

## Chapter 21

### Antibacterials

**ANTIBIOTICS:** Antibiotics should be used only where the benefits are scientifically demonstrable and substantial. The choice of a particular agent should take into account antimicrobial spectrum, clinical efficacy, safety, previous clinical experience, potential for selecting resistant organisms and associated risk of superinfection, cost, as well as patient factors (including hypersensitivity, age, renal or hepatic impairment). The relative importance of each of these factors will be influenced by the severity of the illness and whether the drug is to be used for prophylaxis, empirical therapy or therapy directed at one or more identified pathogens. As far as possible, therapy should be directed against specific organisms and guided by microbiology. Directed antimicrobial therapy for proven pathogens should use the most effective, least toxic, narrowest spectrum agent available. Choice of parenteral or oral formulations should be determined by the site and severity of infection, with preference for oral therapy wherever feasible. The dosage should be high enough to ensure efficacy and minimise the risk of resistance selection and low enough to minimise the risk of dose-related toxicity. Antibiotic combinations should only be used when it has been proven that such combinations are necessary to achieve efficacy or to prevent the emergence of resistant organisms. Empirical antimicrobial therapy should be based on local epidemiological data on potential pathogens and their patterns of susceptibility. Indications should be evidence-based. Duration of therapy should be as short as possible and should not exceed 7 days unless there is proof that this duration is inadequate. Prophylactic antibiotics should be restricted to a limited range of drugs of proven efficacy in situations where they have been proven to be effective or where the consequences of infection are disastrous. Surgical prophylaxis should be such as to achieve high plasma and tissue levels during, and immediately following, the operation. This will usually be best achieved by parenteral dosing commencing just before the operation. A single dose should be used unless it has been demonstrated that the benefits of longer-term prophylaxis outweigh the risk of resistance selection or propagation. Because of their potent capacity for selecting resistant organisms and the risk of patient sensitisation, topical antibiotics should be restricted to proven indications and topical antiseptics substituted wherever possible. Appropriate specimens for microscopy, culture and susceptibility testing should be obtained before commencing antibacterial therapy. A Gram stain or direct antigen detection may allow specific therapy before the pathogen has been cultured.

**BETA-LACTAM ANTIBIOTICS:** penicillins, cephalosporins (including cephamycins), monobactams, carbapenems; inhibit transpeptidase, thus preventing cross-linking of cell wall peptidoglycan; active against Gram positive and Gram negative bacteria; bactericidal; activity depends on duration of exposure; induce an increased release of chemoattractants from bacteria; some classes lead to markedly increased levels of free endotoxins

**PENICILLIN:** kills only growing organisms; no or slight postantibiotic effect; bactericidal; penetrates well into mammalian cells; mainly active against Gram positive bacteria; inactivated by  $\beta$ -lactamases; most active antibiotic against non-enterococcal streptococci; spectrum includes *Actinomyces* (97% susceptible), anaerobic cocci (100% susceptible), anaerobic Gram positive bacilli, *Bacteroides ureolyticus* (MIC ? 0.25 mg/L), *Borrelia recurrentis*, *Capnocytophaga canimorsus* (95% susceptible), *Cardiobacterium hominis*, *Clostridium* (100% susceptible), *Corynebacterium diphtheriae* (resistance not yet confirmed in Australia), *Corynebacterium pseudotuberculosis*, *Eikenella corrodens* (99% susceptible), *Enterococcus* (in Australia, 2% resistant), *Erysipelothrix* (100% susceptible at 0.06 mg/L), *Eubacterium*, *Fusobacterium* (100% susceptible), Group II f (? 0.06 mg/L), *Helicobacter pylori*, *Listeria* (0.25 mg/L), *Moraxella* (? 0.06-0.5 mg/L), *Neisseria gonorrhoeae* (in Australia, 6% resistant due to  $\beta$ -lactamase and 10% chromosomal resistance; 98% total resistance in Vietnam), *Neisseria meningitidis* (in Australia, < 5% MIC > 1 mg/L), *Pasteurella* (resistance not yet confirmed in Australia), penicillinase negative *Staphylococcus aureus* (? 0.03 mg/L; 5% of *Staphylococcus aureus* isolated), streptococci including *Streptococcus agalactiae* (< 5% resistance in Australia), *Streptococcus canis* (< 5% resistance in Australia), *Streptococcus* groups C and F (< 5% resistance in Australia), *Streptococcus milleri* (< 5% resistance in Australia), *Streptococcus pneumoniae* (in Australia, 9% intermediate or fully resistant), *Streptococcus pyogenes* (resistance not yet reported), *Treponema pallidum*, Enterobacteriaceae 100% intrinsic resistance, *Moraxella catarrhalis* 85% acquired

