

Chapter 10

Infections of the Reticuloendothelial System

BONE MARROW INFECTIONS

Agents: *Brucella*, *Salmonella typhi*, *Mycobacterium*, *Histoplasma capsulatum*

Diagnosis: hematological examination of bone marrow (infection causes an increased M/E ratio; in chronic infection, there is a myeloid hyperplasia and increased plasma cells; *Mycobacterium kansasii* causes a severe hypoplasia of hematopoietic cells); Gram stain, Ziehl-Neelsen stain, culture of bone marrow in biphasic medium for 3 w, aerobic and anaerobic bacterial cultures and fungal cultures at 25°C and 35°C on solid media, and culture for mycobacteria as indicated and quantity of specimen allows

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Treatment:

***Brucella*:** doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day for 45 d, ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally twice a day for 30 d

***Salmonella typhi*:** chloramphenicol, cotrimoxazole

***Mycobacterium tuberculosis*:** 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)

Other Mycobacteria: ethionamide, cycloserine, viomycin, ethambutol

***Histoplasma capsulatum*:** amphotericin B, flucytosine, ketoconazole

EHRlichiosis

Agent: *Ehrlichia canis*, *Ehrlichia chaffeensis* and *Ehrlichia sennetsu* (monocytic; tick vector—*Dermacentor variabilis* and *Amblyomma americanum* in Southern and Eastern USA), *Ehrlichia ewingii* and *Anoplasma phagocytophilum* (granulocytic; tick vector—*Amblyomma americanum* and *Ixodes persulcatus*)

Diagnosis: incubation period < 3 w; fever, malaise, headache, nausea, vomiting, anorexia, myalgia, arthralgia, chills, sweating, cough, diarrhoea, abdominal pain, thrombocytopenia, leucocytopenia, increased liver enzyme levels; maculopapular rash (rare in granulocytic); encephalopathy, pulmonary complication (respiratory failure, acute respiratory distress, pharyngitis; pulmonary infiltrates, pulmonary edema on chest X-ray) may occur in monocytic (may evolve with severe multiorgan failure); disseminated intravascular coagulation, meningitis, gastrointestinal bleeding and renal failure also occur; immunohistologic examination of acute phase bone marrow and liver biopsy; PCR (positive in 71%); morulae in Wright-Giemsa stained peripheral or buffy coat smears (positive in 61%); thrombocytopenia and leucopenia in 49%

Treatment: doxycycline

HEPATITIS

Agents:

Prenatal: *human cytomegalovirus*, *rubella virus*, *simplexvirus*, *human coxsackievirus B*, *simplexvirus 3*, *Listeria monocytogenes* (intrauterine infection with septicemia; mortality high), *Treponema pallidum subsp pallidum*

Neonatal: *simplexvirus*, *human cytomegalovirus*, *human echovirus*, *Reovirus*, *measles virus* (fatal in children with leukemia), *Listeria monocytogenes* (acquired from environment; majority recover)

Pediatric: *simplexvirus 3*, *human parvovirus B19*

Adult: hepatitis A (infective hepatitis; acute viral disease of worldwide occurrence, particularly in Third World areas; global incidence 600,000 - 3M/y ; ≈ 2000 notified cases/y in Australia (≈ 27% in NSW; causes 3% of fever in returned travellers); incidence 13/100,000 in USA but 33% serological evidence of prior infection; 0.02% of new episodes of illness in UK; 80% of hepatitis in travellers; global mortality 2400-12,000/y; case-fatality rate 0.1-0.3% overall, 1.8% in

> 50 y.o.; antibody positivity varies from 30% in Switzerland to \approx 100% in Africa, Asia, Latin America, Mexico and South America; from shellfish from contaminated waters, raw produce, uncooked foods and cooked foods not reheated after contact with infected food handler; 50% no identified source, 12-26% household or sexual contact, 10% drug users and men who have sex with men; incubation period 15-50 d; duration of illness 2 w-3 mo), hepatitis B (serum hepatitis; \approx 8000 notified cases/y (52% in NSW) in Australia; global mortality rate 1-2M/y (tenth leading cause of death); case-fatality rate generally 1% but up to 67% in some outbreaks; prevalence of HBsAg varies from 0.2-0.5% in Australia up to 80% in Taiwan; very common in China, SE Asia, Sub-Saharan Africa, Pacific Islands and the Amazon Basin; 181,000 new cases/y, 1.25 M with chronic infection, and 5000 deaths from related cirrhosis or hepatocellular carcinoma in USA; low incidence in W Europe and Australia (\approx 300 notified cases/y (\approx 35% in Queensland)); carrier rate from 0.5% in USA and Canada and 1% in Australia to 5-15% of adults in developing nations; 385 M chronic carriers worldwide; Australian Aborigines have a very high carrier rate; becomes chronic in 90% infected at birth, 25-50% at 1-5 y; transmission by sex (40% heterosexual, 15% men having sex with men), blood and blood products, secretions (eg., saliva, semen), body fluids, contaminated needles/sharp instruments, human bites and intimate contact); incubation period 3-20 w; > 90% of HbeAg-positive mothers transmit to newborns through blood exposure at time of birth), hepatitis C (20% of all cases of acute hepatitis; injecting drug users (80% of cases), those who received a blood transfusion prior to 1992 (5-10%), hemodialysis patients, health care workers (prevalence 1-2%), hemophiliacs, those with transplants before 1992, intranasal cocaine users, those with body piercing, sexual contacts of infected persons, persons with multiple sex partners, individuals with tattoos, those sharing household items with infected individuals, those indulging in fisticuffs, patients of infected healthcare workers; also transmitted from infected mother to newborn (3-5% risk if mother has chronic infection); 15-35% clear infection spontaneously within 2-6 mo, 65-85% develop chronic infection, 5-20% with chronic infection progress to cirrhosis after 20 y (20% after 40 y; increased risk with alcohol consumption, HIV or hepatitis B coinfection, older age at time of infection, male), 3-5% with cirrhosis develop liver failure or hepatocellular carcinoma after 30-40 y; 170 M carriers worldwide; infection rates vary from < 0.5% in Scandinavian countries to 8-14% in Egypt; \approx 200,000 infected in Australia with \approx 134,000 having developed chronic infection, and

\approx 11,000 new infections/y); most common bloodborne infection and most common cause of liver transplant in USA (> 4 M infected; 30,000 new infections and 10,000 deaths annually; leading cause of death in HIV-infected patients in at least 1 US hospital), 8.9 M infected in Europe, 200 M worldwide), hepatitis D (delta hepatitis; superinfection of hepatitis B; transmitted in company with hepatitis B; 5% of HBsAg carriers infected worldwide; endemic in Russia, Romania, southern Italy, Africa and S America, rare in Australia (21 notified cases in 1999); associated with illicit drug usage and blood transfusions, less commonly sexually transmitted; chronic disease rare in acute cases but 70-80% chronic in HBsAg carriers; accelerates development of liver cancer; mortality 2-20%), hepatitis E (acute disease; enterically transmitted; water-borne epidemics in India, Nepal, Pakistan, Burma, former Soviet Union, Africa, Mexico, Middle East; 50% of non-A-C hepatitis in developing countries; endemic in Asia and South America; most common cause of acute sporadic hepatitis in Sudanese children; case-fatality rate up to 25% in pregnancy; 2 notified cases in Australia in 1999), hepatitis G (chronic; no known symptoms; prevalence 1-2% of blood donors, 30% of drug users, 10-30% of hepatitis C patients; transmitted by blood transfusion), *simplexvirus 1* (associated with pregnancy, thymic dysplasia, celiac disease, corticosteroid therapy, leukemias and lymphomas, severe burns, renal transplantation, AIDS; death within 1 w), *simplexvirus 3*, *human cytomegalovirus*, *Epstein-Barr virus*, several viral hemorrhagic fevers including *yellow fever virus* and *Lassa virus*, adenovirus, *human parvovirus B19*, *Staphylococcus aureus* (in toxic shock syndrome), *Listeria monocytogenes* (associated with debilitating and neoplastic diseases, immunosuppressive therapy, renal transplantation, cardiac prosthetic devices), *Escherichia coli*, *Salmonella typhi*, *Shigella*, *Pseudomonas pseudomallei*, *Brucella*, *Yersinia pseudotuberculosis*, *Campylobacter jejuni*, *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare*, *Mycobacterium leprae* (in 90% of lepromatous cases, 20% of tuberculoid), *Treponema pallidum subsp pallidum*, *Leptospira*, Rocky Mountain spotted fever, Boutonneuse fever, Q fever (abattoir and farm workers), *Borrelia recurrentis*, *Actinomyces*, *Nocardia*, *Aspergillus*, *Mucor*, *Candida*, *Histoplasma*, *Leishmania*, *Plasmodium*, *Toxoplasma*, *Schistosoma*, *Echinococcus*, *Entamoeba histolytica* (hepatic amoebiasis (amoebic hepatitis); early stage of invasion of liver via intrahepatic portal vessels; results from intestinal amoebiasis; may be self-limiting or progress to a liver abscess), *Capillaria hepatica*, *Fasciola hepatica*; also alcohol, phenothiazine (chlorpromazine), anesthetics (halothane), antituberculous drugs (rifampicin, isoniazid, pyrazinamide), methyl dopa, contraceptive pills, organic solvents (eg., carbon tetrachloride, 'glue')

