

Chapter 11

Infections of the Skeletal System

JOINT PAIN IN CHILDREN

Single Joint:

Without Constitutional Symptoms: chondromalacia patellae, osteochondritis dissecans, other osteochondritides, Osgood-Schlatter's disease, Sever's disease, Pertle's disease, slipped femoral epiphysis

Signs of General Disease: leukemia, histiocytosis, sickle cell hemoglobin

With Constitutional Upset: acute infections of joints and bones, juvenile rheumatoid arthritis, Henoch-Schonlein purpura, sickle cell hemoglobin, subacute bacterial endocarditis

Multiple Joints: juvenile rheumatoid arthritis and other connective tissue disorders, multiple septic arthritis or osteomyelitis, rheumatic fever, anterior poliomyelitis, rickets, scurvy, purpura, non-accidental injury

ARTHRITIS

Agents: Reiter syndrome (48% of inflammatory arthritis in young men; oligoarticular and asymmetrical, predominantly lower extremity), ankylosing spondylitis (18% of inflammatory arthritis in young men), rheumatoid arthritis (8% of inflammatory arthritis in young men), psoriatic arthritis (7% of inflammatory arthritis in young men), systemic lupus erythematosus (5% of inflammatory arthritis in young men), acute rheumatic fever (3% of inflammatory arthritis in young men), Behcet's disease (2% of inflammatory arthritis in young men), gouty arthritis (2% of inflammatory arthritis in young men), Henoch-Schonlein purpura (2% of inflammatory arthritis in young men; may be complication of *Epstein-Barr virus* infection), septic arthritis (1% of inflammatory arthritis in young men), Crohn's arthritis (1% of inflammatory arthritis in young men), sarcoid arthritis (1% of inflammatory arthritis in young men), Lyme arthritis (in 52% of cases; 29% knee, 14% shoulder, 12% hip, 11% ankle, 9% wrist, 8% hand, 6% foot, 3% toes), yersinosis (in 11% of *Yersinia enterocolitica* and 55% of *Yersinia pseudotuberculosis* cases), Kawasaki syndrome (in 29% of cases), dermatomyositis (in 25% of cases), acute viral hepatitis (in 15% of cases), scleroderma (localised form; in 10% of cases), brucellosis (arthritis in 9% of cases; arthralgia in 55%), *Ross River virus* (poly, especially knees and wrists), *rubella virus* (transient poly), Mucha-Habermann disease, osteochondrosis (limited to maturing lower skeleton), Sweet's syndrome, Takayasu's arteritis

Diagnosis: erythrocyte sedimentation rate 47 mm/h in ankylosing spondylitis, elevated in all cases of foreign body arthritis, 90% of discitis cases, 80% of cases of Kawasaki syndrome, also in Mucha-Habermann disease, multicentric osteomyelitis (mild to moderate), Sweet's syndrome and Takayasu's arteritis

Synovial Fluid Examination:

Normal: straw-coloured, clear, no fibrin clot, good mucin clot, < 200 leucocytes/ μ L, < 25% polymorphs, glucose \approx 100% blood level

Reiter syndrome: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/ μ L, > 50% polymorphs, glucose \approx 75% blood level

Ankylosing Spondylitis: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/ μ L, > 50% polymorphs, glucose \approx 75% blood level

Rheumatoid Arthritis: clear to turbid, large (2-4+) fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/ μ L, > 66% polymorphs, glucose \approx 50-75% blood level

Psoriatic Arthritis: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/ μ L, > 50% polymorphs, glucose \approx 75% blood level

Acute Gout or Pseudogout: turbid, large (2-4+) fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/ μ L, > 70% polymorphs, glucose \approx 90% blood level

Rheumatic Fever: slightly turbid, 1-2+ fibrin clot, good mucin clot, 18,000 leucocytes/ μ L, 50% polymorphs, difference between blood and synovial fluid glucose = 10

Tuberculous Arthritis: turbid, large (2-3+) fibrin clot, poor mucin clot, \approx 20,000-25,000 leucocytes/ μ L, polymorphs variable (usually 60%), glucose < 50% blood level; acid-fast stain positive in 20%, cultures positive in 80%, biopsy positive in 95%

Other Bacterial Septic Arthritis: very turbid or purulent, large (2-4+) fibrin clot, poor mucin clot, 10,000-100,000 leucocytes/ μ L, > 80% polymorphs, glucose < 50% blood level; Gram stain positive in 50-75%, culture positive