resistance due to  $\beta$ -lactamase (probably all resistant in clinical practice), *Staphylococcus aureus* 95% acquired resistance due to  $\beta$ -lactamase; shows synergism with monocytes; shows microbicidal activity against bacteria ingested by monocytes or macrophages; no effect on opsonisation, chemotaxis or neutrophil penetration; significant inoculum effect

**Indications:** clostridial abortifacient and puerperal infection; actinomycosis; anthrax; bacteraemia and septicemia due to *Capnocytophaga canimorsus*, *Leptotrichia buccalis*, *Leuconostoc*; acute bronchiolitis and bronchopneumonia; acute bronchitis; cat bites; cellulitis due to *Erysipelothrix rhusiopathiae*; dental infections; dermatophilosis; diphtheria; dog bites; endocarditis due to *Corynebacterium*; erysipelas; erysipeloid; necrotising ulcerative gingivostomatitis; gonorrhoea; hepatic abscess and hepatic granuloma due to *Actinomyces*; hepatitis due to *Staphylococcus aureus* (susceptible strains), *Listeria monocytogenes*, *Treponema pallidum*, *Borrelia recurrentis*, *Actinomyces*; impetigo; ischioanal abscess; local and generalised sepsis due to *Clostridium botulinum*; mastitis; infections (including postneonatal pyogenic meningitis) due to *Pasteurella multocida*; mouth abscess; otitis externa due to *Streptococcus*, *Corynebacterium diphtheriae*, *Actinomyces*; streptococcal and gonococcal peritonitis; peritonsillar abscess; streptococcal and meningococcal pneumonia; streptococcal psoas abscess; rheumatic fever; salivary calculus; scarlet fever; acute maxillary sinusitis; splenic abscess due to *Propionibacterium*; all streptococcal infections; surgical prophylaxis in amputation; syphilis; systemic infection prophylaxis in hyposplenism/splenectomy; tetanus; Vincent's angina

**Side Effects:** hypersensitivity reactions (1-10%; commonly urticaria, uncommonly angioedema, rarely anaphylactic shock within 72 h; later, urticarial rash (common), fever (uncommon), haemolysis (rare), serum sickness-like reaction (rare); 3-6% cross reaction with cephalosporins; skin test predictive; desensitisation possible), gastrointestinal disturbances (nausea, diarrhoea) with oral preparations, skin reactions (rash, urticaria), pain and inflammation at injection site common; superinfection common with prolonged treatment and/or with broad spectrum penicillins; bronchospasm, vomiting, erythema, toxic epidermal necrolysis, Stevens-Johnson syndrome, colitis uncommon; interstitial nephritis, blood dyscrasias, electrolyte disturbances (potassium metabolic effects), platelet dysfunction and bleeding, haemolytic anaemia, haemolytic uraemic syndrome rare; aseptic meningitis; all penicillins cause neutropenia by myelosuppression; therapeutic efficacy may be decreased by chloramphenicol, tetracycline and erythromycin; serum levels increased and prolonged by probenecid (desired effect); probably safe in therapeutic amounts during pregnancy; modify dosage in severe renal dysfunction (CNS toxicity and aminoglycoside inactivation) and monitor serum levels when possible (maximum permissible blood level 128 mg/L); further dose required after haemodialysis; unpredictable enhanced warfarin effect

**BENZYL PENICILLIN (PENICILLIN G):** narrow spectrum (Gram positive) very acid unstable,  $\beta$ -lactamase unstable penicillin; parenteral (i.m. or i.v. 4 times a day); 59% protein binding, no significant change in protein binding in elderly; active against *Enterococcus faecalis*, *Haemophilus influenzae*, *Neisseria meningitidis*, non- $\beta$ -lactamase-producing *Staphylococcus aureus* (85% of methicillin susceptible strains resistant in Australia), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Pseudomonas* 100% intrinsic resistance; *Moraxella catarrhalis* 94% acquired resistance due to  $\beta$ -lactamase (probably all resistant in clinical practice); in WHO Model List of Essential Drugs; mode of elimination renal; incompatible with lincomycin, tetracycline, vancomycin

