (latex agglutination, tube agglutination)

Treatment:

Cutaneous-lymphatic Form: surgery; potassium iodide up to 3-4 g 8 hourly as a saturated (1 g/mL) solution continuing for 1 mo after clinical cure, ketoconazole 200-400 mg orally (< 20 kg: 50 mg; 20-40 kg: 100 mg) daily for 3-6 months, itraconazole 100 mg orally daily with meals for 120 d (not in pregnancy)

Pulmonary and Disseminated Forms: amphotericin B to total dose 2-3 g, ketoconazole 400-500 mg daily

Maintenance: itraconazole

ASPERGILLOSIS: in farmers, poultry workers and immunocompromised; 151% increase in annual incidence (1.91 to 4.8/M) between 1970 and 1976 in USA; associated with use of corticosteroids and/or antimicrobials, immunosuppressive agents, leucopenia; acute lymphocytic leukemia in 40% of patients, acute myelogenous leukemia in 20%, chronic myelogenous leukemia in 10%, Hodgkin's disease in 5%, lymphoma in 5%, other diseases of lymphoreticular system (aplastic anemia, chronic lymphocytic leukemia, mycoides fungoides, multiple myeloma) in 10%, 'autoimmune' disease (systemic lupus erythematosus, polyarteritis nodosa) in 5%; 95% lung, 20-70% gastrointestinal tract, 15-50% brain, 10-40% liver, 10-40% kidney, 10-30% thyroid; also heart, sinus, eye, spleen, diaphragm, tongue, testis, rare meningitis in AIDS

Agents: *Aspergillus fumigatus* (75%), *Aspergillus flavus*, *Aspergillus glaucus*, *Aspergillus terreus*, *Aspergillus ustus*

Diagnosis: visualisation of hyphae; confirmed by culture

Aspergilloma: hyphae in mass in bloody sputum from lung; sputum and biopsy culture

Invasive Aspergillosis: 60% of isolates in allogeneic bone marrow transplant recipient, 60% in neutropenics, 50% in persons with hematological cancer, 30% in malnutrition, 20% in HIV infection, 20% in solid organ transplantation, 20% in corticosteroid users, 10% in those with underlying pulmonary disease; only 38% alive 3 mo after diagnosis; sputum culture in neutropenic patient; KOH preparation and culture of biopsy of sterile site; sandwich ELISA for galactomannan on serum (sensitivity 94%, specificity 85%), counterimmunoelectrophoresis (precipitating antibodies), radioimmunoassay (usually positive), immunodiffusion (restricted availability; positive result suggests diagnosis if serial specimens are obtained), complement fixation test, precipitins; serial quantitative assay for antibodies may be better than culture (recovered from blood in < 5%, cutaneous lesions in < 10%), or attempts to detect antigen in immunocompromised patients; halo sign on CT indicative of invasive pulmonary aspergillosis

Treatment:

Severe: amphotericin B under expert supervision (rate of response 55%) ± flucytosine or rifampicin; reduce immune suppression

Mild or Moderate: itraconazole

NEOSARTORYA INFECTIONS: occasional opportunistic infections

Agents: *Neosartorya fischeri* systemic infection in transplant recipients, mixed pulmonary infection in patient with multiple myeloma; *Neosartorya pseudofischeri* localised and invasive infections; *Neosartorya hiratsukae* cerebral infection

Diagnosis: visualisation of hyphae; confirmed by culture

Treatment: itraconazole 400 mg daily

ZYCOMYCOSIS: lung, spleen, kidney, CNS, gastrointestinal tract, heart, sinus, eye, liver, pancreas; rhinocerebral associated with diabetes mellitus (with or without associated acidosis or hyperglycemia; 75% of cases), hematological neoplasia, malnutrition, severe (third degree) burns, immunosuppression, following homotransplantation, uremia; cerebral associated with pulmonary or disseminated fungal infection, hematologic malignancy; pulmonary associated with leukemia, lymphoma and leucopenia (75% of cases), diabetes mellitus (with or without associated acidosis or hyperglycemia), renal failure, third degree burns, corticosteroid therapy, cytotoxic therapy; gastrointestinal rare, associated with protein-calorie malnutrition (especially children in tropical and subtropical countries with kwashiorkor), diabetes mellitus, hematological malignancy, uremia, acidosis due to diarrhoea, amoebic colitis, therapy with corticosteroids, ulcerative colitis, abdominal surgery; disseminated associated with leukemia, lymphomas, anemias, multiple myeloma, solid tumours, agranulocytosis, uremia, third degree burns, intravenous narcotic abuse, hemodialysis and deferoxamine, organ transplantation, wounds, neonatal state, lung disease; cutaneous associated with diabetes mellitus, burns, under Elastoplast dressings, AIDS; localised following surgery rare—brain abscess following neurosurgery, prosthetic valve, vascular graft; renal associated with chronic or acute renal failure

Agents: *Rhizopus*, *Absidia*, *Mucor*, rarely *Cunninghamella elegans*, *Cunninghamella bertholetiae*, *Basidiobolus haptosporus*

Diagnosis: temperature > 38.3°C in 61% of cases; histology and culture of infected tissue (necrotic lesion or sterile site)

Treatment: aggressive surgical debridement; amphotericin B 1 mg/kg/d i.v. for 2-3 mo; control of underlying predisposing conditions (diabetes, immunosuppression, immunodeficiency); hyperbaric oxygen

PENICILLIOSIS: in acute lymphoblastic leukemia; focal infections and fatal, progressive disseminated infection (lungs, heart, blood, mediastinum, superior vena cava)

Agent: *Penicillium*, including *Penicillium marneffeii* in AIDS (geographic distribution limited to SE Asia)

Diagnosis: fever in 99%, weight loss in 75%, anemia in 75%, skin lesions in 70%, pulmonary disease in 50%, hepatosplenomegaly in 50%, lymphadenopathy in 40-50%, meningitis very rare; Grocott methenamine silver, periodic acid Schiff and Wright's staining (1-8 μ m pleomorphic elongated cells reproducing by fission) and culture at 25°C and 37°C of biopsies, bone marrow aspirate, touch smears of skin specimens

