Chapter 9

Infections of the Cardiovascular System

Aplastic Crisis

Agent: *human parvovirus B19* in persons with underlying hemolytic disorders

Diagnosis: dot hybridisation, capture ELISA on serum (Biotrin and Dako 100% sensitivity and specificity), PCR

Treatment: supportive

Chronic Anemia

Agent: *human parvovirus B19* in immuncompromised (especially HIV/AIDS)

Diagnosis and Treatment: as above

Babesiosis (Piroplasmosis): America, Ireland, Scotland; transmitted by *Ixodes* tick (black-legged tick, sheep tick) that feeds on deer as an adult but on mice and man in immature stages

Agent: *Babesia bovis* and *Babesia divergens* in splenectomised persons (usually fatal), *Babesia microti* in persons with intact spleen (usually self-limited)

Diagnosis: organisms seen in erythrocytes in Giemsa stained blood films; serology by indirect fluorescent antibody titre; inoculation of patient's blood into splenectomised hamsters or guinea pigs, followed by microscopy of animal's blood

***Babesia bovis* and *Babesia divergens*:** rapid onset, fever, chills, jaundice, dark urine with hemoglobinuria, hypotension, severe anorexia, renal insufficiency

***Babesia microti*:** gradual onset, fever, chills, diaphoresis, myalgia, anemia, fatigue, headache, pulmonary complication (cough, acute respiratory distress; pulmonary edema on chest X-ray)

Treatment: usually not necessary for patients with intact spleen; chloroquine phosphate 1.5 g orally initially followed by 500 mg orally daily for 2 w or clindamycin 1.2 g i.v. 12 hourly (child: 20-40 mg/kg daily in 3 divided doses) or 600 mg orally 8 hourly for 7-10 d + quinine 600 mg orally 8 hourly (child: 25 mg/kg daily in 3 divided doses) for 7-10 d or pentamidine isethionate produce symptomatic improvement but do not reduce parasitemia; exchange transfusion reliably affects rapid reduction of parasite load

(There have been a few reports of intaerythrocytic parasitoses with *Nuttalia* and *Entopolypoides*.)

Malaria (Ague, Cameroon Fever, Chagues Fever, Chills and Fever, Coastal Fever, Congestive Remittent Fever, Corsican Fever, Intermittent Bilious Fever, Intermittent Fever, Jungle Fever, Marsh Fever, Miasmatic Fever, Paludism, Remittent Congestive Fever, Remittent Gastric Fever, Tropical Fever): Africa, Southeast Asia, India, South America; 300-500 M clinical cases/y worldwide (2 M deaths/y); ≈ 700 notified cases/y in Australia (≈ 42% in Queensland); incidence 0.9/100,000 in USA; case-fatality rate 4%; claimed to be responsible for 50% of all human deaths from disease since Stone Age; transmitted by female *Anopheles* mosquito bite and, occasionally, congenitally, by blood transfusion (most frequently *Plasmodium malariae*) and by syringes (especially in drug addicts); variable incubation period (not < 7 d); greatly increases risk of HIV infection and death from AIDS

Agents: 73% *Plasmodium vivax*, 22% *Plasmodium falciparum*, 3% *Plasmodium ovale*, 2% *Plasmodium malariae*, 0.4% mixed; malaria due to simian plasmodia—*Plasmodium brasilianum*, *Plasmodium cynomolgi*, *Plasmodium inui*, *Plasmodium knowlesi*, *Plasmodium simium*—is very rare, may be acquired in nature or the laboratory, and is of moderate severity

Diagnosis: fever, chills, splenomegaly, decreased consciousness; sometimes dehydration, non-bloody diarrhoea, vomiting, jaundice, headache, muscle pains, anorexia; geographic history, transfusion or i.v. drug addict; Giemsa or Romanowski stain of thick and thin blood smears (3 in 48-72 h); indirect immunofluorescence when clinical diagnosis consistent with malaria but parasite not detected in thick blood films; dipstick antigen tests accurate when used by health professionals but not when used by travellers; indirect hemagglutination (experimental), immunodiffusion, ELISA (antibody); hyperbilirubinemia (total bilirubin 9.4 mg/dL), moderately elevated SGPT (15-56 U/mL) and SGOT, blood urea nitrogen 101 mg/dL, creatinine 6.8 mg/dL, anemia (hematocrit 24%, hemoglobin 8.3 g, erythrocyte count decreased), thrombocytopenia (platelets 180,000/μL)

Congenital: fever in 100%, splenomegaly in 93%, irritability in 85%, hepatomegaly in 84%, icterus in 79%

Vivax Malaria (Benign Tertian Malaria, Tertian Ague, Vivax Fever): usually non-fatal; incubation period 12-18 d; fever, headache, myalgia, malaise, nausea; after some time, paroxysms of fever and chills, ending in profuse sweating tend to occur every other day; tendency to relapse; sometimes associated with anemia, hepatomegaly and nonspecific hepatitis; occasionally complicated by spontaneous splenic rupture