Diagnosis: anorexia, malaise, extreme fatigue, right upper quadrant tenderness, nausea, vomiting, acute jaundice; epidemiological history; light-coloured stool, dark urine; computed tomography of abdomen (positive in 93% of cases of focal hepatic candidiasis), ultrasound; serology; Gram, Giemsa, Ziehl-Neelsen and silver-methenamine stains, bacterial, fungal and viral culture of biopsy; viral culture of throat swab, feces; increased urine urobilinogen, serum alanine aminotransferase

> 2.5 times upper limit of normal; serum aldolase increased in viral hepatitis, less consistently in chronic hepatitis; serum β -glucuronidase increased in viral hepatitis; serum isocitrate dehydrogenase increased in viral hepatitis; serum iron and total iron-binding capacity increased in infectious hepatitis; serum sorbitol dehydrogenase increased in acute hepatitis; rheumatoid factor may be present; 80% of cases of chronic active hepatitis have anti-nuclear antibodies titre > 320; anti-smooth muscle antibody test +++ in hepatitis A and B, ++ in chronic active hepatitis, cryptogenic cirrhosis and primary biliary cirrhosis; cytoplasmic mitochondrial smooth muscle fluorescence in chronic active hepatitis and other liver disease; white cell count decreased in *simplexvirus* hepatitis

Hepatitis A: usually asymptomatic or unrecognised in children; in > 80% of adults, marked jaundice, diarrhoea, dark urine, flu-like symptoms (fever, headache, nausea, abdominal pain, fatigue, weakness, arthralgias, myalgias); may have clay coloured stools, skin rash and extreme aversion to tobacco smoke; ELISA tests for hepatitis A IgM antibody (persists 3-6 mo post infection) and total hepatitis A antibody (also antigen; capture IgA in protracted cases); immune adherence hemagglutination test for hepatitis A IgM antibody (not always reliable), seroconversion of hepatitis A IgG antibody; counterimmunoelectrophoresis; immunoelectron microscopy of stool; increase in ALT and AST; bilirubin normal or elevated

Hepatitis B: incubation period 4 w - 6 mo; may be asymptomatic, but usually fatigue, weakness, anorexia, nausea, fever, malaise and fullness or discomfort in right upper quadrant; jaundice in 20-50%; less frequently, hemorrhage due to diminished synthesis of prothrombin complex, altered mental status, Guillain-Barré syndrome, peripheral neuropathy, myokymia, neuropsychiatric dysfunction, red cell aplasia, thrombocytopenia, agranulocytosis, aplastic anemia, myocarditis, pericarditis, superficial/hemorrhagic gastritis, acute pancreatitis, renal failure, membranous glomerulonephritis, urticaria, papular acrodermatitis, arthralgia, vasculitis, pleural effusion; fatal fulminant hepatitis in 1% of acute infections; becomes chronic in 90% of infants, 60% of < 5 y.o. and 2-6% of adults; annual rate of development of cirrhosis 1-3% (5 y survival rate 30%); radioimmunoassay most sensitive; turkey erythrocyte passive haemagglutination test slightly less sensitive but simple, rapid and considerably less expensive; enzyme immunoassay (Auszyme I) 98% sensitivity and 99% specificity; hepatitis B surface antigen (HBsAg) indicates current infection but not necessarily infectivity; hepatitis B e antigen (HBeAg) indicates high infectivity in HBsAg⁺ individual; anti-hepatitis B surface antibody (anti-HBs) indicates post-infection, immunity or (if IgM anti-HBc negative) chronic infection; anti-hepatitis B core antibody (anti-HBc; IgM diagnostic of acute infection); anti-hepatitis B e antibody (anti-HBe) indicates low infectivity in a HBsAg⁺ individual

IgM HbcAb +ve = acute infection

HBsAb +ve HBcAb -ve HBV DNA -ve = hepatitis B immunisation

HBsAb +ve HBcAb +ve HBV DNA -ve = recovered from HBV

HBsAb +ve HBcAb \pm HBV DNA < 10³ copies = occult hepatitis B

HBsAb -ve HBcAb +ve HBeAb -ve HBsAg +ve = acute HBV or chronic hepatitis B

HbsAb -ve HbcAb +ve HbeAb -ve HbsAg -ve = occult hepatitis B

HBsAb -ve HBcAb +ve HBeAb +ve HBsAg +ve = healthy or inactive carrier

HbsAb -ve HbcAb +ve HbeAb +ve HbsAg -ve = occult hepatitis B

serum alanine aminotransferase > 10-20X normal in acute cases, 2-10X normal in chronic cases, < 2X normal in 'healthy' carrier state; total serum bilirubin 2.5-34.8 mg/dL; serum glutamic-oxaloacetic transaminase > 10X upper limit normal in all cases

Hepatitis C: incubation period > 21 d; generally asymptomatic in acute phase; malaise, weakness and anorexia in 25-35%; fatigue and malaise with advanced liver disease; arthritis in 23%, paresthesia in 17%, myalgia in 15%, pruritus in 15%, sicca symptoms of mouth and/or eyes in 11%, mixed cryoglobulins in 40%, low thyroxine level in 10%, antinuclear antibodies in 10%, anti-smooth muscle antibodies in 7% of chronic infections; glomerulonephritis, lichen planus, porphyria cutanea tarda, Raynaud's syndrome, systemic vasculitis, lymphoma, diabetes mellitus, corneal ulceration, autoimmune phenomena, uveitis, sialadenitis and peripheral neuropathy also occur; 1 case of acute disseminated encephalomyelitis reported; infection becomes chronic in 75-85%, with 60-70% having evidence of active liver disease and cirrhosis occurring in 20% of total within 20 y; test for anti-HCV by ELISA (false positives and negatives) and recombinant immunoblot assay (expensive and number of samples give indeterminate results) if positive, reverse transcriptase PCR for hepatitis C virus RNA (negative result does not necessarily exclude infection); genotyping; serum alkaline phosphatase 310 IU/mL, total serum bilirubin 2.6 mg/dL, serum glutamic-oxaloacetic transaminase > 100 U/mL; serum ALT and AST may be elevated in acute cases

Hepatitis D: incubation period 2-8 w; abrupt onset of signs and symptoms of hepatitis B; HbsAg +ve or IgM anti-HBc +ve + anti-HDV +ve