Candida Septic Arthritis: 46,000-56,000 leucocytes/ μ L, 79-97% polymorphs, glucose 18-113 mg/dL, protein 2.8-3.7X serum

Arthritis Associated With Intestinal Diseases: turbid, large fibrin clot, fair to poor mucin clot, 5,000-50,000 leucocytes/ μ L, > 50% polymorphs, glucose \approx 75% blood level

Degenerative Joint Disease: clear to slightly turbid, small (0-1+) fibrin clot, good mucin clot, \approx 700-2000 leucocytes/ μ L, < 25% polymorphs, glucose \approx 100% blood level

Foreign Body Arthritis: \approx 60% inflammatory

Traumatic Arthritis: straw-coloured, bloody or xanthochromic, small (0-1+) fibrin clot, good mucin clot, 50-1200 leucocytes/ μ L, < 25% polymorphs, glucose \approx 100% blood level, protein 2-3X normal

REACTIVE ARTHRITIS (REITER SYNDROME)

Agents: *Shigella*, *Salmonella*, *Yersinia enterocolitica*, *Yersinia pseudotuberculosis*, *Campylobacter* (hips and lower back; uncommon), *Vibrio parahaemolyticus*, *Clostridium difficile*, *Chlamydia*, human immunodeficiency virus, *Cyclospora*, others

Diagnosis: micro and culture of synovial fluid (very high cell count, glucose 80 mg/dL, culture negative), blood tests (moderate anemia, moderate neutrophilia, ESR raised; Rose-Waaler and latex negative; serology may be positive; specific organisms may be cultured); culture of feces (for enteric organisms listed); culture and immunofluorescence of any urethral discharge; HLA typing

Shigella: typically sets in 10 d after enteritis; days 1-11 urethritis, days 3-7 conjunctivitis, day 4-month or more polyarthritis (may become permanent or recurrent, with erythrocyte sedimentation rate increased in each recrudescence)

Yersinia: in adults, joint symptoms resembling rheumatoid arthritis; in children, polyarthritis and erythema nodosum resembling rheumatic fever; direct agglutination test, indirect immunofluorescence of intestinal biopsy

Treatment: appropriate antimicrobial treatment of any relevant organisms isolated (*Shigella*, *Salmonella*, *Yersinia*: gentamicin, cefotaxime, doxycycline, ciprofloxacin; *Campylobacter*: erythromycin; *Clostridium difficile*: metronidazole, vancomycin; *Chlamydia*: tetracycline, doxycycline, erythromycin); bed rest and aspirin; phenylbutazone + indomethacin

ANKYLOSING SPONDYLITIS: chronic arthritis of spine; immune response to bacterial antigen cross-reacts with joint antigen, giving autoimmune damage; strong association with HLA B27 genotype

Agent: *Klebsiella*

Diagnosis: synovial fluid examination; HLA typing

Treatment: phenylbutazone + indomethacin

RHEUMATIC FEVER: an acute febrile disease occurring as a sequela, nearly always after a latent period of 2 to several weeks, to an untreated or inadequately treated streptococcal respiratory tract disease (especially pharyngitis)

Agent: *Streptococcus pyogenes*

Diagnosis: manifestations and their severity vary widely, but usually (\approx 75% of cases) include polyarthritis with intense migrating arthralgia; there may be no objective features or clinically evident arthritis with heat, redness, swelling and tenderness; knees, ankles, elbows and wrists most affected joints; > 1 joint involved in \approx 50% of patients; with therapy, average duration of attacks is about 3 mo; carditis occurs in about 1/3 of cases; chorea is not common and erythema marginatum and subcutaneous nodules are now even less so, but these conditions are diagnostically important should they occur

Prophylaxis: benzathine penicillin (\leq 20 kg: 450 mg; > 20 kg: 900 mg) i.m. at 3-4 weekly intervals or phenoxymethylpenicillin 250 mg orally 12 hourly or (if penicillin hypersensitive) erythromycin 250 mg orally 12 hourly or erythromycin ethyl succinate 400 mg orally 12 hourly; continue minimum 5 y (until at least 18 y) if without carditis or evident valve disease, minimum 10 y (until at least 25 years) if mild or moderate carditis or mild residual valve disease, for life if severe carditis or moderate to severe residual valve disease, or before surgery

SEPTIC ARTHRITIS: can be life threatening and frequently associated with significant morbidity