Falciparum Malaria (Acute Pernicious Fever, Aestivo-Autumnal Fever, Aestivo-Autumnal Malaria, Algid Malaria (Gastrointestinal Symptoms Predominate), Chagues Fever, Continued Malarial Fever, Falciparum Fever, Malignant Tertian Fever, Malignant Tertian Malaria, Pernicious Intermittent Fever, Pernicious Malaria, Plasmodium Falciparum Malaria, Quotidian Malaria, Subtertian Fever, Subtertian Malaria Fever, Subtertian Malignant Tertian Malaria, Tertian Malignant Malaria, Tropical Malaria): severe and, in nonimmune persons, rapidly fulminating; incubation period 8-15 d; high fever, chills, headache, myalgia, rapid pulse rate, splenomegaly, sometimes delirium; often a high level of parasitemia (to 72%) and capillary obstruction; initial fever may last several days, with some remissions; after initial illness, periodic pattern of paroxysms, with fever and chills, usually lasting 12-24 h and tending to be repeated every 48 h; coma, excessive destruction of erythrocytes, convulsions and heart failure may lead to death; the disease may produce very serious complications (cerebral malaria, hemoglobinuric falciparum malaria) and neurologic sequelae (memory impairment and diffuse white matter damage on magnetic resonance imaging)

Ovale Malaria (Ovale Tertian Malaria, Plasmodium Ovale Fever): relatively mild; incubation period 12-18 d; clinical manifestations similar to those of vivax malaria but paroxysms of fever and chills less severe; after initial stage, paroxysms tend to occur every other day; recovery often spontaneous; relapses not unusual

Malariae Malaria (Quartan Malaria, Quartan Ague, Quartan Fever): incubation period 20-40 d; clinical manifestations similar to those of vivax malaria but paroxysms of fever and chills commonly occur at intervals of 3 d; recovery often spontaneous but tendency for recrudescences to occur over many years; children may develop malarial nephropathy

Differential Diagnosis: fever and chills can suggest acute viral or bacterial infection; jaundice, anemia and splenomegaly other causes of hemolytic anaemia; leucopoenia and thrombocytopenia hematolgic malignancy, other severe infections; proteinuria and edema other causes of nephrotic syndrome; acute renal failure other causes of acute renal failure; hepatosplenomegaly and lymphocytic infiltration of hepatic sinusoids lymphoma; altered mental status, seizures and coma viral or bacterial meningitis, encephalitis, Reye's syndrome; bilateral pulmonary infiltrates acute respiratory distress syndrome related to shock from various causes

Treatment:

Uncomplicated *Plasmodium falciparum*: artemether + lumefantrine (5-14 kg: 1 20 + 120 mg tablet; 15-24 kg: 2 tablets; 25-34 kg: 3 tablets; > 34 kg: 4 tablets) orally with fatty food at 0, 8, 24, 36, 48 and 60 h, quinine sulphate 10 mg/kg to 600 mg orally 8 hourly for 7 d + doxycycline 2.5 mg/kg orally 12 hourly for 7 d (not in pregnant or < 8 y) or clindamycin 5 mg/kg to 300 mg orally 8 hourly for 7 d (in pregnant and < 8 y)

Severe (Altered Consciousness, Jaundice, Oliguria, Severe Anemia, Hypoglycemia, Vomiting, Acidotic, Parasite Count > 100,000/mm^3 Or > 2% Erythrocytes Parasitised): artesunate 2.4 mg/kg i.v. immediately and repeated at 12 h and 24 h, then once daily until oral therapy possible, then as above; if parenteral artesunate not available, quinine dihydrochloride 20 mg/kg i.v. over 4 h or 7 mg/kg i.v. over 30 min then 10 mg/kg i.v. over 4 h, after 4 h 10 mg/kg i.v. over 4 h 8 hourly

Others: chloroquine phosphate 10 mg/kg base to 620 mg orally as a single dose initially, then 5 mg/kg to 310 mg at 6, 24 and 48 h (severe cases: 10 mg base/kg rate controlled i.v. infusion over 8 h, followed by 15 mg/kg over 24 h or 3.5 mg base/kg i.m. or s.c. every 6 h until patient can take oral drugs) then primaquine 0.5 mg/kg base to 30 mg orally daily with food or, if nausea, 0.25 mg/kg to 15 mg orally 12 hourly with food for 14 d (*Plasmodium vivax*) or 0.25 mg/kg to 15 mg orally daily with food for 14 d (*Plasmodium ovale*) (avoid in persons with G6PD deficiency or, in mild cases, administer 45 mg base orally weekly for 6 w; avoid during pregnancy; not required in congenital or transfusion)

Prophylaxis:

Areas Without Chloroquine Resistant *Plasmodium falciparum*: chloroquine phosphate 5 mg/kg base to 310 mg orally once a week 1 w before entering to 4 w after leaving area, hydroxychloroquine sulphate 5 mg/kg base to 310 mg once a week 2 w before entering to 4 w after leaving area; where chloroquine cannot be administered: proguanil hydrochloride (< 2 y: 50 mg; 2-6 y: 100 mg; 7-10 y: 150 mg; > 10 y: 200 mg) orally daily 1 d before entering to 4 w after leaving area, doxycycline 1 mg/kg to 100 mg (not < 8 y) orally daily 1 d before entering to 2 d after leaving area (short stay only), mefloquine 250 mg orally weekly

Areas With Chloroquine Resistant *Plasmodium falciparum*: atovaquone + proguanil (11-20 kg: 62.5 + 25 mg; 21-30 kg: 125 + 50 mg; 31-40 kg: 187.5 + 75 mg; > 40 kg: 250 + 100 mg) orally with fatty food daily 1-2 d before entering to 7 d after leaving area, doxycycline 2.5 mg/kg to 100 mg orally daily (not < 8 y) 2 d before entering to 4 w after leaving area, mefloquine (5-9 kg: 31.25 mg; 10-19 kg: 62.5 mg; 20-29 mg: 125 mg; 30-44 kg: 187.5 mg; > 44 kg: 250 mg) orally weekly 2-3 w before entering to 4 w after leaving area, proguanil (< 2 y: 50 mg; 2-6 y: 100 mg; 7-10 y:

150 mg; >10 y: 200 mg) orally daily 1 w before entering to 4 w after leaving area + chloroquine 5 mg base/kg to 310 mg base orally weekly 1 w before entering to 4 w after leaving area if others contraindicated or not tolerated

To Prevent Delayed Attacks of *Plasmodium vivax* and *Plasmodium ovale*: primaquine 0.3 mg/kg to 15 mg daily for 14 d or 0.9 mg/kg to 45 mg weekly for 8 w (tafenoquine may replace)

Personal Protective Measures: wear light coloured long-sleeved shirts and long trousers in the evening; apply insect repellent containing not more than 35% diethylmetatoluamide sparingly to exposed skin; at dusk, spray aerosolised 'knock down' insecticide (eg., containing pyrethrins) in living and sleeping areas; sleep in a screened or air conditioned room or use bed netting of small mesh and good quality that is not damaged and is, preferably, impregnated with permethrin; use mosquito coils or electrically operated insecticide generators containing pyrethroids; avoid outside activities between dusk and dawn; avoid stagnant water; avoid perfume and aftershave

Prevention and Control: mosquito control, treatment of cases

MYOCARDITIS AND PERICARDITIS

Agents: *human coxsackievirus B2-B5* (myocarditis of the newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis; > 50% of all cases), *human coxsackievirus A*, *human echovirus 6, 19*, several arboviruses, *mumps virus* (in 0.04% of mumps cases; may be fatal or followed by endocardial fibroelastosis), *measles virus*, *influenza A virus*, *influenza B virus*, adenovirus (common in paediatric HIV infection), *human cytomegalovirus* (common in pediatric HIV infection), rubella, *human hepatitis A virus*, *hepatitis B virus*, *simplexvirus 3*, *rabies virus*, *Lassa virus*, *human parvovirus B19* (in infants and heart transplant recipients), *Epstein-Barr virus, Neisseria meningitidis* (4% of purulent pericarditis), *Haemophilus influenzae* (3% of purulent pericarditis), *Pseudomonas aeruginosa*, *Campylobacter jejuni*, *Staphylococcus aureus* (23% of purulent pericarditis), *Actinobacillus actinomycetemcomitans* (rare), group C *Streptococcus* (rare), *Yersinia enterocolitica*, Q fever, *Listeria monocytogenes* (cardiac transplantation and others), *Actinomyces* (rare), *Mycoplasma pneumoniae*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, Rocky Mountain spotted fever (in 5% of infections), *Corynebacterium diphtheriae* (toxic manifestation occurring 2 d - 1 mo after onset of, especially, pharyngeal diphtheria), *Mycobacterium tuberculosis*, *Streptococcus pneumoniae* (33% of purulent pericarditis), *Rickettsia helvetica*, *Haemophilus aphrophilus* (rare), *Streptococcus pyogenes* (11% of purulent pericarditis), other Gram negative organisms (19% of purulent pericarditis), anaerobes (2% of purulent pericarditis), *Candida* (cardiac surgery, impaired host defences, severe debilitating disease), *Aspergillus* (pericarditis in 4% of disseminated cases), *Trichinella spiralis* (rare)

Diagnosis: viral culture of throat swab, feces, myocardium; serology; immunofluorescent antibody test on impression smear of myocardium; PCR of endomyocardial biopsy; bacterial and fungal culture of pericardial fluid or pericardium; histology of pericardium; latex agglutination and counterimmunoelectrophoresis of serum and pericardial fluid; blood cultures; when hemorrhagic pericardial effusions of undetermined cause are determined, the heart and great vessels should be evaluated as potential sources of the hemorrhage

***Human parvovirus B19*:** PCR; bone marrow biopsy (pure red cell aplasia, giant proerythroblasts, vacuolisation of cytoplasm and intranuclear inclusions in paltry surviving precursors)

Diphtheric Myocarditis: thready pulse, faint heart sounds, cardiac arrhythmia; cardiac failure may occur

Pericardial Actinomycosis: 68% dyspnoea, 68% pleural effusion, 63% tachypnoea, 63% cough, 58% hepatomegaly, 53% fever, 53% chest pain

Treatment:

Influenza Virus: i.v. ribavirin

***Human parvovirus B19*:** human immunoglobulin 0.5-1 g/kg/d i.v. for 4-5 d, erythropoietin

Other Viruses: non-specific

***Actinomyces*:** benzylpenicillin 12-20 MU/d i.v. for 4-6 w, then phenoxymethylpenicillin or amoxycillin 2-4 g/d orally for 6-12 mo; tetracycline or erythromycin ± rifampicin 300 mg/d; clindamycin; chloramphenicol; third generation cephalosporin

***Neisseria meningitidis,* Streptococci:** benzylpenicillin

***Haemophilus influenzae*, *Listeria monocytogenes*:** ampicillin

***Pseudomonas aeruginosa*:** azlocillin + tobramycin

***Campylobacter jejuni*:** erythromycin

***Staphylococcus aureus*:** vancomycin

***Actinobacillus actinomycetemcomitans*, *Rickettsia*:** tetracycline, chloramphenicol

Coxiella burnetii: doxycycline, tetracycline, erythromycin, rifampicin

***Yersinia enterocolitica*:** pefloxacin 400 mg twice daily + tobramycin 75 mg twice daily

***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 isonazid and rifampicin (to 6 mo) + prednisone 40-80 mg daily, decreasing over several weeks