Hepatitis E: incubation period 2-9 w; immunoelectron microscopy of stool during incubation and early infection; IgM anti-HEV +ve; enzyme immunoassay, Western blot assay (IgM elevated 1 mo after infection, IgG after 6-8 w);

Q Fever: indirect fluorescent antibody titre, complement fixation test

Focal Hepatic Candidiasis: serum alkaline phosphatase increased in 92% of cases; total serum bilirubin increased in 36% of cases, direct in 33%

Parasites: complement fixation test, bentonite flocculation, indirect hemagglutination, latex agglutination, direct agglutination, indirect immunofluorescence, immunodiffusion, counterimmunoelectrophoresis

Capillaria hepatica: acute or subacute hepatitis with high eosinophilia; may be splenomegaly, pneumonitis, fever, constipation and abdominal distension; case-fatality rate high; microscopy of biopsy or autopsy specimen for ova

Fasciola hepatica: fever, pain in right hypochondrium, hepatomegaly, hypergammaglobulinemia, marked eosinophilia; ELISA

Treatment: ursodeoxycholic acid in chronic

Viruses: mainly non-specific; discontinue steroids

Simplexvirus: 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

Hepatitis B (e Antigen Positive, Chronic Active Disease for ≥ 6 mo and on Liver Biopsy): lamivudine 100 mg orally daily until HbeAg is undetectable and replaced by anti-Hbe on 2 occasions at least 3 mo apart (may cause severe and fatal infection if resistance develops), interferon α -2 4.5-10x10⁶ U s.c. 3 times a week for 6 mo or 5x10⁶ units s.c. daily for 6 mo

Unresponsive: interferon α -2 9-10x10⁶ U s.c. 3 times a week for further 6 mo; famciclovir; lamivudine

Renal Transplant Recipient: lamivudine, famciclovir

Liver Transplant Recipient: lamivudine 12 mo + long term hepatitis B immunoglobulins

Hepatitis C: pegylated interferon α -2b \pm ribavirin (not if anemia, hemoglobinopathy, white blood cell count < 1500/mL, platelet count < 100,000/mL, pregnant or unable to practise contraception, decompensated cirrhosis, severe psychiatric illness, cardiovascular disease, seizure disorder or poorly controlled diabetes mellitus; low probability of effectiveness) \pm amantadine for 6 mo if genotype 2 or 3, 1 y if genotype 1 or 4

Staphylococcus aureus: cloxacillin, penicillin

Listeria monocytogenes: penicillin, cotrimoxazole

Escherichia coli: gentamicin

Salmonella typhi: chloramphenicol, cotrimoxazole

Shigella: cotrimoxazole, ampicillin (not amoxicillin)

Burkholderia pseudomallei: cotrimoxazole + ceftazidime or meropenem or imipenem

Brucella: doxycycline + rifampicin or streptomycin, ciprofloxacin + rifampicin

Yersinia pseudotuberculosis: gentamicin, cefotaxime, doxycycline, ciprofloxacin

Campylobacter jejuni: erythromycin

Coxiella burnetii: tetracycline 500 mg orally 6 hourly for 14 d, doxycycline 100 mg orally 12 hourly for 14 d, rifampicin 600 mg (child: 7.5 mg/kg) orally daily, erythromycin 500 mg orally 6 hourly (child: 30 mg/kg/d in 4 divided doses) for 14 d

Mycobacterium tuberculosis: 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 μ M/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)

Mycobacterium avium-intracellulare: 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

Mycobacterium leprae: dapsone + isoniazid, sulphonamides

Treponema pallidum subsp pallidum: penicillin

Leptospira: oxytetracycline

Rickettsia: tetracycline, chloramphenicol

Borrelia recurrentis: penicillin, tetracycline, doxycycline (may be associated with Jarisch-Herxheimer reaction)

Actinomyces: penicillin ± streptomycin, tetracycline, erythromycin, third generation cephalosporin

Nocardia: sulphonamides, cotrimoxazole

Fungi: amphotericin B

Leishmania, Plasmodium: chloroquine, hydroxychloroquine sulphate, amodiaquine, mepacrine, quinine, primaquine, proguanil, pyrimethamine

Toxoplasma: sulphadiazine 1-1.5 g orally or i.v. 6 hourly for 3-6 w then 500 mg orally 6 hourly or 1 g orally 12 hourly + pyrimethamine 50-100 mg orally loading dose then 25-50 mg daily for 3-6 w (continue if necessary)

Sulphadiazine Hypersensitive: substitute clindamycin 600 mg orally or i.v. 6 hourly for 3-6 w (continue 8 hourly if necessary)

Schistosoma: praziquantel, niridazole, sodium stibogluconate

Echinococcus: thiabendazole

Entamoeba histolytica: chloroquine + emetine hydrochloride

Capillaria hepatica: no known treatment

Fasciola hepatica: bithionol

Prophylaxis:

Hepatitis A:

Postexposure: 0.02 mL/kg human immune globulin i.m. as a single dose within 2 w of exposure (close contact with persons having acute hepatitis A—household, sexual contacts, prisons, institutions for mentally retarded, day care centres; persons with repeated exposures within past 2 w to food prepared by IgM hepatitis A virus antibody positive handler handling high risk foods and with poor hygiene)

Preexposure: Travellers to Endemic Regions, People Attending Day Care Centres or Institutions Where Hepatitis A is Prevalent, Sewerage Workers, HIV Negative Homosexual Men, Food Handlers, Recipients of Blood Products, People With Significant Chronic Liver Disease, Illegal Drug Users: 2 doses of inactivated virosome vaccine provides 20 y protection (combined hepatitis A and B vaccine also available); care in handling feces, blood, other secretions and possibly contaminated objects

Hepatitis B: vaccine (low prevalence: health personnel, dialysis patients, institutionalised patients, drug addicts, male homosexuals, persons with history of sexually transmitted disease, persons who have had multiple sex partners, those who have had sex with injection drug user, household members, sex partners and drug-sharing partners of person with chronic infection, persons receiving clotting factor concentrates; high prevalence: all infants; months 0, 1, 2 and 12; inoculation in deltoid rather than buttock as gives better titres; 17% soreness at vaccination site, 15% fever, fatigue, headache, nausea; immunity 5 y but 30% require booster < 3 y after initial course; 2 types—plasma-derived and recombinant DNA; latter may require larger and repeated doses for hemodialysis patients and immunosuppressed patients; avoid in patients with risk of CNS disease) (combined hepatitis A and B vaccine also available), care in handling contaminated blood and secretions

Perinatal Exposure (Infants Born to HBsAg Positive Mothers): hepatitis B immune globulin (HBIG) 0.5 mL i.m. within 12 h of birth, followed by vaccine 0.5 mL i.m. at same times as HBIG or within 7 d, repeated at 1 and 6 mo

Percutaneous Exposure (Acute Exposure to HBsAg by Accidental Needle Stick or Mucosal Exposure):

Where Risk of Source of Infection Being Positive is High or Known to be HBsAg Positive: HBIG 0.06 mL/kg to maximum 5 mL i.m. as a single dose within 24 h, repeat at 1 mo or vaccine 0.5-1 mL at same time as HBIG or within 7 d, repeated at 1 and 6 mo if unvaccinated or partially vaccinated

Where Risk of Source of Infection Being Positive is Low or Source Unknown: vaccine only administered within 7 d of exposure; otherwise, no prophylaxis

Sexual Exposure (Sexual Contact of Persons with Acute Hepatitis B during Previous Month): HBIG 0.06 mL/kg to 5 mL maximum i.m. + hepatitis B vaccine within 14 d

Hepatitis C (Percutaneous Exposure): if source HCV antibody negative and unlikely to be in window period, none; otherwise, HCV RNA testing at 4-6 w and HCV antibodies and ALT at 4-6 mo; consider early therapy if seroconversion

Mycobacterium avium Complex in HIV/AIDS, CD4 < 50/μL: azithromycin 1.2 g orally weekly, clarithromycin 500 mg orally 12 hourly, rifabutin 300 mg orally daily

Toxoplasma gondii in HIV/AIDS, CD4 < 200/μL: cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times daily

LIVER CARCINOMA may be caused by hepatitis B virus transforming hepatic cell. Liver cancer is especially common in those with persistent hepatitis B infection.