Penicillium marneffeii: fever, marked weight loss, anemia, generalised papular skin lesions, lymphadenopathy, hepatomegaly

Treatment:

Severe: amphotericin B

Mild: itraconazole; flucytosine 150 mg/kg/d + ketoconazole 400 mg/d for 90 d

Maintenance: itraconazole

FUSARIOSIS: in immunocompromised, especially acute leukemia; skin, lung, blood, kidney, sinus, eye, gastrointestinal tract, heart, spleen, CNS, liver, pancreas, urine, i.v. line tip, bone marrow, testis; death rate approaching 100%

Agents: *Fusarium solani*, *Fusarium oxysporum*, *Fusarium chlamydosporum*, *Gibberella fujikuroi*, *Fusarium anthophilum*, *Gibberella intermedia*

Diagnosis: persistent fever, skin lesions (ecthyma-like lesions, target lesions, multiple subcutaneous nodules; 60% of patients), orofacial involvement, fungemia, myalgias; blood cultures positive in 60%; histology and culture of skin biopsies

Treatment: control of underlying disease and recovery from neutropenia (granulocyte infusions + GM-CSF); surgical resection; voriconazole; amphotericin B 1.0-1.5 mg/kg daily, liposomal amphotericin B 5-15 mg/kg daily

TRICHOTHECENE MYCOTOXINS: used as biowarfare agents

Agent: *Fusarium*

Diagnosis: cutaneous exposure causes rapid erythema, blistering and necrosis of skin; eye exposure causes tearing, conjunctivitis and blurred vision; respiratory exposure causes nasal burning and epistaxis, sore throat, cough, dyspnoea and chest pain; high doses cause nausea, burning skin, lethargy and incoordination within minutes, bleeding, cough, dyspnoea, chest and abdominal pain, diarrhoea and blistering of skin within hours; severe poisoning causes extensive mucosal bleeding, hypothermia and shock; gas chromatography, mass spectrometry, ELISA or radioimmunoassay on urine

Treatment: none proven; gastric infusion of activated charcoal and high doses of corticosteroids beneficial in mice

Prevention: protective clothing and face masks

SYSTEMIC HANSENULA INFECTIONS: immunosuppression, use of intravenous device, previous treatment with antibacterial drugs; 59% from blood, 18% from CSF, 6% from mediastinal lymph nodes, 6% from endocardium, 6% from kidney, 6% from spleen

Agents: 92% *Hansenula anomala*, 8% *Pichia angusta*

Diagnosis: blood cultures, histology and culture of biopsy specimens

Treatment: amphotericin B

SYSTEMIC BIPOLARIS INFECTIONS: in multiple myeloma; sinus, lungs

Agent: *Bipolaris*

Diagnosis: histology and culture of biopsy specimens

Treatment: amphotericin B (usually not successful), itraconazole

SYSTEMIC PSEUDALLESCHERIA BOYDII INFECTIONS: cancer patients on steroids, chronic pulmonary disease, hematological malignancy during therapy, neutrophil dysfunction, near-drowning; heart, blood, brain, lungs, kidney

Agent: *Pseudallescheria boydii*

Diagnosis: culture of blood, sputum and urine

Treatment: ketoconazole, fluconazole, flucytosine

SACCHAROMYCES CEREVISIAE INVASIVE INFECTIONS: severe immunosuppression, prolonged hospitalisation, prior antibacterial therapy, prosthetic cardiac valves; pneumonia, liver abscess, sepsis, disseminated infection with cardiac tamponade

Agent: *Saccharomyces cerevisiae*

Diagnosis: smear and culture of biopsy

Treatment: amphotericin B to total dose 300-1400 mg

SYSTEMIC *DIPODASCUS CAPITATUS* INFECTIONS: leukemia; pneumonia, focal infection of liver, spleen, kidney, brain, skin, oesophagus, stomach, bacteremia, myocarditis, endocarditis

Agent: *Dipodascus capitatus*

Diagnosis: blood cultures; smear and culture of sputum, sinus, biopsy

Treatment: prolonged amphotericin B + flucytosine

SYSTEMIC *EXOPHIALA DERMATITIDIS* INFECTION: pneumonia, brain abscess; chronic granulomatous disease

Agent: *Exophiala dermatitidis*

Diagnosis: micro and culture of biopsy

Treatment: surgical resection of pulmonary lesion; amphotericin B, flucytosine, ketoconazole + transfused white cells, followed by prolonged course of fluconazole

SCEDOSPORIOSIS: posttraumatic cellulitis, septic arthritis and osteomyelitis, onychomycosis, otomycosis, fungal balls in paranasal sinuses, lungs and bronchi in immunocompetent; endophthalmitis in i.v. drug use; systemic infection (endophthalmitis, endocarditis, metastatic abscesses) in immunocompromised

Agents: *Scedosporium apiospermum*, *Scedosporium prolificans*

Diagnosis: micro and culture of appropriate specimen

Treatment: surgery; itraconazole; amphotericin B in lipid 5-15 mg/kg/d

SYSTEMIC PROTOTHECOSIS: gallbladder, liver, duodenum

Agents: *Prototheca wickerhamii*, *Prototheca zopfii*

Diagnosis: elevated IgG, elevated erythrocyte sedimentation rate, eosinophilia, raised liver enzymes; microscopy and culture of biopsy, stool

Treatment: short course of amphotericin B followed by oral ketoconazole for 3 mo

DISSEMINATED *PNEUMOCYSTIS JIROVECI* INFECTION: AIDS, hematologic malignancy, lymphoreticular malignancy, immunosuppressive therapy; 46% lymph nodes, 36% bone marrow, 36% spleen, 32% liver, 18% gastrointestinal tract, 18% retina, 16% adrenal, 16% thyroid, 14% kidneys, 12% vessels, 10% heart, 8% pancreas, 6% external auditory canal, 4% brain, 4% thymus, 4% pleura, 2% middle ear/mastoid, 2% hard palate, 2% ureters, 2% Virchow-Robin spaces, 2% diaphragm, 2% pericardium, 2% retroperitoneal tissue