***Mycoplasma*, *Ureaplasma*:** tetracycline, erythromycin

***Candida*:** amphotericin B + pericardiectomy

***Aspergillus*:** itraconazole, amphotericin B

Trichinella spiralis: albendazole, mebendazole

Prophylaxis (*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)

CARDITIS

Agents: adenovirus, *human echovirus 7, 11, 30*, *poliovirus*, *Streptococcus pyogenes* (rheumatic fever; carditis due to host immune response and local cross-reactive antigen; < 200 cases/y in USA); highest incidence in 3-4 y group

Diagnosis:

Viral: isolation from infected tissue

Rheumatic Fever: carditis in 40-50% of cases, polyarthritis in 75%, chorea in 15%, erythema marginatum in 10%, subcutaneous nodules, previous rheumatic fever or rheumatic heart disease, arthralgia, fever; acute phase reactants; prolonged PR interval; heart murmurs (tend to be variable from day to day), cardiac enlargement, pericardial friction rub, tachycardia persisting during sleep, congestive cardiac failure; recent scarlet fever; anti-streptolysin O test (normal in ≈ 20% of early cases; peaks at 2-4 w; false positives due to activity of other substances neutralising hemolytic properties of streptolysin O (eg., serum β-lipoprotein in liver disease) and bacterial growth in serum specimens), anti-DNAse B test (consistently elevated; rises later than ASOT, peaks at 4-6 w and remains elevated longer than ASOT; magnitude of response may be suppressed by antimicrobial therapy; detergents, heavy metals, azide and other chemicals interfere with enzyme and colour reaction), anti-hyaluronidase, anti-streptozyme (almost all patients have levels > 200 U); culture of nasal and throat swabs and swab of impetiginous lesions

Treatment:

Viral: non-specific

Rheumatic Fever: benzathine penicillin 1.2 MU (child: 600 000 U) i.m. once as a single dose, phenoxymethylpenicillin 250 mg orally 8 hourly for 10 d, or erythromycin 250 mg orally 6 hourly (child: 40 mg/kg/d in 4 divided doses) for 10 d for initial attack, followed by continuous, long term (well into adulthood, perhaps life-long) benzathine penicillin 900 mg (< 20 kg: 450 mg) i.m. every 3-4 w, phenoxymethylpenicillin 250 mg orally 12 hourly, or erythromycin 250 mg orally 12 hourly or erythromcyin ethyl succinate 400 mg orally 12 hourly (penicillin hypersensitive); aspirin or non-steroidal anti-inflammatory drugs for synovitis/arthritis

ENDOCARDITIS: 4% of community acquired and 1% of nosocomial bacteremia; commonly associated with aortic regurgitation, mitral regurgitation, congenital aortic stenosis (bicuspid valve), prosthetic heart valves, tricuspid regurgitation, ventricular septal defects, patent ductus arteriosus, coarctation of the aorta, arteriovenous fistula; native valves in 76%

Agents: 31-46% oral streptococci (*Streptococcus milleri*, *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus sanguis;* 25-27% in late, and 1-6% in early, infections in prosthetic valve patients; 10% in drug addicts; 19% in recurrent episodes; 18% in children), 16% anaerobic and microaerophilic Gram positive cocci, 10-32% *Staphylococcus aureus* (50-61% in drug addicts; 7-20% in early, and 11-15% in late, infections in prosthetic valve patients; 26% in recurrent episodes; cause of > 50% of cases of acute progressive infective endocarditis; more frequent in children (37% of cases) and in elderly; involves previously normal valves in ≈ 50% of cases; only cause of eustachian valve endocarditis; should be considered in any patient with staphylococcal bacteremia), 8-10 % enterococci (9% in late, and 3-4% in early, infections in prosthetic valve patients; 8% in drug addicts; 13% in recurrent episodes; 14% in bone marrow transplant recipients), 7-14% *equines* (associated with gastrointestinal lesion, especially colon carcinoma), 7-9% coagulase negative staphylococci (25-44% in prosthetic valve patients; 2% in drug addicts; 4% in recurrent episodes; 57% of cases in bone marrow transplant recipients; 12% in children), 7% Gram negative bacilli (*Pseudomonas* (3% of primary, and 4% of recurrent, episodes; *Pseudomonas aeruginosa* 14% of cases in drug addicts, 4% in children; *Pseudomonas alcaligenes* in bone marrow transplant recipients; *Burkholderia cepacia* 0.6% in children, associated with cystic fibrosis and chronic granulomatous disease, also in injection