Agents: almost any organism may be introduced directly or hematogenously; *Staphylococcus aureus* (63% of hospital admissions; neonates, children over 2 y, 25% of total adult cases, usually chronic underlying disease, especially diabetes and rheumatoid arthritis; also Stage I and Stage III prosthetic infections; most common cause of chronic infective arthritis; 17% methicillin resistant), 20% streptococci (mainly *Streptococcus pyogenes* (15% of total adult cases; hematogenous spread from respiratory or skin infection; also Stage III prosthetic infections), *Streptococcus agalactiae* (Stage III prosthetic infections), *Streptococcus pneumoniae* (50% primary focus in lung, middle ear; associated meningitis, endocarditis; alcohol abusers; 6% of community acquired infections; mortality 19% in adults, <1% in children; 56% in knee in adults; bacteremia in 72% of adult cases), Group C streptococci), *Enterococcus faecalis* (seventh most common cause of chronic infective arthritis), 10% Gram negative bacilli (chronic debilitating diseases, such as diabetes, malignancy, immunosuppressive drugs; urinary tract

infection may precede; neonates; alcoholics; also Stage III prosthetic infections; *Proteus* second and *Klebsiella* fifth most common cause of chronic infective arthritis; *Haemophilus influenzae* (infants 1-18 mo, young children, debilitated adults; preceding meningitis in 30%, osteomyelitis in 22%; 8% of all *Haemophilus influenzae* systemic disease in children), *Haemophilus parainfluenzae*, *Brucella* (in 9-37% of infections), *Salmonella* (< 20 y; related to sickle cell disease; *Salmonella typhi* (fourth most common cause of chronic infective arthritis), *Salmonella paratyphi C*, *Salmonella choleraesuis*, *Salmonella typhimurium* (in renal transplant recipients), *Capnocytophaga*, *Mycoplasma hominis* (associated with prostheses), *Eikenella corrodens* (in 50% of infections related to human bites or fist fight injuries), *Kingella kingae* (mainly infants and young children; $\approx \frac{1}{2}$ of cases in knee), *Pseudomonas aeruginosa* (complicating puncture wounds of foot in children; i.v. drug abusers; third most common cause of chronic infective arthritis), *Burkholderia cepacia*, *Serratia marcescens* (i.v. drug abusers; may involve sternoclavicular or sacroiliac joint), *Moraxella catarrhalis* (rare), *Ureaplasma urealyticum* (in hypogammaglobulinemia), *Streptobacillus moniliformis* (rare complication of rat-bite fever), *Campylobacter fetus subsp fetus* (uncommon), *Moraxella osloensis* (rare), *Pasteurella multocida* (polyarticular) and *Pasteurella pneumotropica* (dog and cat bite or exposure), *Haemophilus paraprophilus*, *Legionella pneumophila* (1 case reported in immunosuppressed patient), 4% *Mycobacterium tuberculosis* (reactivation of latent disease; chronic, insidious, monoarticular; knee most common; most do not have concomitant active pulmonary tuberculosis; PPD almost always positive; differs from Poncet's disease, which is polyarthritis occurring during acute tuberculosis infection but in which no mycobacterial infection can be found), *Neisseria gonorrhoeae* (gonococcal arthritis (blenorrhagic arthritis, gonorrhoeal arthritis); 17% of community acquired infections; 50% of total adult cases; arises as a consequence of disseminated gonococcal disease; previously healthy adult, predominates in young women, often within 1 w of onset of menses or last trimester of pregnancy; initial migratory polyarthritis, synovitis or tenosynovitis (wrist, dorsum of hands or feet, Achilles' tendon), typical skin lesions during septicemic phase of disseminated gonococcal disease or localised arthritis, often with purulent joint fluid, in post-septicemic stage; knee or wrist most common), *Neisseria meningitidis* (2% of meningococcal infections; in 5% of children and 11% of adults with acute meningococcal disease (allergic, hemarthrosis and iatrogenic probably more common than septic); oligoarticular; appears as meningitis is resolving; also in chronic meningococemia and primary infections), *Staphylococcus epidermidis* (catheter induced in neutropenics; Stage I and Stage III prosthetic infections; sixth most common cause of chronic infective arthritis), *Listeria monocytogenes* (rare), anaerobes (Stage II prosthetic infections), *Arcanobacterium haemolyticum* (posttraumatic), *Corynebacterium xerosis* (following vascular surgery), *Arcanobacterium pyogenes*, *Corynebacterium diphtheriae*, *Corynebacterium kutscheri*, *Neisseria mucosa* (rare), *Erysipelothrix rhusiopathiae*, *Candida* (*Candida albicans* and *Candida tropicalis* 17% of hospital acquired infections; especially in knee in cancer patients; insidious onset, indolent course; may occur in debilitated patient; males > females; usually 40s-50s; also *Candida parapsilosis* and *Candida glabrata* in prostheses), *Scedosporium* (penetrating trauma, surgery)