Agent: *Pneumocystis jiroveci*

Diagnosis: Wright-Giemsa, Papanicolaou, Gomori methenamine silver stain, direct immunofluorescence of appropriate specimen

Treatment: cotrimoxazole 5/25 mg/kg oral or i.v. 6-8 hourly for 3 w then 80/400-160/800 mg orally daily or 160/800 mg orally 3 or 4 d/w or 12 hourly 2 d/w; pentamidine isethionate 4 mg/kg to 300 mg i.v. daily for 3 w then 300 mg i.v. or aerosolised every 2-4 w

Maintenance Therapy in HIV/AIDS: cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3 times weekly, dapsone 100 mg orally 3 times weekly, pentamidine 300 mg i.v. or aerosolised every 2-4 w

Prophylaxis (CD4 Cell Count < 200/ μ L): cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3-4 times a week or 12 hourly twice a week, pentamidine 300 mg i.v. or aerosolised every 2-4 w, dapsone 100 mg orally 3 times a week

VISCERAL LEISHMANIASIS (ASSAM FEVER, BUNDWAN FEVER, CACHECTIC FEVER, CACHEXIAL FEVER, DEATH FEVER, DUM-DUM FEVER, INFANTILE LEISHMANIASIS, KALA-AZAR, NONMALARIA REMITTENT FEVER, PONOS, SAHIB DISEASE): endemic in 62 countries including India, Mediterranean, East Africa, Middle East, S Africa, China, Latin America; 500,000 new cases/y worldwide, with 41,000 recorded deaths; human (only reservoir for *Leishmania donovani donovani*), dog, fox, rodent, jackal reservoirs; transmission by sandfly (*Phlebotomus* and *Lutzomyia*) bite; incubation period weeks to months; untreated cases usually fatal

Agents: *Leishmania donovani* (India and East Africa), *Leishmania chagasi* (New World), *Leishmania infantum* (Mediterranean); rarely, *Leishmania tropica*

Diagnosis: incubation period > 21 d; prolonged or intermittent fever, marked splenomegaly, hepatomegaly, intermittent cough, diarrhoea, malaise, poor weight gain, wasting; if cell-mediated immunity insufficient, disease may be mild or asymptomatic, with limited pathology; geographic history; history of sandfly bites; fever, splenomegaly; anti-K39 IgG strip test on fingerstick blood (sensitivity 100%, specificity 98%), ELISA (sensitivity 98%, specificity 100%), PCR, examination of splenic pulp smears (positive in 98%), bone marrow smears (positive in 90%), liver biopsy (positive in 70%), thin smears of buffy coat of blood (positive in 60%), lymph node aspirate or biopsy; histological appearances of chronic infection of reticuloendothelial system with presence of parasites in bone marrow, liver, lymph nodes and spleen; culture of tissue or blood; indirect hemagglutination titre, direct agglutination titre, complement fixation test, latex agglutination, Montenegro

skin test; progressive anemia with leucopenia and thrombocytopenia, falling serum albumin, greatly increased γ -globulin, raised erythrocyte sedimentation rate and serum viscosity and, later, serum bilirubin

Treatment: meglumine antimonate 20 mg antimony/kg/d for 20-40 d, amphotericin B 7-20 mg/kg total dose i.v. for up to

20 d, liposomal amphotericin B 10-20 mg/kg total dose i.v. in 5-10 doses over 10 d, amphotericin B colloidal suspension 10-15 mg/kg total dose over 5 d, pentamidine 15-30 doses over 3-4 w, miltefosine, metronidazole 25 mg/kg daily i.v. for 5 d, followed by 40 mg/kg orally daily in divided doses for 7 d, sodium stibogluconate 10 mg/kg i.m. or i.v. 8 hourly for 10 d, paromomycin 11 mg/kg i.m. daily for 21 d

VISCERAL LARVA MIGRANS (LARVA MIGRANS VISCERALIS, PARASITIC LARVAL GRANULOMATA, VLM SYNDROME)

Agents: *Toxocara* (toxocariasis, *Toxocara* infection, *Toxocara* infestation; principally *Toxocara canis*, less frequently *Toxocara cati*), occasionally *Ascaris lumbricoides*, *Baylisascaris procyonis* (from raccoons), *Capillaria hepatica*, *Diriofilaria*, *Gnathostoma*, *Toxascaris leonina*

Diagnosis: symptoms depend on number of larvae and on tissues invaded; may be no localised reaction or may be hepatomegaly or hepatosplenomegaly, pneumonitis (tropical eosinophilic pneumonia) or pulmonary infiltrates, allergic phenomena and neural and ocular lesions of varying severity; granulomatous lesions characteristic; fever, rigours, pruritic rash, abnormal behaviour

Toxocara: ELISA, bentonite flocculation (needs evaluation; 1:5 titre may be diagnostic if indirect hemagglutination also positive), indirect hemagglutination (generally reliable although status of disease activity may be uncertain; diagnostic titre 1:400)

Visceral Form: usually benign, but rare deaths due to severe neurologic or myocardial involvement; exposure to dogs and cats or eating raw chicken; 1-5 y old with history of pica; malaise, weight loss, wheezing, cough; surgical liver biopsy; marked eosinophilia (usually > 30%), anemia, neutrophilia in children, increased serum γ -globulin (including increased IgE), raised isohemagglutinin titres

Ocular Form: 5-20 y old; history of pain unusual; failing vision, strabismus, whitish retinal granuloma, endophthalmitis, uveitis; hematological tests usually normal; unnecessary enucleation because of misdiagnosis of retinoblastoma

Ascaris: acute localised manifestations (hepatic, pancreatic, bile duct, intestinal obstruction, peritonitis, appendicitis) and allergic reactions (bronchospasm, pulmonary infiltration, urticaria)

Treatment: corticosteroids in severe cases; thiabendazole 25 mg/kg 12 hourly orally daily for 5 d, diethylcarbamazine 2 mg/kg 8 hourly orally for 7-10 d