heroin abusers and patients with prosthetic heart valves), *Stenotrophomonas maltophilia* (associated with i.v. drug abuse and prosthetic valve surgery), *Haemophilus* (1% of primary, and 2% of recurrent, episodes; oral source; *Haemophilus influenzae* 0.6% in children; *Haemophilus aphrophilus* 0.6% in children; *Haemophilus parainfluenzae* 2% in children; *Haemophilus paraphrophilus*, *Aggregatibacter segnis*, *Haemophilus aegytius)*; *Kingella kingae* (5-20% of early, and 10-18% of late, infections in prosthetic valve patients; also native valves); *Prevotella melaninogenica* (oral source; polymicrobial), *Fusobacterium nucleatum* and *Fusobacterium necrophorum* (oral source), *Bacteroides*, *Brucella* (1% in children), *Cardiobacterium hominis* (oral source), *Actinobacillus actinomycetemcomitans* (oral source; associated with periodontitis and prosthetic valves), *Eikenella corrodens* (oral source), *Yersinia enterocolitica*, *Flavobacterium meningosepticum* (in rheumatic heart disease, open heart surgery and i.v. drug abuse), *Salmonella enterica subsp enteric* serotype *paratyphi C*, *Salmonella choleraesuis* and other *Salmonella* (54% AIDS patients, 34% oncology patients; also elderly with previous valvular heart disease; 70% fatality rate), *Coxiella burnetii* (0.6% in children; 17% chronic; 37% mortality), *Chlamydophila pneumoniae*, *Legionella* (prosthetic valves), *Streptobacillus moniliformis* (rare complication of rat bite fever), *Alcaligenes* (0.6% in children), *Achromobacter xylosoxydans xylooxydans* (catheter related in bone marrow transplant recipients), *Campylobacter fetus* subsp *fetus* (0.6% in children), *Escherichia coli* (3% in children; 47% previous heart disease; 47% from urinary tract; 47% nosocomial; 84% new or changing murmur; 58% mitral valve; case-fatality rate 53%), *Proteus mirabilis* (0.6% in children), other Enterobacteriaceae, *Suttonella indologenes* (rare), *Moraxella osloensis, Acinetobacter calcoaceticus, Capnocytophaga canimorsus, Agrobacterium tumefaciens* (prosthetic valve), *Bordetella bronchiseptica*, *Aeromonas*, *Tropheryma whipplei*), 3% *Streptococcus pyogenes* (1% in recurrent episodes; 0.6% in children) and other β-haemolytic streptococci (including *Streptococcus agalactiae* (postpartum and postabortion, diabetics and alcoholics; 83% affecting native valve; case-fatality rate 44-47% overall, 100% if affecting prosthetic valve; 2% in recurrent episodes; 1% in children), Group C *Streptococcus* (*Streptococcus zooepidemicus*, *Streptococcus equisimilis*, rarely *Streptococcus equi*) and *Streptococcus canis* (rare)), 3% other streptococci (including *Streptococcus pneumoniae*), 2% *Corynebacterium* (especially *Corynebacterium jeikeium* (6-8% in early, and 2-4% in late, infections in prosthetic valve patients; 2% in drug addicts; 14% in bone marrow transplant recipients); *Corynebacterium xerosis* (0.6% in children; also in i.v. drug abusers with AIDS); *Corynebacterium pseudodiphtheriticum* (1% in children); non-toxigenic strains of *Corynebacterium diphtheriae*), 2% fungi (10% in drug addicts; 6-10% in early, and 2-6% in late, infections in prosthetic valve patients; mainly *Candida* (3% in recurrent episodes; 14% in bone marrow transplant recipients; *Candida parapsilosis* in i.v. drug addicts, invasive procedure, prosthetic devices, hyperalimentation, 0.6% in children; also *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Chrysosporium* (associated with prostheses), *Drechslera* (post surgery for ventricular septal defect), *Aspergillus* (coronary artery surgery, liver transplantation); *Aspergillus flavus* 0.6% in children; *Aspergillus fumigatus* 0.6% in children), *Pseudallescheria boydii* (in prosthetic valves and in AIDS); rarely, *Curvularia lunata*), *Neisseria gonorrhoeae* (0.6% in children), *Erysipelothrix rhusiopathiae* (animal contact (slaughterhouse workers, fish handlers, butchers, farmers), alcohol abuse; case-fatality rate 38%), *Listeria monocytogenes* (complicating rheumatic fever or prosthetic heart valve, malignancy, immunosuppressed, following coronary artery bypass surgery; case-fatality rate 29%), *Rothia dentocariosa* (rare; i.v. drug abuse, poor dentition, congenital heart disease), *Mycobacterium chelonae* and *Mycobacterium fortuitum* (infecting prosthetic valves), *Lactobacillus* (very rare; oral source; usually patient with preexisting structural heart disease and recent dental infection or manipulation; mortality 5-25%), *Propionibacterium acnes* (oral source), *Veillonella parvula* (oral source; polymicrobial; rare), *Neisseria mucosa* (i.v. drug abuser; oral source), *Neisseria sicca*, *Neisseria subflava* (i.v. drug abusers with AIDS; oral source), *Neisseria flavescens* (i.v. drug abusers with AIDS), *Neisseria elongata, Oerskovia* (prosthetic valves), *Rothia mucilaginosa* (i.v. drug abusers, cardiac valve disease, vascular catheter, immunocompromised), *Enterococcus faecalis* (5% in children), *Micrococcus* (0.6% in children), *Bacillus cereus* (infrequent; valvular heart disease, i.v. drug abuse), *Acinetobacter* (rare), *Actinomyces* (rare), *Staphylococcus lugdunensis* (mainly community acquired, usually preexisting cardiac abnormality), *Peptostreptococcus magnus* (oral source), *Aerococcus viridans* (rare), *Bartonella, Mycoplasma hominis, Pasteurella dagmatis, Yersinia enterocolitics, Cunninghamella bertholletiae* (after kidney transplantation)

Diagnosis: prior heart disease in 60-80%; constitutional symptoms in 90-100%, fever in 85-100%, heart murmur in 60-95%, emboli in 33%, petechiae in 30-79%, microscopic hematuria in 30-50%, heart failure in 25-66%, splenomegaly in 23-60%, mycotic aneurism in 2-11%; 2-dimensional echocardiogram (abnormalities in 34%; vegetations usual in *Streptococcus viridans* infections and in 40% of Q fever endocarditis; right bundle branch block in gonococcal endocarditis), colour flow Doppler technology, transesophageal echocardiography; blood cultures (take 3 sets before starting therapy; positive in 80%; bone marrow culture and combined arterial/venous blood cultures if negative); complement fixation tests, microagglutination tests, indirect fluorescent antibody titre, ELISA (antibody), counterimmunoelectrophoresis of serum; histology and PCR of diseased valves; elevated erythrocyte sedimentation rate in 90-100% of cases; total hemolytic complement decreased when

glomerulonephritis also present; white cell count elevated in 20-66% of cases; rheumatoid factor in 50-80% of bacterial cases; anemia in 40-80%