HEPATIC ABSCESS: mortality 23%; pyogenic liver abscesses cause 0.007-0.03% of hospital admissions in temperate districts but ≈ 0.09% in Thailand

Agents: 50% mixed anaerobes (especially Gram positive cocci; also *Odoribacter splanchnicus*); *Staphylococcus aureus*, coliforms, *Actinomyces*, *Burkholderia pseudomallei*, *Yersinia pseudotuberculosis*, *Chromobacterium violaceum* (in 44% of infections), *Listeria monocytogenes* (in diabetes), *Streptococcus milleri*, *Edwardsiella tarda* (rare), *Haemophilus influenzae* (adult), *Haemophilus parainfluenzae*, *Klebsiella pneumoniae* (in diabetics; especially serotype K1), *Entamoeba histolytica* (resulting from hepatic amoebiasis; may rupture into peritoneum, pericardium, pleura or lung), *Schistosoma*, *Toxocara*

Diagnosis: incubation period > 21 d in amoebic; night sweats in 75% of amoebic; liver enlargement in 69-76% of bacterial, 95-100% of amoebic (presenting complaint in 40%); fever in 63-100% of bacterial, 35-95% of amoebic (< 38°C in 60%; presenting complaint in 40%); nausea/vomiting in 60-75% of amoebic; raised right diaphragm in 60% of amoebic; epigastric pain and tenderness in 48-52% of amoebic; right upper quadrant pain and tenderness in 47-69% of bacterial, 66-100% of amoebic (presenting complaint in 30%), 57% of actinomycotic; chills in 42-70% of amoebic; right shoulder pain in 40% of amoebic (presenting complaint in 3%); anorexia/weight loss/fatigue in 33-100% of amoebic (presenting complaint in 5%), 3% of actinomycotic; back pain in 30% of amoebic; diarrhoea in 25-66% of amoebic (50% bloody; presenting complaint in 15%); right chest pain in 6-50% of amoebic; hiccoughs occasionally in amoebic; right pleural effusion in 35% of amoebic; geographic history; epidemiological history; ultrasonography; radioactive isotope scan (positive in 89% of pyogenic; large, single defect in right lobe in amoebic); arteriogram (positive in 77% of pyogenic); upper gastrointestinal X-ray (positive in 19% of pyogenic; elevated right hemidiaphragm in 60% of amoebic); micro and culture of biopsy, aspirated fluid (in amoebic, trophozoites found only at periphery of cavitory lesions and aspirates may be falsely negative; sensitivity is only 20-30%); serology (amoebic; complement fixation test (evaluated), bentonite flocculation (evaluated), indirect hemagglutination (commercially available; with counterimmunoelectrophoresis, most sensitive (70%) and specific (70-80% in acute, > 90% in convalescent)), latex agglutination (commercially available), indirect immunofluorescence (evaluated), immunodiffusion (agar gel diffusion; commercially available), immunoelectrophoresis, counterimmunoelectrophoresis (commercially available; with indirect haemagglutination, most sensitive and specific), ELISA (commercially available; dot ELISA for antibody as sensitive as indirect hemagglutination and better than plate ELISA and has 100% specificity); animal inoculation (monkey, ferret); trophozoites or cysts in stool (25% of amoebic); white cell count > 10,000/μL in 87% of pyogenic and 62-90% of amoebic (42-60% 10,000-20,000/μL); elevated prothrombin time in 80% of amoebic; anemia in 95% of actinomycotic, 31-70% of amoebic (haemoglobin 10-14 g/dL in 66-70%), also in pyogenic; hematocrit 80-100% of normal in 52% of amoebic, < 35% in 50% of pyogenic; elevated ESR in 95% of actinomycotic; leucocytosis in 93% of actinomycotic; serum albumin decreased in 23-60% of amoebic, 3 g/dL in 33% of pyogenic; serum alkaline phosphatase > 10 IU/mL in 55-60% of pyogenic, increased in 91% of actinomycotic and in 23-60% of amoebic (< 130 IU in 60% of acute cases but > 130 IU in 90% of chronic cases); serum bilirubin 2 mg/dL in 53% of pyogenic, increased in 13-26% of amoebic; serum glutamic-oxaloacetic acid transaminase > 40 U/mL in 51% of pyogenic, < 40 IU in 45-73% of amoebic; serum lactic dehydrogenase normal in 93% of amoebic; globulin elevated in 56% of amoebic

Differential Diagnosis (Amoebic): pyogenic liver abscess, hepatic neoplasm, hydatid cysts; male gender, insidious onset, fever, history of chronic diarrhoea (only in 30-40% of patients), right pleuritic pain, single hepatic lesion of right lobe, liver enlargement, liver tenderness, liver filling defect favour diagnosis

Treatment: aspiration +:

Chromobacterium violaceum: chloramphenicol

Actinomyces: penicillin, tetracycline

Klebsiella pneumoniae: ceftriaxone

Other Bacterial: ciprofloxacin + metronidazole

Entamoeba histolytica: metronidazole 750 mg orally or i.v. 8 hourly (child: 35-50 mg/kg/d in 3 doses) for 10 d or tinidazole 2 g orally daily for 3-5 d or 600 mg twice daily for 10 d (child: 50 mg/kg/d for 3-5 d); emetine 1 mg/kg/d to 60 mg maximum in 2 divided doses for 5 d, followed by chloroquine phosphate 600 mg base orally daily for 2 d, then 300 mg base orally daily for 2-3 w (child: 10 mg base/kg to 300 mg maximum daily for 2-3 w) if no response to metronidazole in 72 h; percutaneous or surgical drainage if no response to chemotherapy after 5 d, abscess > 10 cm, or suspected impending rupture; if concomitant cyst passing detected, presume cysts pathogenic and treat with diloxanide

furoate 500 mg 3 times daily (child: 20 mg/kg/d in 3 divided doses) for 10 d or diodohydroxyquine to eliminate carrier state

HEPATIC GRANULOMA

Agents: 20% *Mycobacterium tuberculosis*, 2% *Brucella*, 2% *Schistosoma*, 1% fungi (*Histoplasma capsulatum*, *Cryptococcus neoformans*, *Coccidioides immitis*, *Ajellomyces dermatitidis*, *Candida*, *Torulopsis*, *Aspergillus*), 1% viruses (*human cytomegalovirus*, *Epstein-Barr virus*, *human hepatitis A virus*, *human hepatitis B virus*, *influenzavirus B*); atypical mycobacteria, *Mycobacterium bovis* BCG, *Mycobacterium leprae* (in 90% of lepromatous cases, 20% of tuberculoid), *Francisella tularensis*, *Klebsiella granulomatis*, *Burkholderia pseudomallei*, *Listeria monocytogenes*, *Nocardia*, *Actinomyces*, *Salmonella typhi*, *Salmonella paratyphi B*, *Coxiella burnetii*, *Treponema pallidum subsp pallidum*, *Chlamydia*, *Toxocara*, *Fasciola*, *Capillaria*, *Strongyloides*, *Ascaris*, *Ancylostoma*, *Entamoeba histolytica*, *Toxoplasma*, *Plasmodium*, Pentastomida; 35% sarcoidosis, 10% cirrhosis, 2% lymphomas, 1% drug-induced and toxic; others