VISCERAL GNATHOSTOMIASIS: SE Asia and S America; large range of freshwater fish, amphibians, reptiles, crustaceans, birds and mammals act as second intermediate hosts; pulmonary, gastrointestinal, genitourinary, ophthalmologic, ear, nose, throat

Agent: *Gnathostoma spinigerum*

Diagnosis: isolation of parasites when possible; eosinophilia; history of travel to SE Asia or S America and ingestion of raw or undercooked fish, poultry or pork

Treatment: removal of worm where appropriate

TRYPANOSOMIASIS

Agents: *Trypanosoma brucei gambiense* (Gambian fever, Gambian sleeping sickness, Gambian trypanosomiasis, Mid-African sleeping sickness, West African trypanosomiasis), *Trypanosoma brucei rhodesiense* (East African trypanosomiasis, Rhodesian sleeping sickness, Rhodesian trypanosomiasis; prevalence 12 M), *Trypanosoma cruzi* (American trypanosomiasis, barbeiro fever, Brazilian trypanosomiasis, careotrypanosis, Chagas-Cruz disease, Chagas disease, Chagas-Mazza disease, Cruz trypanosomiasis, South American trypanosomiasis; Central and S America; transmission mostly indoors)

Diagnosis: skin nodule, fever, lymphadenopathy, circinate rash, mental changes; geographic history; insect vector bite (*Glossina* in African trypanosomiasis, reduviid bugs (triatomine (cone nose) bugs of genera *Triatoma*, *Rhodnius* and *Panstrongylus*) in trypanosomiasis due to *Trypanosoma cruzi*); electrocardiogram (myocarditis); thick and thin blood films and buffy coat examination (febrile stage)

American Trypanosomiasis: incubation period 1-3 w; children 1-5 y old; chagoma (erythematous, warm mass at site of and within few h of bite) persists for 2-3 mo, becomes fibrotic and encapsulated, most commonly on cheek or around eye

Acute: fever, toxic anemia, rash, edema of eyelids with unilateral conjunctivitis, regional adenitis, moderate hepatomegaly or splenomegaly, epistaxis, convulsions, acute myocarditis, cardiac arrhythmias and congestive heart failure, meningoencephalitis

Chronic: fever, adenitis, anemia, monocytosis, weight loss, autonomic neuropathy causing gastrointestinal lesions (megaesophagus, megacolon), myocardial degeneration, biventricular cardiac failure (greater on right than left), meningoencephalitis, pulmonary or systemic embolism

serology (Machado-Geurrein test, indirect fluorescent antibody titre, hemagglutination inhibition test); culture of blood and bone marrow aspirate on biphasic blood agar (NNN) medium; xenodiagnosis (6 clean, uninfected, laboratory-bred reduvid bugs allowed to feed on patient and hindgut examined for epimastigotes after 2 w)

African Trypanosomiasis: incubation period < 21 d; skin nodule (trypanosomal chancre) at site of bite firm, tender, indurated, inflamed, may ulcerate, persists 2-3 w, precedes other manifestations of illness by weeks to years; chills, intermittent fever 2-3 w duration, accompanied by erythematous skin eruption; debilitation, anemia, dyspnoea, edema, headache weeks to months; lymphadenopathy symmetric, predominantly cervical, persists for several months; CNS involvement, muscular pain and spasms, emaciation; hepatosplenomegaly; parasitemia frequently visible on blood smear; early sleeping stage lassitude, apathy, fatigue, later asleep most of time, terminal coma; Kerandel's sign (severe pain over area of nerve distribution following light tap on nerve); Giemsa stained smears of fluid aspirated from an enlarged lymph gland, bone marrow aspirate, CSF; serology (ELISA most sensitive, may give false positives if CSF used; IgM increase in blood and in CSF when nervous system involvement)

Trypanosoma brucei gambiense: subacute or chronic with mild onset; more severe encephalitis; less visceral involvement; more lymphadenopathy; death in untreated cases usually after several years as result of severe malnutrition and/or intercurrent infections

Trypanosoma brucei rhodesiense: acute with sudden onset and much more acute rapid course; less severe encephalitis; more visceral involvement, including heart; less lymphadenopathy; death in untreated cases usually within weeks or months

Treatment:

Trypanosoma brucei:

Hemolymphatic Stage: suramin 100-200 mg test dose then 1 g (child: 20 mg/kg) i.v. on days 1, 3, 7, 14, 21; *Trypanosoma brucei gambiense* only: pentamidine isethionate 4 mg/kg i.m. daily for 10 d

Organisms in CSF: suramin 200 mg test dose i.v. followed by 20 mg/kg to 1 g on days 1, 3 and 8, followed by melarsoprol (commencing on day 12) 2-3.6 mg/kg daily for 3 d, course repeated after 1 w at 3.6 mg/kg daily at intervals of 1-5 d for total of 10 doses and 25 mg/kg over 1 mo; nitrofurazone 1-2 g daily in 3 or 4 divided doses for 5-7 days; difluoromethylornithine hydrochloride monohydrate 100 mg/kg 6 hourly infused over 1 h for up to 14 d, followed by 75 mg/kg orally 6 hourly for 30 d

Trypanosoma cruzi: nifurtimox 8-10 mg/kg orally daily in 4 divided doses for 120 d (1-10 y: 15-20 mg/kg daily for 90 d; 10-16 y: 12.5-25 mg/kg daily for 90 d; 50% cure rate), lampit, benzimidazole

Prophylaxis (*Trypanosoma brucei gambiense*): pentamidine isethionate 250 mg i.m. given as a single dose

FILARIASIS: 120 M infected worldwide; no deaths reported; Africa, Eastern Mediterranean, Asia, South America; transmission by mosquitoes, infected arthropods; incubation period weeks to years

Agents: *Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori*, *Loa loa*, *Onchocerca volvulus*, *Mansonella ozzardi*, *Mansonella perstans*, *Mansonella streptocerca*, *Meningonema peruzzii*, *Dirofilaria*