Staphylococcus aureus: right-sided usually involves tricuspid valve, occurs mainly in young users of injecting drugs but also as nosocomial infection associated with indwelling central venous catheters, and presents acutely with fever, chills, leucocytosis, bacteremia and with focal, rounded, sometimes cavitary infiltrates on chest radiograph; left-sided usually associated with community acquired bacteremia of unknown origin and carries high mortality

Q Fever: work in abattoir or on farm; usually preceded by atypical pneumonia and acute hepatitis; fever in 67% of cases, cardiac failure in 66%, hepatosplenomegaly in 57%, increased γ-globulin in 94%, increased ESR in 89%, increased SGOT in 83%, increased alkaline phosphatase in 80%, thrombocytopenia in 67%; serology (complement fixation test, indirect immunofluorescence); isolation from cardiac valves; liver biopsy

Erysipelothrix rhusiopathiae: erysipeloid present in 36%

***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

Differential Diagnosis: acute rheumatic fever, marasmic endocarditis, systemic lupus erythematosus, vasculitis, atrial myxoma, atrial thrombus, hpyernephroma, carcinoid, *human cytomegalovirus* in patients recently having valve replacement

Treatment: benzylpenicillin 45 mg/kg to 1.8 g i.v 4 hourly + di(flu)cloxacillin 50 mg/kg to 2 g i.v. 4 hourly + gentamicin 4-6 mg/kg (child: < 10 y: 7.5 mg/kg; $\geq$ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function)

Nosocomial, Immediate Penicillin Hypersensitive, Patients with Prosthetic Valves, Community-associated Methicillin Resistant *Staphylococcus aureus* Suspected: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly slowly over 60 min (monitor blood levels and adjust dose to trough 10-20 mg/L) + gentamicin 4-6 mg/kg (child: < 10y: 7.5 mg/kg; $\geq$ 10 y: 6 mg/kg) i.v. daily (monitor blood levels and adjust dose to trough 0.5-1 mg/L) + early removal and replacement of prosthesis

Streptococci with Benzylpenicillin MIC $\leq$ 0.12 mg/L:

Uncomplicated: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 14 d + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor plasma levels); benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w

Complicated (Large Vegetation, Multiple Emboli, Symptoms > 3 mo, Secondary Sepsis): benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor plasma levels)

Streptococci with Benzylpenicillin MIC > 0.12 & $\leq$ 0.5 mg/L: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor palsma levels)

Streptococci with Benzylpenicillin MIC > 0.5 but < 4 mg/L, *Abiotrophia*, *Granulicatella*, Susceptible Enterococci, *Rothia dentocariosa*, Culture Negative Where Q Fever or Fungal Infection Not suspected: gentamicin 1 mg/kg i.v. 8 hourly for 6 w (monitor plasma levels and adjust dose to trough 0.5-1 mg/L) or (in elderly) netilmicin 1 mg/kg i.v. 8 hourly for 14 d + benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 6 w or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 6 w

Streptococci With Benzylpenicillin MIC > 4 mg/L, Penicillin Hypersensitive: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly slowly over 60 min (monitor blood levels and adjust dose to trough 10-20 mg/L) for 4-6 w + gentamicin 1 mg/kg i.v. 8 hourly (monitor blood levels and adjust dose to trough 0.5-1 mg/L for 4-6 w or (for elderly) netilmicin 1 mg/kg i.v. 8 hourly

Vancomycin Resistant Enterococci: linezolid, quinupristin-dalfopristin

***Neisseria*, *Haemophilus parainfluenzae, Haemophilus aprophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*:** cefotaxime 50 mg/kg to 2 g i.v. 8 hourly for 4 w or ceftriaxone 50 mg/kg to 2 g i.v. daily for 4 w

***Fusobacterium*, *Prevotella*:** metronidazole, tetracycline $\pm$ lincomycin

***Brucella*:** streptomycin 1 g twice a day i.m. for 30 d + doxycycline 100 mg twice a day orally for 90 d + rifampicin 900 mg/d orally for 90 d + cotrimoxazole 5/25 mg/kg/d in 4 equally divided doses for 90 d, or oxytetracycline 500 mg orally 6 hourly for 12 w + gentamicin 120 mg i.m. 8 hourly for 4 w; + surgery (valvular replacement with biprosthetic valve)

***Salmonella*:** ampicillin 2 g i.v. 6 hourly for 6 w (child: 150-200 mg/kg i.v. daily in divided doses) + gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly (trough < 1.5 mg/L) for 6 w; ciprofloxacin, ceftriaxone, cefotaxime

Streptobacillus moniliformis, Actinomyces: benzylpenicillin 12-20 MU (neonates: 500,000-1 MU; child: 200,000-400,000 U/kg) i.v. daily in divided doses for 30 d

***Legionella*:** erythromycin 4 g i.v. daily in divided doses for 2-6 mo (consider change to 2 g orally daily after 2 mo) + rifampicin 600 mg orally for up to 14 mo; ciprofloxacin 600 mg i.v. daily in divided doses + rifampicin 1200 mg orally daily for 10 w