Diagnosis: histology, microscopy and culture of biopsy; serology; counterimmunoelectrophoresis; bromosulphophthalein retention increased in 80% of sarcoidosis, 73% of tuberculous and 56% of fungal; cholesterol abnormal in 33% of tuberculous, 17% of fungal, normal in sarcoidosis; serum alanine aminotransferase decreased in 50% of sarcoidosis, 47% of tuberculous, 25% of fungal; serum bilirubin increased in 37% of tuberculous, 18% of sarcoidosis, normal in fungal; serum gamma globulin increased in 86% of fungal, 83% of sarcoidosis, 68% of tuberculous

Tuberculosis: fever of unknown origin, frequently with chills, anemia, meningeal involvement, loss of weight and asthenia, symptoms < 6-8 mo

Treatment:

Mycobacterium tuberculosis: 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)

Other Mycobacteria: 4-6 of ethionamide, cycloserine, viomycin, ethambutol, pyrazinamide, capreomycin

Brucella*, *Francisella tularensis*, *Klebsiella granulomatis: streptomycin

Burkholderia pseudomallei*, *Nocardia*, *Toxoplasma: cotrimoxazole + ceftazidime or meropenem or imipenem

Listeria monocytogenes: ampicillin

Salmonella: chloramphenicol

Actinomyces: penicillin

Fungi: amphotericin B 0.75 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 14 d

Entamoeba histolytica: metronidazole, emetine + chloroquine

Schistosoma: praziquantel, niridazole, sodium stibogluconate

Plasmodium: chloroquine

Fasciola: bithionol

Capillaria: no known treatment

Pentastomida: levamisole

Other Parasites: thiabendazole

Viral: mainly non-specific

Unknown: isoniazid + steroids

BACILLARY PELIOSIS: blood-filled peliotic changes in hepatic or splenic parenchyma; especially in AIDS

Agents: *Bartonella henselae*, *Bartonella quintana*

Diagnosis: Warthin-Starry stain of biopsy

Treatment: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 3-4 mo (not < 8 y), erythromycin 10 mg/kg to 500 mg orally 6 hourly for 3-4 mo, erythromycin ethyl succinate 20 mg/kg to 800 mg orally 6 hourly for 3-4 mo

MALARIAL SPLENOMEGALY: occurs in areas where malaria is endemic

Agent: *Plasmodium* species

Diagnosis:

Hyperreactive Malarial Splenomegaly (Tropical Splenomegaly Syndrome): elevated serum IgM level, high malarial antibody titre, lymphocytic infiltration of hepatic sinusoids; parasitemia rare; decreases with long-term corticosteroid therapy

Nonimmune Malarial Splenomegaly: serum IgM and malarial antibody levels not elevated; occurs in the absence of immunity during acute malarial attacks, recrudescences or epidemics

Treatment:

Hyperreactive: corticosteroids

Nonimmune: antimalarials

SPLENIC ABSCESS

Agents: *Staphylococcus aureus*, *Salmonella*, *Escherichia coli*, *Propionibacterium acnes*, *Propionibacterium avidum*, *Listeria monocytogenes*, *Clostridium difficile*, *Shigella flexneri* (extremely rare), *Streptococcus pneumoniae* (rare), *Streptococcus equinus* (rare), *Mycobacterium tuberculosis* (in AIDS), *Allelomyces dermatitidis* (rare), others

Diagnosis: computed tomography, ultrasonography; culture of biopsy or surgical specimen

Treatment: resection +:

Staphylococcus aureus: cloxacillin

Salmonella, Escherichia coli: chloramphenicol

Propionibacterium: penicillin

Listeria monocytogenes: ampicillin

Clostridium difficile: vancomycin, metronidazole

Mycobacterium tuberculosis: 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)

Streptococci: benzylpenicillin 18 MU/d i.v. + gentamicin 240 mg/d i.v. for 2 w, then amoxycillin 1.5 g/d oral + clindamycin 900 mg/d oral

Ajellomyces dermatitidis: amphotericin B, ketoconazole

LYMPH GLAND INFECTIONS

Agents: 36% *Mycobacterium* (23% of cervical lymph node infections in children; 20% *Mycobacterium tuberculosis* (5% of tuberculosis cases; 5% of cervical lymph node infections in children), 12% *Mycobacterium avium-intracellulare*, 4% *Mycobacterium kansasii*; *Mycobacterium scrofulaceum* (frequent cervical in children); infrequent *Mycobacterium chelonae*, *Mycobacterium fortuitum* (cervical), *Mycobacterium haemophilum*, *Mycobacterium malmoeense*), 35% fungal (27% *Histoplasma capsulatum*, 3% *Ajellomyces dermatitidis*, 2% *Coccidioides immitis*, 2% *Cryptococcus neoformans*, 1% *Sporothrix schenckii*, rare *Aspergillus*), 3% *Staphylococcus aureus* (79% of cervical lymph node infections in children); *Brucella* (in 50% of infections), *Corynebacterium pseudotuberculosis*, *Listeria monocytogenes*, *Yersinia pestis* (pea-sized to orange-sized inguinal, axillary), *Francisella tularensis* (painful; neck, axillary, epitrochlear), *Toxoplasma gondii* (localised or general)

Diagnosis: Gram stain, Ziehl-Neelsen stain, fluorescent antibody stain, direct immunofluorescence and culture of lymph node; histology; serology

Cervical: mildly tender, small to moderate nodes usually secondary to viral upper respiratory tract infection; large, tender anterior nodes associated with pharyngitis/tonsillitis; large tender nodes with skin erythema and fever occur in Kawasaki syndrome, *Epstein-Barr virus* infections and cat scratch disease; acute suppurative secondary to local staphylococcal skin infection, streptococcal tonsillopharyngitis or dental infection; chronic or subacute unilateral usually mycobacterial

Tuberculosis: nodes usually in supraclavicular area or posterior cervical triangle, more commonly bilateral; pulmonary tuberculosis may be present; constitutional symptoms prominent

Brucella: acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Other Bacterial Infections: fever usually present; nodes may be warm and tender; pharyngitis may be present

Toxoplasmosis: IgM-IFA, DS-IgM-ELISA, serial IgG tests; biopsy

Differential Diagnosis: cat scratch disease (usually unilateral and suppurates—similar to nontuberculous mycobacterial infection; history of cat scratch; skin tests), infectious mononucleosis (blood picture, heterophil antibody test, specific tests for *Epstein-Barr virus*), lymphoma (involvement of other sites may be present), leukemia (blood picture, bone marrow examination)

Treatment:

Suppurative: di/flucloxacillin 25 mg/kg to 500 mg orally 6 hourly for 7 d, cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7 d

Brucella: doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day for 45 d, ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally twice a day for 30 d

Staphylococcus aureus: di/flucloxacillin 25 mg/kg to 500 mg orally 6 hourly for 7 d, cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7 d

Corynebacterium pseudotuberculosis: erythromycin or penicillin + surgical drainage or excision

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

Listeria monocytogenes: erythromycin 500 mg orally 6 hourly (child: 30 mg/kg daily in 4 divided doses) for 5 d

Mycobacterium tuberculosis: 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)

Other Mycobacteria: ethionamide, cycloserine, viomycin, ethambutol

Francisella tularensis: streptomycin, tetracycline

Yersinia pestis: streptomycin

Fungi: resection; amphotericin B, miconazole (not *Aspergillus*)

Toxoplasma gondii: cotrimoxazole, sulphadiazine + pyrimethamine, spiramycin

LYMPHADENOPATHY: 0.3% of new episodes of illness in UK

Agents: in addition to the above specific infections, a number of agents cause more or less characteristic lymphadenopathy

Preauricular: acute hemorrhagic conjunctivitis (in 77% of cases), epidemic keratoconjunctivitis (in 85% of cases)

Postauricular: rubella (also suboccipital and postcervical)