Diagnosis: clinical; bentonite flocculation test (1:5 titre diagnostic if indirect hemagglutination assay also positive), indirect haemagglutination assay (1:400 titre diagnostic if bentonite flocculation test also positive), ELISA (sensitive but non-specific), indirect immunofluorescence; eosinophilia sometimes

Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori: demonstration of microfilariae in peripheral thick blood films taken at night and by histological examination of biopsy material

Acute: recurrent lymphangitis (with *Brugia*, not severe and usually affecting lower limbs with enlargement of femoral and popliteal lymph nodes); may be fever, headache and urticarial rash ('filarial fever')

Chronic: fibrosis and lymphatic obstruction, leading to hydrocele and/or elephantiasis (enlargement of legs, arms, breast and genitals)

Loa loa: adult worms migrate through subcutaneous tissues producing painful transient erythematous inflammation ('fugitive swelling', 'Calabar swelling'), migratory angioedema, urticarial vasculitis, and occasionally across eye beneath conjunctiva; microfilariae in films of peripheral blood collected repeatedly at midday and midnight and concentrated by Knott's technique; occasionally, adult filariae under conjunctiva or in biopsy material of swelling; white cell count 9900/ μ L, 31% eosinophils

Onchocerca volvulus: chronic; dermatitis (irritating pruritic rash) and sometimes hyperkeratosis, depigmentation; subcutaneous encapsulated tumours (onchocercomata containing adult worm) with muscular pain, sclerosing

lymphadenitis, eye disease (conjunctival hyperemia, iritis, corneal opacities, chorioretinitis, optic nerve disease leading to blindness (river blindness)); in Africa, loss of skin elasticity causing hanging groin syndrome; in S America, pouches under eyes causing 'leonine facies'; adult filaria in excised nodules, microfilaria in shavings of skin; histology of lymph nodes; radioimmunoassay; Mazzotti test; patch test

Mansonella: eosinophilia; recovery of microfilariae from blood by Knott's concentration

Mansonella ozzardi: asymptomatic or urticaria, lymphadenopathy, articular pains, pruritic skin eruptions, headaches, hydrocele

Mansonella perstans: usually mild or asymptomatic but can cause arthropathy, Calabar swellings and pyrexia

Mansonella streptocerca: rare; cutaneous edema, rash, red macules

Meningonema peruzzii: acute encephalomyelitis or mild illness with headache, fatigue and drowsiness

Dirofilaria: often asymptomatic; abscesses or nodules ('coin lesions') in heart, lungs, subcutaneous tissue, eye

Treatment: ivermectin 200 µg/kg single oral dose, flubendazole 750 mg i.m. weekly for 5 w, albendazole, diethylcarbamazine

PREVENTION AND CONTROL: control of vectors, treatment of cases

SCHISTOSOMIASIS (BILHARZIASIS, HAEMIC DISTOMIASIS, SNAIL FEVER): worldwide incidence 200 M/y (Africa, Near East, rain forest belt in Central Africa, Western Pacific, Kampuchea, Laos; absent from Australia and Papua New Guinea); dermatitis (within 1-2 d of cercarial penetration), enteritis (*Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi*, *Schistosoma intercalatum*, *Schistosoma mattheei*), Katayama syndrome (4-8 w after primary infection), urinary infection (chronic *Schistosoma haematobium* infection), intestinal polyps, hepatosplenic schistosomiasis (hepatosplenic bilharziasis; caused by tissue reaction to trapped eggs; varies from formation of a few hepatic granulomas to occurrence of severe hepatosplenic fibrosis, hepatosplenomegaly and portal hypertension), pulmonary schistosomiasis (lung schistosomiasis, pulmonary bilharziasis; caused by a reaction of lung tissues to eggs of *Schistosoma mansoni* and, very rarely, *Schistosoma haematobium* and *Schistosoma japonicum*), CNS schistosomiasis (*Schistosoma mansoni*, *Schistosoma haematobium*, *Schistosoma japonicum*, localisation of granulomata leading to paresis of different types; reported in both acute and chronic stages)

Agents: *Schistosoma mansoni* (Africa, Middle East, S America, Caribbean; mature adults in mesenteric vessels; eggs in liver or feces), *Schistosoma japonicum* (Japan, China, Philippines; 600,000 sufferers; 25% of transmission due to animal reservoirs; mature adults in intestine or mesentery; eggs in spleen or liver), *Schistosoma haematobium* (Africa, Middle East; mature adults in bladder or mesentery; eggs in urine or liver), *Schistosoma mekongi* (only in Mekong River basin), *Schistosoma intercalatum* (worms and eggs in mesenteric portal system, vesical system not involved; mainly colonic and rectal involvement), *Schistosoma mattheei*

Diagnosis: bentonite flocculation test (1:5 titre diagnostic if cholesterol lecithin flocculation test also positive), complement fixation test, counterimmunoelectrophoresis, fluorescent antibody staining of serum, indirect hemagglutination titre, FAST-ELISA; light microscopy of stool (acid-ether concentrate), urine (concentrate; midday for *Schistosoma haematobium*), aspirate, puncture, unstained biopsy of rectum; anemia (erythrocyte count and hemoglobin decreased)

Schistosoma japonicum and Schistosoma mekongi: urticarial rash and fever followed by dysentery, bloody and mucoid stools, epigastric pain, acute hepatitis, high eosinophilia, weight loss and hyperemia; may be liver cirrhosis, splenomegaly and ascites in late stage

Schistosoma mansoni: pruritic papular rash followed by dysentery, bloody and mucoid stools, abdominal pain, nausea, vomiting, eosinophilia, hepatosplenomegaly or liver cirrhosis

Schistosoma intercalatum: similar to, but milder than, *Schistosoma mansoni*

Schistosoma haematobium: microscopic and macroscopic hematuria, painful and frequent micturition; chronic sequelae hydronephrosis, renal failure and squamous cell carcinoma of bladder

Treatment:

Schistosoma haematobium, Schistosoma mansoni: praziquantel 20 mg/kg orally for 2 doses after food 4 h apart

Schistosoma japonicum, Schistosoma mekongi: praziquantel 20 mg/kg orally for 3 doses after food at 4 hourly intervals