Diagnosis: mono- or oligoarticular, lower > upper extremity, fever, local inflammation, pain with motion; micro (predominance of polymorphs), culture (mycobacteria and *Legionella* in Bactec 13A medium), counterimmunoelectrophoresis and latex agglutination of synovial fluid; blood cultures; white cell count 18,000-100,000/ μ L; increased erythrocyte sedimentation rate

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: surgical drainage in all hip joint infections, inadequate closed drainage, persistent febrile course, inaccessible joint; needle drainage in other cases except prosthetic, where resection of prosthesis and all foreign bodies (including cement fragments) and debridement of involved tissues is required (especially in fungal infections)

Organism Not Known:

< 5 y **Old:** di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 3-6 d + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. once daily for 3-6 d, then di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly or (if *Haemophilus influenzae* likely) amoxicillin-clavulanate 15 mg/kg to 500 mg orally 8 hourly for minimum 21 d total

Sexually Active Young Adult: single dose ceftriaxone 125 mg i.m. or single dose ciprofloxacin 500 mg orally + doxycycline 100 mg twice a day for 7 d

Adult: flucloxacillin + gentamicin or flucloxacillin + oral ciprofloxacin

With Prosthesis: vancomycin + third generation cephalosporin

Neisseria: benzylpenicillin 150 000 U/kg i.v. daily in divided doses for 7 d, ceftriaxone 50 mg/kg to maximum 3 g i.v. daily for 7 d, cefoxitin 100 mg/kg i.v. daily in divided doses for 7 d, erythromycin 50 mg/kg daily orally in 4 divided doses for 7 d

Kingella kingae: benzylpenicillin 4 MU i.v. at once, then 2 MU i.v. 4 hourly (neonates: 100,000 U/kg daily in 3 or 4 divided doses; < 45 kg: 250,000 U/kg daily in divided doses) for at least 10 d, followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses)

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)

Staphylococcus aureus: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 2-4 w, then di(flu)cloxacillin 25 mg/kg to 1 g orally 6 hourly for at least 6 w total ± probenecid 10 mg/kg to maximum 500 mg orally 6 hourly for minimum 6 w total; if methicillin resistant, vancomycin 20 mg/kg to 1 g i.v. slowly 12 hourly for 2-6 w, then rifampicin 7.5 mg/kg to 300 mg orally 12 hourly + sodium fusidate 12 mg/kg to 500 mg orally 12 hourly

Penicillin Hypersensitive: cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 25 mg/kg to 1 g i.v. or i.m. 8 hourly, then cephalexin 25 mg/kg to 1 g orally 6 hourly; if severe, clindamycin 10 mg/kg to 450 mg i.v. slowly 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, then clindamycin 300-450 mg orally 6-8 hourly (child: 10 mg/kg to 450 mg orally 6 hourly)

Streptococci, Capnocytophaga, Arcanobacterium haemolyticum, Streptobacillus moniliformis: benzylpenicillin 100 000-150 000 U/kg/d i.v. for 10-14 d (4 w for *Streptococcus pneumoniae*)

Brucella: streptomycin 1 g twice a day i.m. for 14-21 d + rifampicin 900 mg/d orally for 45 d + doxycycline 100 mg orally twice daily for 45 d

Haemophilus influenzae, Eikenella corrodens: cefotaxime 2 g i.v. 4 hourly (child: 200 mg/kg daily in 4 divided doses) or ceftriaxone i.v. for 4-6 days, then amoxicillin-clavulanate for total period of 21 d; chloramphenicol

Listeria monocytogenes: ampicillin 2 g i.v. 8 hourly for 10 d, then amoxicillin 500 mg orally 3 times daily

Salmonella: joint aspiration, surgical drainage; chloramphenicol 500 mg orally 6 hourly (child > 2 w: 50 mg/kg orally daily in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg daily in 4 divided doses) for 15 d

Coliforms, Pseudomonas aeruginosa, Serratia marcescens: gentamicin or tobramycin 5 mg/kg/d i.v. for 4-6 w (+ ticarcillin in immunocompromised host with *Pseudomonas aeruginosa*)

Burkholderia cepacia: imipenem

Corynebacterium: i.v. cefotaxime 2 g 3 times daily for 21 d, followed by oral erythromycin 500 mg 4 times daily for 14 w