***Flavobacterium meningosepticum*:** sulphadiazine + rifampicin

***Pseudomonas aeruginosa*:** azlocillin 3 g i.v 4 hourly (child: 225 mg/kg i.v. daily in 3 divided doses) + amikacin 5 mg/kg i.v. 8 hourly

Burkholderia cepacia: cotrimoxazole ± polymyxin B + valvectomy or valve replacement

***Stenotrophomonas maltophilia*:** cotrimoxazole + ticarcillin + rifampicin

Escherichia coli: ceftriaxone ± aminoglycoside

Acinetobacter: polymyxin, ampicillin-sulbactam, imipenem, cefperazone-sulbactam

***Alcaligenes*:** imipenem

***Bartonella*:** doxycycline 2.5 mg/kg to 100 mg doxycycline 12 hourly for 6 w (not < 8 y) + gentamicin 1 mg/kg i.v. 8 hourly for 14 d or rifampicin 7.5 mg/kg to 300 mg orally 12 hourly for 14 d

Other Gram Negative Bacilli: gentamicin 5 mg/kg i.v. daily (trough < 1.5 mg/L) for 6 w or tobramycin 5 mg/kg daily for 6 w + ticarcillin for 4-6 w; early consultation with cardiovascular surgeon and clinical microbiologist or infectious diseases physician

Staphylococci: early surgery +

Left-sided:

Methicillin Susceptible: di/flucloxacillin 50 mg/kg to 2 g i.v. 4 hourly for 4-6 w

Methicillin Resistant: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly over 60 min for 4-6 w (monitor blood levels and adjust dose to trough 10-20 mg/L)

Tricuspid Valve: di/flucloxacillin 50 mg/kg to 2 g i.v. 4 hourly for 4 w

***Bacillus*:** clindamycin

***Lactobacillus*:** benzylpenicillin 15-20 MU (neonates: 500,000-1 MU; older children: 200,000-400,000 U/kg) i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly (trough <1.5 mg/L)

***Erysipelothrix rhusiopathiae*:** benzylpenicillin 12-20 MU/d i.v. for 4-6 w

***Corynebacterium jeikeium*:** vancomycin

Other *Corynebacterium*: penicillin ± aminoglycoside; vancomycin

Listeria monocytogenes: ampicillin or penicillin, cotrimoxazole

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

***Coxiella burnetii*:** tetracycline 2 g orally daily in divided doses + clindamycin 600 mg i.v. 8 hourly; rifampicin 10 mg/kg to 600 mg orally daily + cotrimoxazole 2/10 mg/kg to 160/800 mg orally twice daily; doxycycline + hydroxychloroquine for 2 y in chronic cases

Pasteurella: penicillin, ampicillin, mezlocillin, piperacillin, cefuroxime, ceftriaxone, cefotaxime

Fungi: valve replacement essential to management; amphotericin B (increase to 1 mg/kg daily; total dose of 2 g or more) + ketoconazole; fluconazole

Surgery where appropriate therapy fails to control infection or refractory congestive cardiac failure occurs.

Test of Progress: fall in circulating immune complexes levels

Prophylaxis: required with most congenital cardiac defects, previous endocarditis, hypertrophic cardiomyopathy, mitral valve prolapse with regurgitation, prosthetic valve, rheumatic and other acquired valvular dysfunction, surgically constructed systemic-pulmonary shunts or conduits

Bronchoscopy with Rigid Bronchoscope, Dental Procedures (Dental Extractions, Surgical Drainage of Dental Abscess, Maxillary or Mandibular Osteotomies, Surgical Repair or Fixation of Fractured Jaw, Periodontal Procedures (Including Probing, Scaling, Root Planing, Surgery), Dental Implant Placement and Reimplantation of Avulsed Teeth, Endodontic (Root Canal) Instrumentation or Surgery Only Beyond the Apex, Subgingival Placement of Antibiotic Fibres or Strips, Initial Placement of Orthodontic Bands (but not Brackets), Intraligamentary Local Anesthetic Injections, Prophylactic Cleaning of Teeth or Implants Where Bleeding is Anticipated), Surgical Procedures Breaking Respiratory Mucosa, Tonsillectomy and/or Adenoidectomy: 0.5% chlorhexidine applied to gingival

margin before local anasthesia for dental surgery; amoxycillin 50 mg/kg to 2 g orally as a single dose 1 h before procedure; amoxy(ampi)cillin 50 mg/kg to 2 g i.v. just before procedure or i.m. 30 min before procedure

Penicillin Hypersensitive, On Long-term Penicillin or Having Taken β-lactam Antibiotic More Than Once in Previous Month: clindamycin 15 mg/kg to 600 mg orally single dose 1 h before procedure or i.v. over at least 20 min, ending just before procedure commences; lincomycin 15 mg/kg to 600 mg i.v. over at least 1 h, ending just before procedure commences; vancomycin 25 mg/kg to 1.5 g i.v. (child 30 mg/kg to 1.5 g) over at least 1 h, ending just before procedure commences; teicoplanin 10 mg/kg to 400 mg i.v. just before procedure or i.m. 30 min before procedue; cephalexin 50 mg/kg to 2 g orally 1 h before procedure (not those on long-term penicillin or having taken related beta-lactam > once in previous month or with immediate penicillin hyprsensitivity)