Prevention and Control: mass chemotherapy; control of snails *Bulanus* (*Schistosoma haematobium*), *Biomphalaria* and *Oncomelnicera* (*Schistosoma mansoni*, *Schistosoma japonicum*); controlled sanitation

KATAYAMA SYNDROME (ACUTE SCHISTOSOMIASIS)

Agents: *Schistosoma mansoni* (primary and secondary), *Schistosoma japonicum* (primary and secondary), *Schistosoma haematobium* (primary; rare)

Diagnosis: fever, cough, hepatosplenomegaly, myalgias, urticaria, eosinophilia; pulmonary infiltration visible radiologically; at least 3X1g stool samples concentrated by modified Ritchie technique and examined for ova; ova in urine; immunofluorescent antibody tests on serum

Treatment: praziquantel as above + dexamethasone

CYSTICERCOSIS (CYSTICERCAL DISEASE, CYSTICERCIASIS, CYSTICERCOUS DISEASE, *TAENIA SOLIUM* CYSTICERCOSIS): eggs in food contaminated by infected person or autoinfection; areas of low socioeconomic development in Central and S Africa, Mexico (causes 1.9% of all human deaths), Central and S America, Southern Asia; subcutaneous tissues, skeletal muscles, brain, eye, heart, lungs, liver; presentation time may be delayed for up to 30 y, with mean presentation time being 5 y

Agent: *Taenia solium*, one case due to *Taenia crassiceps* reported

Diagnosis: subcutaneous or muscular disease often asymptomatic but subcutaneous nodules or intramuscular swellings occur; if larvae become lodged in vital organs, differing manifestations, according to site of disease and number of larvae, may result; cerebral cysticercosis frequently causes epileptiform fits; death may ensue; computed tomography of brain; X-ray of large muscle; hemagglutination of serum ($\geq 1:128$) and CSF ($\geq 1:8$), ELISA, enzyme-linked immunoelectrotransfer blot assay (sensitivity 98%, specificity 100%), indirect fluorescent antibody titre; histology of biopsied nodules; 53% of patients have intestinal taeniasis

Posterior Fossa Syndrome: lymphocytosis, elevated protein level and diminished glucose level of CSF

Meningoencephalitis: eosinophilia of CSF

Treatment: praziquantel 50 mg/kg orally daily in 3 divided doses for 15 d + dexamethasone 12-16 mg orally daily or prednisone 30-40 mg orally daily in neurocysticercosis; albendazole; surgery for ventricular involvement and in cases of raised intracranial pressure

TRICHINELLOSIS (TRICHINA WORM INFECTION, TRICHINELLIASIS, TRICHINIASIS, TRICHUROSI, TRICHINOUS MYOSITIS, TRICHINOUS POLYMYOSITIS)

Agents: *Trichinella spiralis*

Diagnosis: often asymptomatic; fever in 90% of cases, myalgias in 80%, periorbital edema in 75%, headache in 50%, urticarial rash in 20%, peripheral edema in 20%, intermittent diarrhoea in 15-51% (in early stages), nausea in 15%, subconjunctival hemorrhages in 10%, splinter hemorrhages in 10%, vomiting, abdominal discomfort, malaise, myositis, neurologic symptoms; cardiac, pulmonary or cerebral complications or toxemia may occur and can be fatal unless properly treated; unusual presentation of prolonged diarrhoea without fever and with brief muscle symptoms in Canadian Arctic (may affect 20% of Arctic population); worms and larvae in feces 7-14 d after ingestion; histology of cysts in muscle (quadriceps muscle biopsy positive in 91% of cases); ELISA, latex agglutination (screening test), immunodiffusion (if positive in latex agglutination), bentonite flocculation test (positive in 40% of cases; diagnostic titre 1:5), complement fixation test, indirect hemagglutination; neutrophilia with eosinophilia by tenth day, very high eosinophil count by 3-4 w, anemia (erythrocyte count and hemoglobin may be decreased)

Treatment: mebendazole in increasing doses to 600 mg orally 8 hourly for 30 d before surgical removal or in increasing doses to 200 mg/kg daily orally for 16-48 w in order to obtain serum levels > 100 mg/mL 1-3 h after an oral dose if inoperable; albendazole 10 mg/kg orally daily for 8 w

ECHINOCOCCOSIS (HYDATID CYST): wherever man comes into contact with canines in sheep-rearing countries; ≈ 30 notified cases/y in Australia ($\approx 59\%$ in Victoria); ≈ 3 deaths/y in USA; 40-66% of cysts in liver and peritoneum, 22-30% in lungs, 10% subcutaneous, 3% in female genital, 2% in spleen, 2% in bones, 2% in orbit, 2% in parotid glands and neck, 1-3% in kidneys, 1% in brain, 1% in breast

Agents: *Echinococcus granulosus*, *Echinococcus multilocularis*, *Echinococcus oligarthus*, *Echinococcus vogelsi*

Diagnosis: liver enlargement with palpable mass and 'hydatid thrill', hemoptysis, bone fracture, space-occupying lesion in brain; contact with dogs; peripheral eosinophilia; X-ray (calcification); liver scan; arteriography; ultrasound and computed tomographic imaging most reliable; identification of scolices, brood capsules or daughter cysts after surgical removal or autopsy or in aspirated fluid, or fragments from a ruptured cyst in sputum or urine (should be no attempt at aspiration on account of risk of spreading infection); cardiac hydatid cyst life threatening but rare; complement fixation test, indirect hemagglutination titre ($> 1:320$; highly specific but positive in only 51%; remains elevated for many years after infection), counterimmunoelectrophoresis (superior indicator of efficacy of treatment, as titres return to negative within 2 y of successful treatment), RAST (detects hydatid-specific IgE present in hepatic involvement but only in $\approx 25\%$ of cases in which lung infected), bentonite flocculation test (1:5 titre diagnostic if indirect hemagglutination assay also positive), latex agglutination, indirect immunofluorescence, immunodiffusion, passive hemagglutination

Echinococcus granulosus: clinical manifestations depend on number, size and location of cysts