**Indications:** treatment of choice for many infections; in i.v. treatment, when high doses required; abscesses; actinomycosis; anaerobic infections; anthrax; septic arthritis (community acquired, due to *Neisseria*, *Kingella kingae*, *Streptococcus*, *Capnocytophaga*, *Arcanobacterium haemolyticum*, *Streptobacillus moniliformis*); bacteraemia and septicemia due to *Neisseria meningitidis*, *Streptococcus pyogenes*; brain abscess from frontal sinuses, ear or mastoid or due to streptococci, *Actinomyces* or anaerobes; severe streptococcal or clostridial cellulitis; cerebrospinal fluid shunt infections; cervical fascial space infections in normal patients; clostridial myositis; compound fractures prophylaxis if wound soiling, severe tissue damage and/or devitalised tissue; purulent conjunctivitis due to *Neisseria*, *Listeria monocytogenes*; diphtheria prophylaxis in close contacts; disseminated gonococcal and meningococcal disease; endocarditis; severe erysipelas; erythema serpens; necrotising fasciitis due to *Streptococcus pyogenes*; gas gangrene; gonorrhoea; meningococcal and streptococcal haemorrhagic fever; acute leptospirosis; *Listeria monocytogenes* prophylaxis in pregnancy; lymph gland infections due to *Corynebacterium pseudotuberculosis*; meningitis (postneonatal pyogenic in adult; streptococcal, gonococcal and listerial in neonate); myocarditis and pericarditis due to *Actinomyces*, *Neisseria meningitidis*; necrotising ulcerative gingivostomatitis; osteomyelitis and osteochondritis due to *Streptococcus*, *Kingella*

*kingae*; streptococcal and clostridial pelvic sepsis; perinatal and prenatal generalised disease due to *Clostridium*, *Corynebacterium*, *Neisseria gonorrhoeae*, *Peptostreptococcus*, *Streptococcus*; peritonsillar abscess in normal host; pharyngitis; pneumonia (severe community acquired in non-tropical Australia, moderate nosocomial with no specific risk factors, aspiration, moderate to severe anaerobic pleuropulmonary, intensive care, pneumococcal, penicillin susceptible staphylococcal, neonatal); pulmonary abscess; rheumatic fever prophylaxis; salpingitis; streptococcal and enterococcal local and generalised sepsis; acute sinusitis; localised skin lesions due to *Streptococcus pyogenes*, *Neisseria*, *Staphylococcus aureus* (susceptible strains), *Clostridium botulinum*, synergistic gangrene; tertiary and congenital syphilis; systemic infections in patients with C5, 6, 7, 8 deficiency; tetanus; acute throat infections due to *Corynebacterium* and *Arcanobacterium haemolyticum*, streptococcal toxic shock syndrome; tubo-ovarian abscess

**Side Effects:** sensitivity to penicillin, anaphylactic shock in hypersensitive patients; convulsions, bone marrow suppression, megaloblastic marrow, positive direct Coomb's test and associated haemolytic anaemia with very large doses; pain at injection site; requires moderate to significant adjustment of dosage in renal failure (rarely, seizures, interstitial nephritis, sodium overload, hypokalemia) and in dialysis; safe in pregnancy; probenecid increases plasma levels; unpredictable enhanced warfarin effect

**Contraindications:** penicillin hypersensitivity

**BENZATHINE BENZYL PENICILLIN:** narrow spectrum  $\beta$ -lactamase unstable penicillin; i.m. preparation; provides low levels of benzylpenicillin for up to 4 w; in WHO Model List of Essential Drugs

**Indications:** severe impetigo with cellulitis in remote areas, Lyme disease arthritis, rheumatic fever prophylaxis and treatment, scarlet fever, syphilis (noncompliant, congenital, late latent, tertiary), acute streptococcal throat infections in remote areas