Campylobacter fetus subsp fetus: gentamicin, erythromycin, amoxicillin-clavulanate

Mycoplasma hominis: ciprofloxacin 750 mg twice daily, tetracycline, doxycycline

Ureaplasma urealyticum: tetracycline, doxycycline

Candida tropicalis, Candida glabrata: amphotericin B

Other Candida: oral ketoconazole + i.v. miconazole, amphotericin B

Scedosporium: debridement

Test of Progress: complement fixation

VIRAL ARTHRITIS

Agents: *Ross River virus*, *Barmah Forest virus*, *hepatitis A virus*, hepatitis B virus (in 10-42% of cases; usually preicteric), *hepatitis C virus*, *mumps virus* (polyarticular or monoarticular; mainly adult males; self-limited), infectious mononucleosis (in 5-10% of cases), *human cytomegalovirus*, *simplexvirus 1*, *human echovirus*, *simplexvirus 3*, adenovirus (in 8% of *human adenovirus E* serotype 4 infections), group A arboviruses (rash, encephalitis, nephritis and hemorrhage), *human rubella virus* (usually adult women; fingers, wrists and knees; also vaccine), *human parvovirus B19*

Diagnosis: arthralgias common; usually transient; fever; leucocytosis with neutrophilia, raised erythrocyte sedimentation rate, mild anemia; agglutinations (paired sera 2 w apart)

Human parvovirus B19: PCR on synovial fluid or joint aspirate, dot hybridisation, capture ELISA (IgG) on serum

Treatment: corticosteroids, non-steroidal anti-inflammatory drugs (not aspirin)

ARTHRALGIA also occurs in 77% of dengue cases (poly), 73% of acute schistosomiasis attacks, 73% of cases of Mediterranean spotted fever, 56% of influenza A cases, 50% of cases of Rocky Mountain spotted fever, 35% of *human immunodeficiency virus* infections, 25% of loiasis, in infections with *Bacillus anthracis*, *Coxiella burnetii*, *Francisella tularensis*, *Listeria monocytogenes*, *Pasteurella multocida* and *Streptobacillus moniliformis*, in malaria, Marburg virus disease, plague, psittacosis (generalised) and Rift Valley fever; also in arthromyalgia, leukemia (severe) and pigmented villonodular synovitis (+ swelling; knee, hip, ankle, tarsus, elbow)

OSTEOMYELITIS AND OSTEOCHONDRITIS: secondary to an adjacent infection (overlying abscesses or burns, but usually from decubitus ulcers in patients without generalised vascular insufficiency and due to *Staphylococcus*, Gram negative bacilli (especially *Pseudomonas aeruginosa*) and anaerobes; in patients with generalised vascular insufficiency, such as with diabetes or peripheral vascular disease, the small bones of the feet are most commonly infected with *Staphylococcus*, *Enterococcus*, Gram negative bacilli and anaerobes), while necrotising/malignant otitis externa (usually due to *Pseudomonas*) also occurs; osteomyelitis of the fingers is a common complication of fingertip abscess; hematogenous (femur or tibia involved in most childhood cases; vertebrae next most common—45% lumbar, 35% thoracic, 10% cervical, 10% thoracolumbar, 10% lumbosacral, 20% due to *Staphylococcus*, 15% Gram negative rod, 3% *Streptococcus*, 30% from a genitourinary infection, 5% from skin, 5% from respiratory, less acute in adults and surgery is usually not necessary but 10% suffer paraplegia and 5% die; long bone infection is commonly a reactivation and due to *Staphylococcus*, *Peptostreptococcus*, *Pseudomonas aeruginosa*); due to penetrating wounds (animal bites, iatrogenic heel puncture in children, other puncture wounds of the foot; *Pseudomonas* most common); due to compound fracture; due to infection of prosthesis; postoperative (postoperative pubic osteomyelitis may be misdiagnosed as osteitis pubis); multifocal (typical in neonates and drug addicts); 30% femur, 25% tibia, 15% vertebra, 10% humerus, 5% pelvis, 5% fibula, 5% tarsal, 2% radius, 2% rib