Echinococcus multilocularis: disease of liver resembles mucoid carcinoma, with hepatosplenomegaly, jaundice and ascites

Treatment: conservative, with local use of scolicide; aspiration of cavity, injection of 95% ethanol into cystic cavity and slow reaspiration; surgery when cyst producing symptoms or increasing in size or with cardiac cyst; albendazole 7.5 mg/kg to 400 mg orally 12 hourly (not < 6 y)

TOXOPLASMOSIS: worldwide; possibly commonest protozoal infection; 30% of adults in UK have antibodies; ≈ 200 cases (≈ 13 deaths)/y in USA; prevalence 20-100%; intrauterine infection (incidence 50% in women receiving initial infection in pregnancy) produces varying degrees of brain damage, myocarditis, retinochoroiditis and may cause miscarriage; infection in children and adults (principal modes of infection accidental ingestion of oocysts in rare to medium beef, while working in an outside garden or on exposure to cats; also in meat handlers through skin abrasions; other accidental routes of transmission include blood transfusion, laboratories, organ transplantation and autopsies; recent outbreak due to contaminated municipal water reported) may produce no symptoms, fever, mild off-colour feeling, hepatitis-like syndrome, mononucleosis-like syndrome, myocarditis, typhus-like syndrome, atypical pneumonia, lymphadenopathy (27.5% of cases), retinochoroiditis (60% of cases), acute meningoencephalitis (rare; may be terminal in Hodgkin's disease, in leukemia, after irradiation and after immunosuppressive drugs), chronic infection with cysts persisting in CNS, heart, skeleton and smooth muscle

Agent: *Toxoplasma gondii*

Diagnosis:

Acquired Toxoplasmosis: usually asymptomatic or mild and self-limiting; 20% cervical or generalised lymphadenopathy and/or a flu-like illness; overt disease (disseminated toxoplasmosis) relatively rare, characterised by abrupt onset, prolonged remittent fever, maculopapular rash, chorioretinitis, uveitis, internal hydrocephalus, delirium and convulsions; myocarditis or pneumonitis often seen; may be rapidly fatal in persons with impaired immune response (especially those undergoing immunosuppressive therapy and those with AIDS (6.2% of opportunistic infection in AIDS), pediatric heart transplant recipients, lymphoma, leukemia; from accidental ingestion of contaminated substances (eg., in gardening or cleaning cat litter box) or from raw or partly cooked beef, pork, lamb or venison; light microscopy of aspirate, puncture, biopsy of lymph node; Giemsa-stained smear of bronchoalveolar lavage; isolation from blood or other body fluids; serology generally reliable, although status of disease activity may be unclear—indirect fluorescent antibody test (IgG onset to rise 0-2 mo, duration years, rising titre in acute disease, titre present in ocular disease, stable or rising titre in congenital disease in neonate, false positives and negatives; IgM indicates recent infection, onset to rise 0-1 mo, duration 3 w - 18 mo, titre present in acute disease, false positives in patients with anti-nuclear antibodies), latex agglutination (IgG and IgM antibodies), differential agglutination (IgG; differentiates recent infection from remote in adults and older children), complement fixation test (onset to rise 1-5 mo, duration years; rising titre in acute disease, titre present in ocular disease, stable or rising titres in congenital disease in neonate), direct immunofluorescence, ELISA (antibody; IgG, (appears in 1-2 w, peaks at 6-8 w, declines but may persist for life), IgM (appears early and may persist 1 or more years; negative results in immunocompetent usually excludes infection but positive not useful in adults), IgM capture, IgA (positive in infected adults and congenitally infected infants; may persist for months or years; avidity assay useful in first trimester), IgE (presence in adults usually indicates acute infection; present in congenital infection; absence does not exclude infection)), indirect hemagglutination titre (onset to rise 2-5 mo, duration years, rising titre in acute disease, stable or rising titre in congenital disease in neonate; antibodies found in > 1/3 of population), Sabin-Feldman dye test (IgG; onset to rise 0-2 mo, duration years; mainly reference laboratories; negative result practically rules out prior exposure), IgG avidity (urea dissociable; low avidity indicates primary infection), IgE immunosorbent assay; histopathology of enlarged lymph node; mouse inoculation; anemia (erythrocyte count and hemoglobin may be decreased), atypical monocytes

Congenital Toxoplasmosis: many cases asymptomatic but may be severe, with fever, jaundice, rash and hepatosplenomegaly, and complicated by chorioretinitis, encephalitis, hydrocephalus, microcephaly, convulsions, mental retardation, cerebral calcification and cerebral palsy; some signs and symptoms may develop several years after birth; positive IgM and low avidity test in mother at 3-4 mo; isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory)

Toxoplasmosis of Brain: recent onset of a focal neurologic abnormality consistent with intracranial disease or a reduced level of consciousness + evidence by brain imaging (computed tomography or nuclear magnetic resonance) of a lesion having a mass effect or the radiographic appearance of which is enhanced by injection of contrast medium + serum antibodies to toxoplasmin or successful response to therapy for toxoplasmosis

Treatment: sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly for 3-6 w (clindamycin 600 mg orally or i.v. 6 hourly if hypersensitive) + pyrimethamine 50-100 mg (child: 2 mg/kg to maximum 25 mg) orally first dose then 25-50 mg orally daily (child: 1 mg/kg daily; infant: every second or third day) for 3-6 w + folic acid 3-9 mg orally daily; in AIDS,

followed by sulphadiazine 500 mg orally 6 hourly (clindamycin 600 mg orally 8 hourly if hypersensitive) + pyrimethamine 25-50 mg orally daily + folinic acid; spiramycin 50-100 mg/kg to 2-4 g orally daily for 4 w, cotrimoxazole 160/800 mg (child: 1.5/7.5 mg/kg) twice daily for 4 w; azithromycin + pyrimethamine

Pregnancy: spiramycin 3 g daily in divided doses throughout pregnancy

Prophylaxis in AIDS: cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3 times weekly, dapsone 100 mg orally 3 times a week ± pyrimethamine, atovaquone + pyrimethamine, pyrimethamine alone, azithromycin, clarithromycin