**Side Effects:** sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; safe in pregnancy

**Contraindications:** penicillin hypersensitivity

**PROCAINE BENZYL PENICILLIN:** narrow spectrum,  $\beta$ -lactamase unstable penicillin; i.m. preparation; daily dose provides adequate levels for up to 24 h against highly susceptible organisms; in WHO Model List of Essential Drugs

**Indications:** abscess; anthrax; boils; breast abscess; cat and dog bites; less severe streptococcal cellulitis; purulent conjunctivitis due to *Neisseria* in remote areas; diphtheria treatment and carriers; less severe erysipelas; uncomplicated gonorrhoea; human bite and clenched fist injury infections; louse-borne relapsing fever; necrotising ulcerative gingivostomatitis; neurosurgery prophylaxis in CSF leakage; acute otitis media; pelvic inflammatory disease; pericoronitis; mild to moderate community acquired pneumonia; quinsy; rat bite fever; streptococcal local and generalised sepsis; syphilis (late latent and tertiary, HIV infected patients, cardiovascular, neurosyphilis, congenital, prophylaxis); acute streptococcal and gonococcal infections

**Side Effects:** sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients (epinephrine must be injected at once); safe in pregnancy and breastfeeding

**Contraindications:** penicillin hypersensitivity; do not use in newborn babies unless no other penicillin or ampicillin is available (in emergencies)

**PHENETHICILLIN:** Gram positive effective, acid stable, sensitive to  $\beta$ -lactamases; well absorbed; activity equal to phenoxymethylpenicillin

**Indication:** prophylaxis of recurrent streptococcal infections including rheumatic fever

**BICILLIN:** benzathine penicillin + procaine penicillin + benzylpenicillin; i.m. single or daily dose

**Indications:** cat and dog bite infections in remote areas, erysipelas in remote areas, human bite and clenched fist injury infections in remote areas, acute otitis media in remote areas, acute streptococcal throat infections in remote areas

**Side Effects:** as for components

**PHENOXYMETHYLPENICILLIN (PENICILLIN V):** narrow spectrum (Gram positive), acid stable,  $\beta$ -lactamase unstable penicillin; may be given orally; well absorbed but absorption impaired by food (take  $\frac{1}{2}$  -1 h before food); bioavailability 65%; no significant change in absorption in elderly; 66% protein binding; lower activity than benzylpenicillin against staphylococci (in Australia, 85% acquired resistance due to  $\beta$ -lactamase) and streptococci, low activity against *Haemophilus influenzae*, *Pseudomonas* 100% intrinsic resistance; *Moraxella catarrhalis* 94% acquired

resistance due to  $\beta$ -lactamase (probably all resistant in clinical practice); in WHO Model List of Essential Drugs and UNHCR Basic List of Essential Drugs; mode of elimination renal

**Indications:** actinomycosis; septic arthritis due to *Kingella kingae*; acute bronchitis; less severe cellulitis due to *Streptococcus pyogenes*; diphtheria; streptococcal endocarditis; less severe erysipelas; erythema chronicum migrans; gingival and periodontal infection; impetigo; myocarditis and pericarditis due to *Actinomyces*; necrotising ulcerative gingivostomatitis; osteomyelitis and osteochondritis due to *Streptococcus*, *Kingella kingae*; acute streptococcal otitis media; pericoronitis; pneumococcal pneumonia; rat bite fever; prophylaxis and treatment of recurrent streptococcal infections including rheumatic fever; streptococcal local and generalised sepsis; acute sinusitis; surgical prophylaxis (CSF leakage, postsplenectomy); acute streptococcal throat infections; tooth abscess; streptococcal water-related infections

**Side Effects:** sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; dosage adjustment not required in renal failure (rarely, seizures); dose after intermittent haemodialysis; safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; probenecid increases plasma levels; very weak association with oral contraceptive failure

**Contraindications:** penicillin hypersensitivity

**PROPICILLIN:** potassium salt of phenoxypenicillin; similar to phenoxymethylpenicillin but can be administered with food and has higher bioavailability (85%)