Cervical: 38% undiagnosed, 17% benign noninfectious causes, 13% cat scratch disease, 12% malignancy, 9% secondary to tonsillitis, sinusitis, parotitis, mastoiditis, otitis, 3% *Toxoplasma gondii*, 2% *Streptococcus pyogenes*, 1% *Staphylococcus aureus*, 1% *Mycobacterium tuberculosis*, 1% anaerobes, 1% *Epstein-Barr virus*, 1% *simplexvirus 3*, *mumps virus*, tularemia, Lyme disease, *Haemophilus parainfluenzae*, *Haemophilus aphrophilus*, *Streptococcus anginosus*, *Actinomyces israelii*, *Corynebacterium diphtheriae*, *human cytomegalovirus* (rare), Kawasaki syndrome (68% of cases have an acute nonsuppurative cervical mass > 1.5 cm diameter)

Axillary: anthrax, *Pseudomonas aeruginosa* whirlpool-associated dermatitis (painful; in 14% of cases), psittacosis (also enlarged red lymphoid follicles on posterior pharyngeal wall)

Inguinal: anthrax, chancroid (in 32% of cases; tender, unilateral or bilateral), gonorrhoea, granuloma inguinale, herpes genitalis, lymphogranuloma venereum, *Yersinia enterocolitica* (bilateral)

Near Primary Site of Infection: Chaga's disease, *Pasteurella multocida*, staphylococci, streptococci

Generalised: *human adenovirus 4* (in 7% of cases), *human adenovirus 16* (in 58% of cases), AIDS (persisting 3+ mo), algal infection, chromobacteriosis (in 11% of cases), cryptosporidiosis (in 14% of cases), Gambian trypanosomiasis, Rhodesian trypanosomiasis (fulminating), leprosy, protozoan infection, Rocky Mountain spotted fever (in 27% of cases; 13% in first 3 d), syphilis (primary and secondary)

Diagnosis: clinical; ultrasound; serology; culture, histology and special staining of needle aspiration or extirpated node; PCR of biopsy for cat scratch disease

Treatment: dependent on agent

LYMPHANGITIS occurs with *Brugia malayi* and *Wuchereria bancrofti* infections. Ascending lymphangitis is also seen (rarely) in tularemia.

MESENTERIC LYMPHADENITIS

Agents: adenovirus (intussusception common), measles (in 15% of hospitalised cases), *Yersinia pseudotuberculosis*, *Yersinia enterocolitica*, *Mycobacterium tuberculosis*

Diagnosis: viral and bacterial culture of biopsy; serology (monospecific saline agglutination titre $\geq 1:128$ in previously healthy individual; rise or fall in titre; indirect immunofluorescent antibody test)

***Yersinia pseudotuberculosis*:** ESR 10-105 mm/h, white cell count 5 500-18 500/ μ L

Treatment: surgery if indicated

***Yersinia*:** gentamicin, cefotaxime, doxycycline, ciprofloxacin

***Mycobacterium tuberculosis*:** 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 μ M/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)

CAT SCRATCH DISEASE (BENIGN INOCULATION LYMPHORETICULOSIS, BENIGN LYMPHORETICULOSIS, BENIGN RETICULOSIS, CAT SCRATCH FEVER, DEBRÉ-MOLLARET SYNDROME, FELINOSIS, FOSHAY-MOLLARET SYNDROME, INOCULATION ADENITIS, LYMPHORETICULOSIS BENIGNA, MORBUS PETZETAKIS, NONBACTERIAL REGIONAL LYMPHADENITIS, PETZETAKIS DISEASE): usually benign; typical presentation (initial cutaneous lesion at site of inoculation, followed by regional lymphadenitis, which often leads to formation of fistulas through which enlarged suppurating lymph nodes drain) in 88% of cases, inoculation lesion (skin, eye, mucous membrane) in 59%, Parinaud's oculoglandular syndrome in 6%, encephalitis in 2%, severe or chronic systemic disease (including abdominal visceral granulomas) in 2%, erythema nodosum in 0.6%, pneumonitis in 0.2%, breast tumour in 0.2%, thrombocytopenia purpura in 0.1%; also mesenteric adenopathy; fatigue, malaise, weight loss, progressively higher and longer recurring fevers, headache and hepatomegaly in HIV-infected patients; spread through cat flea feces

Agent: *Bartonella henselae*

Diagnosis: adenopathy only in 51%, fever in 31% (71% in AIDS), malaise/fatigue in 28% (36% in AIDS), headache in 13%, anorexia, emesis, weight loss in 13% (36% in AIDS), splenomegaly in 12%, sore throat in 9%, exanthem in 4%, conjunctivitis in 4%, swelling of parotid gland in 2%; severe systemic disease and multiple skin sites in 93% of AIDS patients infected; cat contact with presence of scratch or primary dermal or eye lesion; normal blood cells and differential count; Mantoux tests negative; serology for *Epstein-Barr virus*, *human cytomegalovirus*, *Toxoplasma*, fungal diseases, lymphogranuloma venereum, syphilis, *human immunodeficiency virus*, *simplexvirus*, tularemia, brucellosis and streptococci negative; skin test (cat scratch antigen; positive in 98-99% of cases; not in widespread use because antigen difficult to obtain and not standardised); characteristic histopathologic changes in lymph node or skin lesion; demonstration of small, pleomorphic bacilli in collagen fibres, in abscesses or in granulomas, stained by Warthin-Starry silver impregnation method, Brown-Hopps stain or immunoperoxidase stain; PCR; culture usually unsuccessful

Treatment: spontaneous cure in 2-21 mo in normal patients; often severe in AIDS; azithromycin 10 mg/kg to 500 mg orally first day then 5 mg/kg to 250 mg orally once a day for 4 d; aspiration of abscesses or fluctuant nodes as necessary

Prophylaxis: eradication of cat fleas

EPSTEIN-BARR VIRUS DISEASE: widespread, particularly in young; $\approx 14,000$ cases/y (17 deaths/y) in USA; 0.01% of new episodes of illness in UK; transmitted by contact with external secretions (saliva); incubation period 7-14 d; inflammatory reaction in all reticuloendothelial organs

Agent: *Epstein-Barr virus*, *simplexvirus 6* primary infection in adults gives similar condition; *human cytomegalovirus* and *Toxoplasma gondii* give similar symptoms but without pharyngitis or heterophil agglutinins; lymphadenopathy and rash are rare with *human cytomegalovirus*

Diagnosis:

Children < 8 y: glandular fever: fever in 90%, splenomegaly in 60%, > 25% atypical lymphocytes in 55%, lymphadenopathy in 50%, hepatomegaly in 45%, abnormal liver function tests in 45%, lymphocytes > 50% of leucocytes in 40%, exudative pharyngitis in 40%, heterophil antibody in 5%, autoantibodies absent

Older Children, Young Adults, AIDS Cases and Organ Transplant Recipients: monocytic angina: sore throat ± increased lymph glands