Agents: 55% *Staphylococcus aureus* (60% in children; 30% of neonatal; most common cause of osteomyelitis secondary to contiguous focus), 22% *Staphylococcus aureus* + anaerobes, 5% anaerobes alone (*Bacteroides fragilis*, *Peptostreptococcus*, *Propionibacterium*, *Actinomyces*, rare *Veillonella parvula*), 5% *Streptococcus pyogenes*, 3% *Pseudomonas aeruginosa* (66% in drug abusers; spine, sacroiliac joint, sternoclavicular joint, symphysis pubis, as well as usual large joints, in these patients; second most common cause of osteomyelitis secondary to contiguous focus), 2% *Streptococcus pneumoniae* (< 1% in children), 1% *Mycobacterium tuberculosis* (lower thoracic, proximal femur, distal femur, proximal tibia, ankle); *Streptococcus canis* (sacroiliitis), *Streptococcus agalactiae* (40% of neonatal), other β -hemolytic streptococci (including Group C), *Streptococcus viridans*, enterococci, *Streptococcus milleri*, *Streptococcus equinus* (rare spondylodiskitis and vertebral osteomyelitis as complication of endocarditis), coagulase negative staphylococci, *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Proteus*, *Serratia* (spine, sacroiliac joint, sternoclavicular joint, symphysis pubis as well as usual large joints, in drug addicts), *Mycobacterium fortuitum* (emerging pathogen in AIDS), *Haemophilus influenzae* (3% of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults), *Brucella*, *Salmonella* (associated with hemoglobinopathies, particularly sickle cell disease; more likely in patients with lymphoma or connective tissue disorders), *Neisseria meningitidis*, *Neisseria sicca* (following back injury), *Aeromonas* (post-traumatic), *Clostridium botulinum* (in wound botulism), *Listeria monocytogenes*, *Capnocytophaga*, *Eikenella corrodens* (in 50% of *Eikenella corrodens* infections related to human bites or fist fight injuries), *Nocardia asteroides*, *Haemophilus arophilus* (rare vertebral), *Haemophilus parainfluenzae* (vertebral), *Kingella kingae* (mainly infants and young children), *Actinobacillus actinomycetemcomitans* (uncommon), *Vibrio vulnificus* (trauma in seawater), *Burkholderia cepacia* (cervical), *Moraxella osloensis* (rare), *Acinetobacter calcoaceticus*, *Ochrobacterium antropi* (puncture wound), *Providencia*, *Plesiomonas shigelloides*, *Pasteurella multocida* and *Pasteurella pneumotropica* (dog and cat bite or exposure), *Haemophilus haemoglobinophilus*, *Haemophilus paraprofilus*, *Mycobacterium intracellulare*, *Mycobacterium simiae* (infrequent), mixed aerobes and anaerobes (skull or facial bones secondary to ENT procedures; long bone compound fractures; pelvic bone secondary to intraabdominal sepsis; hand secondary to bites, especially human; foot associated with vascular insufficiency and/or diabetes; cervical spine secondary to retropharyngeal abscess), *Bartonella henselae* (vertebral), *Candida* (especially in drug abusers, also periprosthetic; vertebral in lengthy treatment with broad spectrum antibiotics, major surgery, hyperalimentation, neutropenia, sternal in coronary artery bypass grafting), *Aspergillus* (predisposing factors, liver transplantation), *Drechslera* (associated with prior surgery), *Scedosporium* (penetrating trauma, surgery), *Cryptococcus neoformans*

Diagnosis: X-ray (82% of cases of vertebral osteomyelitis show intervertebral disc space narrowing); micro and culture of aspirate, swab or biopsy; blood cultures; counterimmunoelectrophoresis of serum; erythrocyte sedimentation rate usually elevated; white cell count (acute: 7400 – 73,000/ μ L (mean 21,100/ μ L); chronic traumatic: 8300 – 12,700/ μ L (mean 9800/ μ L); chronic prosthetic: 8300/ μ L); fluorodeoxyglucose-positron emission tomography 96% accurate for hip prosthesis, 81% for knee prosthesis, 91% for other osteomyelitis

Neonatal: 40% multiple bone involvement (never with *Streptococcus agalactiae*); increasing incidence of *Escherichia coli*; often secondary to complications during pregnancy or delivery (preeclampsia, premature rupture of membranes, etc); also iatrogenic—heel or scalp resulting from infected heel-stick or phlebitis; septic arthritis in 70% of staphylococcal and 35% of *Streptococcus agalactiae* cases; fever in 66% of total cases, 40% of staphylococcal infections, never in *Streptococcus agalactiae* cases; white cell count > 210,000/ μ L in 40% of staphylococcal and 10% of *Streptococcus agalactiae* infections; swelling in 75% of patients, decreased movement in 55%, erythema in 30%, tenderness in 15%