**METHICILLIN:** antistaphylococcal,  $\beta$ -lactamase stable, acid unstable penicillin; 33% protein binding; higher activity than phenoxymethylpenicillin against  $\beta$ -lactamase-producing *Staphylococcus aureus* and against *Streptococcus pyogenes*; no longer available (replaced by dicloxacillin or flucloxacillin); methicillin resistant *Staphylococcus aureus* should be regarded as clinically resistant to all  $\beta$ -lactams irrespective of laboratory reports of susceptibility

**Indications:** persistent *Staphylococcus aureus* infection in cystic fibrosis (inhalation)

**Side Effects:** greater nephrotoxicity than cloxacillin and flucloxacillin

**OXACILLIN:** Gram positive effective, acid stable, resistant to most  $\beta$ -lactamases; orally absorbed; 92% protein binding; minimal inoculum effect; most active antibiotic against methicillin susceptible staphylococci; lower activity than methicillin against *Streptococcus pyogenes*; low activity against *Enterococcus faecalis*

**Indications:** endocarditis due to methicillin susceptible *Staphylococcus*, staphylococcal postneonatal pyogenic meningitis, staphylococcal local and generalised sepsis

**Side Effects:** hepatotoxicity in 22%, rash in 32%; safety not established in pregnancy; dosage modification not required in renal dysfunction

**CLOXACILLIN:** narrow spectrum and antistaphylococcal,  $\beta$ -lactamase stable, acid stable penicillin; 95% protein binding; orally absorbed (take  $\frac{1}{2}$  - 1 h before food) but now only used parenterally; activity equal to oxacillin; minimal inoculum effect; Enterobacteriaceae and *Enterococcus* 100% intrinsic resistance; in Australia, 22% *Staphylococcus aureus* resistant (mainly confined to teaching hospitals in eastern Australia); mode of elimination renal; in WHO Model List of Essential Drugs; incompatible with erythromycin, gentamicin, polymyxin B, tetracycline

**Indications:** abscesses; septic arthritis; bacteraemia and septicemia (focus probably intravascular catheter); acute bronchiolitis and bronchopneumonia; cellulitis; chondritis; endocarditis due to methicillin susceptible *Staphylococcus aureus*; staphylococcal enterocolitis; *Erysipelothrix rhusiopathiae* infections (100% susceptible at 0.025 mg/L); acute severe furunculosis; staphylococcal hepatitis; impetigo; mastoiditis; meningitis; musculoskeletal trauma prophylaxis; acute neonatal osteomyelitis and osteochondritis; serious ophthalmia neonatorum due to *Staphylococcus aureus*; bacterial parotitis and submandibular sialadenitis; perichondritis; perinatal generalised disease due to *Staphylococcus aureus* (hospital acquired); staphylococcal pneumonia; scalded skin syndrome; skin infections; methicillin susceptible staphylococcal infections (including lymph gland infections, splenic abscess, toxic shock syndrome); symbiotic gangrene

**Side Effects:** sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; to be given under medical supervision; safe in pregnancy; dosage modification not required in renal dysfunction (rarely, seizures) or dialysis; probenecid increases plasma levels

**FLUCLOXACILLIN (NAFCILLIN):** narrow spectrum and antistaphylococcal  $\beta$ -lactamase stable penicillin; more readily absorbed by oral route than cloxacillin and may cause less gastrointestinal upset (take  $\frac{1}{2}$  - 1 h before food, 4 times a day or twice a day with probenecid); also parenteral; Enterobacteriaceae, *Pseudomonas* and *Enterococcus* 100%

intrinsic resistance; in Australia, 22% *Staphylococcus aureus* isolates from metro hospitals and 10% of isolates from private laboratories resistant (significant geographic variation); serum protein binding 96%; reduced protein binding and clearance in elderly; mode of elimination renal