Endoscopic Retrograde Cholangiography, Biliary Tract Surgery, Esophageal Dilatation, Sclerotherapy for Esophageal Varices, Surgical Procedures Breaking Intestinal Mucosa (Except Endoscopy, Biopsy, Percutaneous Endoscopic Gastrostomy), Prostatic Surgery, Transrectal Prostatic Biopsy, Cystoscopy, Urethral Catheterisation or Urinary Tract Surgery in Presence of Urinary Tract Infection, Urethral Dilatation and Curettage, Therapeutic Abortion, Sterilisation Procedures or Insertion or Removal of Intrauterine Contraceptive Device in the Presence of Infection, Vaginal Delivery in Presence of Infection or Prolonged Labour: (amoxy)ampicillin 50 mg/kg to 2 g i.v. just before procedure or i.m. 30 minutes before procedure then 25 mg/kg to 1 g i.v. i.m. or orally 6 h later + gentamicin 2 mg/kg (child: 2.5 mg/kg) i.v. just before procedure or i.m. 30 min before procedure

Penicillin Hypersensitive: vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. over at least 1 h, ending just before procedure, teicoplanin 10 mg/kg to 400 mg i.v. just before procedure

Patients With Prosthetic Valves Or Previous Endocarditis Undergoing Skin Biopsy: di(flu)cloxacillin 25 mg/kg to maximum 1 g i.v. just before procedure commences or i.m. 30 min before procedure + gentamicin 2 mg/kg (child: 2.5 mg/kg) i.v. just before procedure commences or i.m. 30 min before procedure

If Parenteral Thrapy Impractical: di(flu)cloxacillin 25 mg/kg to maximum 1 g orally 1 h before procedure commences, then 25 mg/kg to maximum 1 g orally 6 h later

Penicillin Hypersensitive: vancomycin 20 mg/kg to maximum 1 g i.v. slowly over 60 min + gentamicin as above

Vascular Graft Infection

Agents: 33% *Staphylococcus aureus*, 16% *Escherichia coli*, 12 % *Staphylococcus epidermidis,* 11% streptococci, 8% *Proteus*, 7% other aerobic Gram negative bacilli, 6% other bacteria (including *Listeria monocytogenes*), 1% *Candida*, rarely *Aspergillus*

Diagnosis: culture of surgical specimen, blood cultures

***Aspergillus*:** persistent back pain, fever, arterial embolusation

Treatment: surgery + vancomycin 20 mg/kg to 1 g i.v. slowly 12 hourly (trough 10-20 mg/L) + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. daily

Mycotic Aneurism: present in 2-11% of endocarditis cases, also due to direct arterial infection

Agents: 18-66% *Salmonella*, 16-44% *Staphylococcus aureus*; *Streptococcus pneumoniae*, other streptococci, enterococci, *Mycobacterium tuberculosis*, *Yersinia enterocolitica*, *Proteus*, *Klebsiella*, *Enterobacter*, *Campylobacter fetus* subsp *fetus*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Listeria monocytogenes*, *Escherichia coli, Haemophilus influenzae, Aspergillus*

Diagnosis: CT scan; aortography; blood cultures; smears and cultures of sputum, urine, bone marrow, surgical specimens

Treatment: surgery + vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. slowly 12 hourly (monitor blood levels and adjust dose to trough 10-20 mg/L) + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. daily

False Aneurism: common in i.v. drug addicts

Agents: 83% *Staphylococcus aureus*, 39% polymicrobial, 22% streptococci, 20% anaerobes, 12% aerobic Gram negative bacilli

Diagnosis: computed tomography (sensitivity 100%), arteriography (sensitivity 96%), digital subtraction angiography (sensitivity 92%); blood cultures, culture of surgical material

Treatment: resection + appropriate antimicrobial

Thrombophlebitis: rarely affects CNS; although 33% of intravenous catheters give positive cultures, only 3% are associated with sepsis; development of infection in intravenous catheters is related to patient being already septic, transient bacteremia from another source, irrigating or otherwise manipulating an occluded, leaking or infiltrated catheter, contaminated fluid being administered, total parenteral nutrition, burned patient, length of time catheter remains in place,

cancer patient, corticosteroids and/or other immunosuppressive therapy, plastic cannulas (as opposed to steel), intravenous therapy in lower extremity

Agents: 40% *Klebsiella-Enterobacter*, 20% *Providencia*, 20% *Proteus*, 12% *Serratia marcescens,* 12% *Staphylococcus aureus* (associated with local trauma), 8% *Pseudomonas aeruginosa*, 8% *Escherichia coli*, 8% *Candida*; *Campylobacter fetus* subsp *fetus*, halophile *Vibrio*, *Aeromonas*, *Corynebacterium striatum* (rare; associated with central venous catheters), *Staphylococcus epidermidis*

Diagnosis: culture of infected material; blood cultures

Treatment: dependent on agent

Prevention: intravenous catheters should be used only when less dangerous methods are not possible; catheter must be inspected daily; three-way stopcocks should be avoided if possible or, if not, should at least be changed at least every 24 hours, because they provide a portal of entry for bacteria or fungi; forced irrigation should be avoided because of possibility of thromboembolism; in placing an intravenous catheter, prepare area with antiseptic solution (chlorhexidine), use sterile drapes and gloves, apply 2% chlorhexidine ointment to the site after insertion, anchor catheter securely, apply sterile dry gauze (not transparent occlusive) dressing, 'date' catheter, use antiseptic/antibiotic impregnated short-term central venous catheter if rate of infection is high despite adherence to other strategies

ARTERITIS

Agent: *Pythium* (in thalassemic farmers), *Aspergillus*

Diagnosis: histology and culture of surgical material

Treatment:

Pythium: aggressive surgery + i.v. sodium iodide

***Aspergillus*:** surgery + amphotericin B

BACILLARY ANGIOMATOSIS: largely in immunocompromised patients, particularly AIDS

Agent: *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 fo 3-4 mo