Young Adults (15-30 y): infectious mononucleosis: lymphadenopathy in 95%, abnormal liver function tests in 95%, lymphocytes > 50% of leucocytes in 90% (> 35% in all) and atypical lymphocytes in all cases (also present with adenovirus, *human cytomegalovirus*, *simplexvirus*, *mumps virus*, *rubella virus*, toxoplasmosis and viral hepatitis and as drug reaction to hydantoinates, paraaminosalicylic acid, phenylbutazone and sulphonamides) but with > 25% atypical lymphocytes in 45% (> 50% lymphocytes with > 10% atypical mononuclears sensitivity 39%, specificity 97%), continued fever in 85%, serum glutamic-pyruvic acid transaminase increased in 84%, serum glutamic-oxaloacetic acid transaminase increased in 83%, serum alkaline phosphatase increased in 81%, heterophil agglutinin antibody (Paul-Bunnell-Davidsohn test) positive (titre 1:128 after absorption by guinea pig and ox cells) in 80-100%, exudative pharyngitis and sore throat (but without conjunctivitis or rhinitis) in 80%, serum gamma globulin increased in 72%, increased leucocytes but decreased neutrophils in 60-80%, bone marrow granulomas in 50%, serum bilirubin increased in 43%, splenomegaly in 40-55%, serum albumin decreased in 36%, autoantibodies in 25%, platelet count slightly decreased in 25-50%, occult hemolysis in 20-40%, blood urea increased in 15-20%, rash in 10-20%, hepatomegaly in 10%, liver damage common; early antigen antibody > 1:20 (sensitivity 90%, specificity 97%; indicates active infection; appears at 1-4 w, duration 6 mo); indirect fluorescent antibody titre or ELISA for IgG, IgA and IgM (viral capsid antigen antibody > 1:650 sensitivity 40%, specificity 100%; IgG appears rapidly after onset, peaks after 1-2 mo, slowly drops to ≈ 1:320, maintained for life; IgM positive in acutely ill, peaks at 2-3 mo); EA:VCA > 0.031 (sensitivity 100%, specificity 97%); Epstein-Barr nuclear antigen antibody positive 2-52 w after onset, persists for life (Pasteur IgG ELISA kit 90% sensitivity, 95% specificity); (generally, VCA IgG negative, VCA IgM negative, EBNA IgG negative = negative; VCA IgG positive, VCA IgM positive, EBNA negative = recent infection; VCA IgG positive, VCA IgM negative, EBNA IgG positive = past infection); cold agglutinins in 10-50% of cases; mitochondrial cytoplasmic fluorescence may be seen in smooth muscle; serum leucine aminopeptidase inconsistently increased; rheumatoid factor may be present; possible complications include hemolytic anemia, aplastic anemia, thrombocytopenia, neutropenia, disseminated intravascular coagulation, airway obstruction, pneumonia, pleural effusion, myocarditis, pericarditis, aseptic meningitis, meningoencephalitis, encephalitis, transverse myelitis, peripheral neuritis, facial nerve palsy, optic neuritis, Guillain-Barré syndrome, hepatic necrosis, Reye's syndrome, splenic rupture

Treatment: aspirin or paracetamol or nonsteroidal anti-inflammatory drug for pain (narcotic analgesics contraindicated); prednisolone 0.5 mg/kg for 1-2 w in patients with severe prostration, significant thrombocytopenia or hemolytic anemia; parenteral dexamethasone 0.5-1 mg/kg to 10 mg daily or hydrocortisone 100 mg 6 hourly in impending airway obstruction; famciclovir in severe cases; antimicrobials, especially ampicillin and amoxicillin, should be avoided unless there is concurrent infection with frank bacterial pathogens; drug reactions, especially skin reactions with ampicillin and amoxicillin (widespread maculopapular reaction), are common in this situation and occur also in other viral infections; if streptococcal pharyngitis is suspected, a 10 d course of penicillin or erythromycin should be given

NASOPHARYNGEAL CARCINOMA: tumour of nasal passages and throat; affects up to 2% of people in Southern China; also in Southeast Asia, northern Africa and among Arctic peoples; *Epstein-Barr virus* transforms epithelial cell (? + cocarcinogen in food)

BURKITT'S LYMPHOMA may be due to *Epstein-Barr virus* transforming B lymphocytes (evidence compelling but not conclusive; cofactor (? malaria) may be required)

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE: tumour often found in organ transplant patients

Agent: ? *Epstein-Barr virus*

ACUTE INFECTIVE LYMPHOCYTOSIS: occurs in children

Agent: ? enterovirus

Diagnosis: absolute lymphocytosis persisting for 2-3 w, eosinophilia common; associated with abdominal pain, diarrhoea and vomiting

Treatment: none

CHRONIC NON-SPECIFIC INFECTIOUS LYMPHOCYTOSIS

Agent: unknown

Diagnosis: moderate leucocytosis with lymphocytosis lasting for months, low normal hemoglobin, normal platelet count and ESR; tests for infectious mononucleosis, *human cytomegalovirus* and toxoplasmosis negative

Treatment: none

ADULT T CELL LEUKEMIA

Agent: *human T-lymphotrophic virus 1*

Diagnosis: immunoprecipitation

Treatment: as for other leukemias

HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION/ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS): worldwide; global prevalence (HIV infection) \approx 40 M ($>$ 25 M in Sub-Saharan Africa; 36% of adult population in Botswana infected; malaria important cofactor); leading cause of death in Africa, causing 25% of deaths in South Africa, and fourth leading cause of death worldwide (\approx 20 M deaths to date); \approx 600 notified cases (\approx 500 deaths)/y in Australia; 0.1% of ambulatory care visits in USA; *Pan troglodytes* (chimpanzee) probable natural host and reservoir; majority of cases sexually transmitted by anal intercourse (risk 0.06-5% per contact), remainder by vaginal intercourse (risk 0.05-0.2% per contact male to female, 0.03-6% female to male), shared use of needles (risk 0.7% per contact), transplantation, blood transfusion (risk 90% per contact), other exposure to contaminated blood (needle puncture risk 0.3% per contact), deep kissing infected individual with bleeding gums, oral sex (infection from fellatio very rare), congenital (\approx 750,000 HIV infected babies born/y globally; virus destroys T4 lymphocytes, weakening resistance to infection by a wide variety of bacteria, protozoa, fungi and viruses and causing an increased incidence of a number of carcinomas

Agent: *human immunodeficiency virus*

Diagnosis: patient history; fever in 87% of primary infections, skin rash in 50-68%; also night sweats, arthralgia, (40-80%) myalgia (40-80%), malaise, headache (40-80%), nausea (10-40%), vomiting (10-40%), diarrhoea (10-40%), anorexia, pharyngitis, weight loss (10-40% $>$ 5 kg), lymphadenopathy (40-80%), sore throat (40-80%), fatigue (40-80%), retro-orbital pain, depression; on examination, 77% have abnormalities of oral cavity (10-40% ulcers), 73% of skin (10-40% genital ulcers) and 57% of lymph nodes; 74% have thrombocytopenia ($<$ 150×10^6 /mL); also leucopenia, meningitis, neuropathy, encephalopathy; in the absence of a known cause of immunosuppression (high dose or long term systemic corticosteroid therapy or other immunosuppressive/cytotoxic therapy, Hodgkin's disease, non-Hodgkin's lymphoma (other than primary brain lymphoma), lymphocytic leukemia, multiple myeloma, any other cause of lymphoreticular or histiocytic tumour, angioimmunoblastic lymphadenopathy, congenital immune deficiency syndrome or acquired immune deficiency syndrome (such as one involving hypogammaglobulinemia) atypical of *human immunodeficiency virus* infection, any disease that is indicative of a defect in cellular immune function (candidiasis of esophagus, trachea, bronchi or lungs; extrapulmonary cryptococcosis; *human cytomegalovirus* infection of organ other than liver, spleen or lymph node in patient $>$ 1 mo; *simplexvirus* causing mucocutaneous ulcer persisting longer than 1 mo, or bronchitis, pneumonitis or esophagitis for any duration affecting patient $>$ 1 mo; Kaposi's sarcoma or primary lymphoma in the CNS in patient $<$ 60 y; meningitis, encephalitis, pneumonitis due to *Pneumocystis jiroveci*, *Toxoplasma* (patient $>$ 1 mo), *Aspergillus*, *Nocardia*, *Candida*, *Strongyloides*, zygomycetes; lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child $<$ 13 y; progressive multifocal leucoencephalopathy; chronic cryptosporidial enterocolitis (diarrhoea persisting $>$ 1 mo); disseminated (site other than or in addition to lungs, skin, cervical or hilar lymph nodes) atypical mycobacteriosis (especially *Mycobacterium avium-intracellulare* complex or *Mycobacterium kansasii*), coccidioidomycosis, histoplasmosis, toxoplasmosis of the brain in $>$ 1 mo, 2 or more bacterial infections (septicemia, pneumonia, meningitis, bone or joint infections) or abscess of internal organ or body cavity other than otitis media or superficial abscesses), or any patient with decreased T helper cells, decreased T helper/T suppressor ratio, increased serum globulins, decreased blastogenesis or anergy should be tested for possible AIDS