Children: bone pain, limp or disuse in all, fever in 85%, joint pain in 66%, history of injury in 45%; 30% femur (60% proximal, 30% distal, 10% middle), 30% tibia (50% distal, 45% proximal, 5% middle), 10% pelvis, 10% humerus, 10% fibula, 3% radius; 20% complicating septic arthritis, 20% growth disturbance, 15% restricted motion, 15% deformity, 15% draining sinus, 10% recurrence, 5% chronicity, 5% pathologic fracture, 1% death

Aspergillus: 1,3- β -D-glucan levels increased

Differential Diagnosis: cellulitis, bone infarction, subperiosteal hematoma, traumatic periostitis, bone cyst, eosinophilic granuloma, osteitis deformans, neurofibromatosis, monoarticular rheumatoid arthritis, osteodystrophy in patient on long term dialysis, recurrent multifocal osteomyelitis with pustularis palmoplantaris (very rare, apparently noninfectious), multiple myeloma, primary or metastatic malignancy, congenital syphilis, pyomyositis, wound infection, soft tissue abscess, acute rheumatic fever, septic arthritis

Treatment: debridement of necrotic bone and loculated purulence, reestablishment of vascularity, grafting bony defects, removal of prostheses; surgery if development of neurological abnormalities in vertebral or cranial osteomyelitis or if spread to hip joint in child; nonsteroidal antiinflammatory drugs +:

General Empirical: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly; cephalozin 50 mg/kg to 2 g i.v. 8 hourly

Immediate Penicillin Hypersensitive: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Acute Neonatal: gentamicin 5-7.5 mg/kg i.v. daily in 2 or 3 divided doses + cloxacillin/flucloxacillin 200 mg/kg daily i.v. in 3 divided doses for 14 d \pm fusidic acid 20 mg/kg 12 hourly by i.v. infusion over 2 h for 14 d, followed by cloxacillin/flucloxacillin orally for 6 mo

Gram Negative Infection Suspected, Child < 5 y Not Immunised Against *Haemophilus influenzae* type b: cefotaxime 50 mg/kg to 2 g i.v. 8 hourly; ceftriaxone 50 mg/kg to 2 g i.v. daily + di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Diabetic Foot or Contiguous Ulcer: debridement or surgery, biomechanical offloading of mechanical impediments to wound healing; ciprofloxacin or clindamycin or piperacillin-tazobactam or ampicillin-sulbactam + aminoglycoside for 4-6 w; rifampicin 600 mg twice daily + ofloxacin 200 mg 3 times daily for 6 mo

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 fortuitum, Nocardia asteroides: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Streptococci: benzylpenicillin 4 MU i.v. once then 2 MU i.v. 4 hourly (child: 150 000-250 000 U/kg daily in 4 divided doses), followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses); drainage at operation and removal of any prosthesis

Methicillin Susceptible *Staphylococcus aureus*: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly, then di/flucloxacillin 25 mg/kg to 1 g orally 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephalozin 50 mg/kg to 2 g i.v. 8 hourly, then cephalexin 25 mg/kg to 1 g orally 6 hourly

Immediate Penicillin Hypersensitive:

Macrolide Susceptible: clindamycin 10 mg/kg to 450 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, then clindamycin 10 mg/kg to 450 mg orally 8 hourly

Macrolide Resistant: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly), then cotrimoxazole 8/40 mg/kg to 320/1600 mg orally 12 hourly or doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not in child < 8 y)

Methicillin Resistant *Staphylococcus aureus*: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly), then rifampicin 7.5 mg/kg to 300 mg orally 12 hourly + sodium fusidate tablets 12 mg/kg to 500 mg orally 12 hourly or fusidic acid 18 mg/kg to 750 mg orally 2 hourly or clindamycin 10 mg/kg to 450 mg orally 8 hourly or cotrimoxazole 8/40 mg/kg to 320/1600 mg orally 12 hourly

***Listeria monocytogenes, Eikenella corrodens*:** ampicillin

***Kingella kingae*:** benzylpenicillin 4 MU i.v. once, then 2 MU i.v. 4 hourly (neonate: 100 000 U/kg daily in 3 or 4 doses; < 45 kg: 250 000 U/kg daily in 6 divided doses) for at least 10 d, followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses)

***Brucella*:** streptomycin 1 g twice a day i.m. for 14-21 d + rifampicin 900 mg/d orally for 45 d + doxycycline 100 mg orally twice daily for 45 d