STRONGYLOIDIASIS: tropical and temperate areas; 42% gastrointestinal disturbance (diarrhoea, malabsorption, abdominal pain, bloating, weight loss), 25% asymptomatic, 22% skin complaints (transient seriginous urticaria, weals on waist and buttocks, persistent rash), 7% pruritus ani, 4% fever; eosinophilic pneumonia due to larval migration through lung; eosinophilia (83% > 400 eosinophils/μL); severe strongyloidiasis in immunocompromised: 66% hyperinfection (50-86% mortality), 21% disseminated (71% mortality), 15% intestinal (20% mortality), may lead to bacteremia and meningitis with enteric organisms; asymptomatic individuals from at-risk populations (immigrants, refugees, war veterans who have served in tropics, requiring corticosteroids and possibly exposed to *Strongyloides*), patients with eosinophilia and history of possible exposure, and patients with suggestive abdominal symptoms or skin manifestations should be tested

Agents: *Strongyloides stercoralis*, *Strongyloides fuelleborni*

Diagnosis: microscopy for larvae and ova in feces 3 or more concentrated specimens); Harada-Mori or agar plate culture; ELISA (IgG to *Strongyloides ratti*; 84-95% sensitivity; does not distinguish between current and past infection); indirect fluorescent antibody titre in patients with long-standing symptoms

Severe Strongyloidiasis: fever in 71% of cases, abdominal pain in 66%, dyspnoea in 56%; diffuse alveolar infiltrates in 56%; isolation of larvae from stool in 59%, sputum in 38%, lung and duodenum at autopsy in 18%

Treatment and Prophylaxis: ivermectin 200 μg/kg/d on days 1, 2, 15, 16; albendazole 400 mg once orally on 3 consecutive days

DISSEMINATED MICROSPORIDIOSIS: HIV, renal transplant recipients

Agent: *Encephalitozoon cuniculi*

Diagnosis: chromotrope-based stains of urine, stools, sputum, conjunctival scrapings; electron microscopy, immunofluorescence, polymerase chain reaction, cultures of affected tissue

Treatment: oral albendazole, topical fumagillin, withdrawal of immunosuppressive therapy

INTERNAL HIRUDINIANSIS: leeches enter and attach themselves to mucous membrane of upper respiratory tract, digestive passage or genitourinary tract

Agents: *Limnatis nilotica* and other *Limnatis* species

Diagnosis: hemoptysis, hematemesis, severe anemia, occasionally death from excessive loss of blood; suffocation may occur in laryngeal or tracheal hirudiniasis ('halzoun') caused by *Limnatis nilotica*; history of drinking or bathing in leech-infested water

Treatment: removal if possible

LINGUATULOSIS (LINGUATULIASIS): uncommon disease in which intestine, lung, nasopharyngeal region, eye (with visual damage) or other organs may be affected

Agent: '*Linguatula serrata*'

Diagnosis: direct visualisation

Treatment: removal if possible

SYSTEMIC INFECTIONS IN IMMUNOCOMPROMISED

Diagnosis: blood cultures; examination and culture of CSF, sputum culture, other investigations as indicated

Agammaglobulinemia

Agents: *human echovirus*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*

Treatment: β-lactamase-resistant cephalosporin

Prophylaxis: amoxicillin, cotrimoxazole, tetracycline, IgG (passive immunisation)

Cell-mediated Immune Disorders

Agents: fungi, *Simplexvirus*, *Legionella*, *Listeria*, *Mycobacterium*, *Nocardia*, *Pneumocystis jiroveci*, *Toxoplasma*

Treatment: dependent on clinical and laboratory evaluation

Prophylaxis: cotrimoxazole, nystatin, interferon, interleukin 2, thymic hormones, transfer factor

Chemotactic Defect

Agents: *Candida*, *Cryptococcus*, *Haemophilus influenzae*, *Staphylococcus aureus*

Treatment: antistaphylococcal drug

Complement Deficiency:**C1, 2, 3, 4, Factor B**

Agents: aerobic Gram negative bacilli, *Haemophilus influenzae*, *Neisseria meningitidis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*

Treatment: β -lactamase-resistant cephalosporin

Prophylaxis: plasma

C5, 6, 7, 8

Agents: *Neisseria gonorrhoeae*, *Neisseria meningitidis*

Treatment: benzylpenicillin

Prophylaxis: plasma

Granulocytopenia

Agents: *Aspergillus*, *Candida*, *Corynebacterium*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, coagulase negative staphylococci

Treatment: aminoglycoside + antipseudomonal penicillin, ciprofloxacin + piperacillin

Breakthrough Bacteremia: if isolate Gram positive, add vancomycin; if isolate Gram negative, switch to new regimen

Catheter-associated Infection: add vancomycin

Severe Oral Mucositis or Necrotising Gingivitis: add clindamycin or metronidazole

Esophagitis: institute trial of oral clotrimazole or ketoconazole or i.v. amphotericin B 0.5 mg/kg/d

Diffuse or Interstitial Pneumonitis: institute trial of cotrimoxazole and erythromycin (continue initial antimicrobials if granulocytopenic)

New Pulmonary Infiltrate: if granulocyte count rising, watch and wait; if granulocyte count not recovering, perform biopsy to establish diagnosis; if biopsy cannot be done, add amphotericin B 0.5 mg/kg/d empirically

Perianal Tenderness: add clindamycin or metronidazole

Persistent Fever and Neutropenia: continue antibacterials; if fever and neutropenia persist for a week, add systemic antifungal therapy empirically

Prophylaxis: cotrimoxazole, nystatin, granulocyte transfusions, passive immunisation, plasma

Hyposplenism/Splenectomy

Agents: *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*

Treatment: β -lactamase-resistant cephalosporin

Prophylaxis: penicillin, pneumococcal vaccine, '*Corynebacterium parvum*'

Microbicidal Abnormality

Agents: *Aspergillus*, *Candida*, *Pseudomonas*, *Serratia*, *Staphylococcus aureus*

Treatment: antistaphylococcal drug + cotrimoxazole