Low Risk Individuals With No Known Exposure: ELISA (false positives in multiparous women, those recently immunised against influenza or hepatitis B, those who have had multiple blood transfusions, and those with autoimmune disease, cirrhosis due to alcohol use, malaria, dengue or hepatitis B); confirmed with Western blot or immunofluorescence assay

Low Risk Individuals With Possible Exposure: ELISA + Western blot (frequent indeterminate reactions in absence of infection with some kits); repeated at 3, 6, 9 and 12 mo after possible exposure; p24 antigen capture if possible exposure within 6-12 w of evaluation or if patient has mononucleosis-like syndrome, followed by antibody test 4-6 weeks later

High Risk Individuals: ELISA and Western blot repeated at 6 w intervals; culture of peripheral blood lymphocytes or testing for proviral DNA in lymphocytes if negative

AIDS (as opposed to *human immunodeficiency virus* infection) is diagnosed by laboratory evidence + presence of one or more of following diseases: multiple or recurrent septicemia, pneumonia, meningitis, bone or joint infection, or abscess of internal organ or body cavity (excluding otitis media or superficial mucosal abscesses) caused by *Haemophilus*,

Streptococcus or other pyogenic bacteria in children < 13 y; disseminated or extrapulmonary coccidioidomycosis; *human immunodeficiency virus*-related encephalopathy; disseminated or extrapulmonary histoplasmosis; cryptosporidiosis or isosporidiosis with diarrhoea persisting > 1 mo; Kaposi's sarcoma; primary lymphoma of the brain; B cell non-Hodgkin's lymphoma; small noncleaved lymphoma or immunoblastic sarcoma of unknown immunologic phenotype; disseminated or extrapulmonary mycobacterial disease; pulmonary or extrapulmonary disease caused by *Mycobacterium tuberculosis*; recurrent nontyphoidal *Salmonella* septicemia; HIV wasting syndrome; candidiasis of esophagus, bronchi, trachea or lungs; *human cytomegalovirus* retinitis with loss of vision; *human cytomegalovirus* disease other than liver, spleen or nodes; lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child < 13 y; *Pneumocystis jiroveci* pneumonia; toxoplasmosis of brain affecting patient > 1 mo; invasive cervical cancer; chronic ulcers (> 1 mo duration), bronchitis, pneumonitis or esophagitis due to *simplexvirus*; recurrent pneumonia; progressive multifocal leucoencephalopathy; in the absence of serological evidence, the diagnosis of AIDS will be accepted if all other indicators listed above are excluded and any of the indicator diseases listed above are present and the T helper/inducer (CD4⁺) lymphocyte count is < 200/μL; any patient with proven *human immunodeficiency virus infection* and with one or more of the indicator diseases listed above or with CD4⁺ T cell count < 200/μL is to be considered as meeting the definition of AIDS; cases of *human immunodeficiency virus* infection with CD4⁺ counts > 200/μL are classified category B if they display any of the following symptoms: bacillary angiomatosis, oropharyngeal candidiasis, vulvovaginal thrush which is persistent or frequent or poorly responsive to therapy, moderate or severe cervical dysplasia/cervical carcinoma in situ, such constitutional symptoms as fever (38.5°C) or diarrhoea lasting > 1 mo, oral hairy leucoplakia, shingles involving at least 2 distinct episodes or > 1 dermatome, idiopathic thrombocytopenic purpura, listeriosis, pelvic inflammatory disease (particularly if complicated by tubo-ovarian abscess), peripheral neuropathy; *human immunodeficiency virus* infections with CD4⁺ counts < 200/μL and any of the above conditions are grouped as category A

Treatment: may be deferred until patient symptomatic or CD4 cell count < 350/μL; [emtricitabine + tenofovir 200 + 300 mg daily (not child) or lamivudine + zidovudine 150 + 300 mg 12 hourly (not child) or lamivudine 150 mg 12 hourly or 300 mg daily + tenofovir 300 mg daily (not child) or abacivir 300 mg 12 hourly or 600 mg daily + emtricitabine 200 mg daily (not child) or abacivir + lamivudine 600 + 300 mg daily (not child) or didanosine (< 60 kg: 250 mg daily; > 60 kg: 400 mg daily) + emtricitabine 200 mg daily (not child) or didanosine (child: 120 mg/m² (150 mg/m² in neurological disease) 12 hourly; adult < 60 kg: 250 mg daily; > 60 kg: 400 mg daily) + lamivudine (child: 4 mg/kg to 150 mg 12 hourly; adult: 150 mg 12 hourly or 300 mg daily)] + efavirenz (10-15 kg: 200 mg daily; 16-20 kg: 250 mg daily; 20-25 kg: 300 mg daily; 25-32.5 kg: 350 mg daily; 32.5-40 kg: 400 mg daily; > 40 kg: 600 mg daily; not in pregnant or likely to become pregnant) or nevirapine 120 mg/m² to 200 mg daily for 2 w then 12 hourly (not in women with CD4 cell count > 250/μL or men with CD4 cell count > 400/μL) delavirdine 400 mg 8 hourly (not < 12 y) or lopinavir + ritonavir 400 + 100 mg 12 hourly (child ≥ 2 y: 230 + 57.5 mg/m² 12 hourly) or atazanavir 400 mg daily or 300 mg daily + ritonavir 100 mg daily (not child) or fosamprenavir 700 mg + ritonavir 100 mg 12 hourly (not child) or fosamprenavir 1400 mg + ritonavir 200 mg daily (treatment naïve only; not child) or indinavir 800 mg 8 hourly (not child) or 800 mg + 100 mg ritonavir 12 hourly (not child) or nelfinavir 25-35 mg/kg to 750 mg 8 hourly or 45-55 mg/kg to 1250 mg 12 hourly or saquinavir 1200 mg 8 hourly (soft gel capsules only; not child) or 1000 mg + ritonavir 100 mg 12 hourly (not child)

Treatment Failure: enfuvirtide 2 mg/kg to 90 mg s.c. 12 hourly (not < 6 y)

Prophylaxis:

Low Risk Exposure: lamivudine + zidovudine 4 + 10 mg/kg to 150 + 300 mg orally 12 hourly for 4 w, emtricitabine + tenofovir 200 + 300 mg orally daily for 4 w

High Risk Exposure: lopinavir + ritonavir 400 + 100 mg orally 12 hourly for 4 w, nelfinavir 25 mg/kg to 1.25 g orally 12 hourly for 4 w

Pregnancy: zidovudine + caesarean section (2% risk of vertical transmission)

HIV WASTING SYNDROME

Agent: *human immunodeficiency virus*

Diagnosis: *human immunodeficiency virus* infection + profound involuntary weight loss of > 10% of baseline body weight + either chronic diarrhoea (at least 2 loose stools/d for ≥ 30 d) or chronic weakness and documented fever (for ≥ 30 days; intermittent or constant) in absence of a concurrent illness or condition other than *human immunodeficiency virus* infection that could explain the findings (eg, cancer, tuberculosis, cryptosporidiosis or other specific enteritis)

Treatment: as for AIDS + increased fluids, calories and protein, smoking cessation, regular exercise; recombinant growth hormone for muscle wasting

VIRUS-ASSOCIATED HEMOPHAGOCYTTIC SYNDROME: fulminant disorder associated with systemic viral infection

Agents: *Epstein-Barr virus*, *human cytomegalovirus*, adenovirus, *simplexvirus 1* and *2*, *human herpesvirus 6*

Diagnosis: multiple organ infiltration of hemophagocytic histiocytes into lymphoreticular tissues

Treatment: supportive