***Burkholderia cepacia*:** imipenem

***Pseudomonas*:** ofloxacin 200 mg/kg orally 3 times daily for 2-4 w (not child), i.v. tobramycin for 7 d

***Vibrio vulnificus*:** doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

***Aeromonas*:** gentamicin

Anaerobes: chloramphenicol, clindamycin

Other Bacteria: ceftriaxone

Fungi: amphotericin B ± flucytosine, itraconazole, fluconazole (all ineffective for *Scedosporium*); debridement with immediate bone grafting desirable if appropriate

Prophylaxis Before Joint Surgery: cloxacillin/flucloxacillin 500 mg i.v. or i.m. immediately specimens taken during surgery + amoxicillin 500 mg i.v. or i.m. at same time and 6 hourly for 48 h + gentamicin on polymethylmethacrylate beads put into joint and left in situ ≈ 19 d

GRANULOMATOUS SYNOVITIS

Agents: *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, *Mycobacterium marinum*, *Mycobacterium goodii*, *Mycobacterium avium*, *Mycobacterium chelonae*

Diagnosis: Ziehl-Neelsen stain, culture and histology of surgical specimen

Treatment: surgery +:

***Mycobacterium avium*:** ethambutol 15 mg/kg (not < 6 y) orally daily + clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly 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 till culture negative 12 mo

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

***Mycobacterium kansasii*:** isoniazid 10 mg/kg to 300 mg orally daily [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally daily + ethambutol 15 mg/kg (not < 6 y) orally daily for 18 mo and 12 months negative cultures

***Mycobacterium marinum*:** clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly, cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly, doxycycline 2.5 mg/kg to 100 mg orally (not < 8 y) 12 hourly for 3-4 mo

Others: 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)

TENOSYNOVITIS

Agent: *Mycobacterium nonchromogenicum* (chronic of knee)

Diagnosis: culture of biopsy

Treatment: ethambutol, sulphonamides, cotrimoxazole, erythromycin, streptomycin + surgical debridement

BURSITIS

Agents: *Staphylococcus aureus*, coagulase negative staphylococci, β -haemolytic streptococci, *Mycobacterium marinum*, *Mycobacterium kansasii*, *Mycobacterium szulgai*, *Brucella abortus*, *Haemophilus influenzae*, *Serratia marcescens*, *Pseudomonas fluorescens*, *Enterobacter cloacae*, *Escherichia coli*, *Prototheca* (olecranon)

Diagnosis: culture of aspirate

Treatment: repeated aspiration + appropriate antimicrobials; surgical drainage if necessary

CARPAL TUNNEL SYNDROME

Agents: 21% *Mycobacterium tuberculosis*, 19% *Mycobacterium* other than *Mycobacterium tuberculosis*, 14% rubella vaccine, 11% *Borrelia burgdorferi*, 11% rubella virus, 5% *Histoplasma capsulatum*, 5% *Sporothrix schenckii*, 3% *Neisseria gonorrhoeae*, 3% toxic shock syndrome, 1% *Staphylococcus aureus*, 2% β -haemolytic streptococci, 0.8% coagulase negative staphylococci, 0.8% *Enterococcus faecalis*, 0.8% *Clostridium histolyticum*, 0.8% guinea worm

Diagnosis: smear and culture of biopsy

Treatment: surgery + appropriate antimicrobial

COMPOUND FRACTURES

Agents: *Staphylococcus aureus*, Gram negative bacilli, *Clostridium perfringens*

Diagnosis: if infection is evident before treatment or develops despite treatment, Gram stain and culture of tissue or swab

Treatment: treatment should be prophylactic; di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly, or cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 25 mg/kg to 1 g i.v. 8 hourly if penicillin hypersensitive (not immediate), or clindamycin 10 mg/kg to 450 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg 8 hourly if immediate penicillin hypersensitivity for 1-3 d + (if wound soiling or tissue damage severe and/or devitalised tissue present) piperacillin + tazobactam 100 + 12.5 mg/kg to 4 + 0.5 g i.v. 8 hourly or ticarcillin + clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly then amoxicillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly or (penicillin hypersensitive) gentamicin (< 10 y: 7.5 mg/kg; child \geq 10 y: 6 mg/kg; adult 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function) or ciprofloxacin 10 mg/kg to 400 mg i.v. or 15 mg/kg to 750 mg orally 12 hourly + clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly then clindamycin 10 mg/kg to 450 mg orally 8 hourly; review patient's immune status to tetanus

PAGET'S DISEASE: localised deformation of bone

Agent: ? *measles virus* persistent infection of osteoclasts