**Indications:** both orally and parenterally, has become treatment of choice for susceptible *Staphylococcus aureus* infections but should not be used for trivial infections; septic arthritis (staphylococcal and organism unknown); bacteraemia and septicemia (infection from respiratory system in children, focus probably open skin infection/cellulitis, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer, focus probably intravascular catheter, unidentified source, due to *Staphylococcus aureus*); staphylococcal blepharitis associated with lid abscess; bullous impetigo; staphylococcal cellulitis; compound fractures prophylaxis; endocarditis treatment and prophylaxis; acute mastitis and breast abscess; mastoiditis; osteomyelitis (acute neonatal, due to *Staphylococcus aureus*); acute localised otitis externa; staphylococcal parotitis and submandibular sialadenitis, pneumonia (staphylococcal, severe community acquired in children, mild to moderate nosocomial in patients with diabetes, coma, head injury); preseptal and postseptal cellulitis; local and generalised sepsis (due to *Bacillus cereus*, organism unknown); complicated or severe acute sinusitis; methicillin susceptible staphylococcal infections (including pyoderma with cellulitis or recurrent, toxic shock syndrome); surgical prophylaxis (cardiovascular, vascular grafts, breast, dialysis access, orthopaedic, muscular, skeletal and soft tissue trauma), neurosurgery; symbiotic gangrene; suppurative wound infections

**Side Effects:** severe, long-lasting cholestasis (rarely fatal), especially in elderly (> 55 y) and if treatment > 14 d (oral or i.v.), after oral or i.v. and up to 6 w after treatment; rash in 10%; adjustment of dosage interval required in renal failure (rarely, seizures) and in continuous venovenous or arteriovenous haemodialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; probenecid increases plasma levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

#### **FLUCLOXACILLIN HYDROXYAPATITE GRANULES**

**Indications:** staphylococcal osteomyelitis

**DICLOXACILLIN:** narrow spectrum and antistaphylococcal; similar to cloxacillin/flucloxacillin; oral (take ½ - 1 h before food) and parenteral; minimal inoculum effect

**Indications:** serious staphylococcal infections

**Side Effects:** as for **FLUCLOXACILLIN** but less hepatotoxic and more likely to produce thrombophlebitis and interstitial nephritis; high dose may cause diarrhoea; safety in pregnancy not established

**AMPICILLIN:** moderate spectrum, very acid stable, ?-lactamase sensitive aminopenicillin; oral (take ½ - 1 h before food) and parenteral; well absorbed; mean peak serum concentration 3.7 mg/L after 0.8 mole oral dose; 45% urinary recovery; 3% bronchial penetration 2-3 h after 1 g oral dose; intraperitoneal penetration 96%; protein binding 15-18%; increased interindividual variability in absorption, reduced clearance, no significant change in  $V_d$  in elderly; no postantibiotic effect; greater activity than benzylpenicillin against some Gram negative organisms; agent of choice against *Enterococcus* (in Australia, *E.faecalis* 0.7% resistant, *E.faecium* 69% resistant); less active than benzylpenicillin against *Streptococcus viridans*; spectrum includes *Borrelia burgdorferi* (MIC 0.25-1 mg/L), *Brucella*, *Erysipelothrix* (100% susceptible at 0.25 mg/L), Group III (? 0.06 mg/L), *Haemophilus influenzae* (in Australia, 28% resistant), *Listeria monocytogenes* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (in Australia, 15% resistance due to both ?-lactamase and altered penicillin binding proteins), *Neisseria meningitidis* (? 0.12 mg/L), *Salmonella*, *Shigella*, *Streptococcus agalactiae* (? 0.12-0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.06 mg/L), *Streptococcus pneumoniae* (in Australia, 3% resistant), *Streptococcus pyogenes* (? 0.12 mg/L); *Staphylococcus aureus* 85% acquired resistance due to ?-lactamase; *Klebsiella* 98% intrinsic resistance due to ?-lactamase (probably all resistant in clinical practice); *Enterobacter*, *Serratia*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia* 96% intrinsic resistance (probably all resistant in clinical practice), *Moraxella catarrhalis* 94% acquired resistance due to ?-lactamase (possibly all resistant in clinical practice); *Pseudomonas aeruginosa* 100% intrinsic resistance; *Stenotrophomonas maltophilia* 100% intrinsic resistance; *Bacteroides fragilis* 100% intrinsic resistance due to ?-lactamase; in Australia, *Escherichia coli* 48% resistance due to ?-lactamase, *Proteus mirabilis* 18% resistance due to ?-lactamase; significant inoculum effect; mode of elimination renal; incompatible with erythromycin, gentamicin, kanamycin, lincomycin, polymyxin B, tetracycline; oral ampicillin largely replaced by oral amoxicillin; in WHO Model List of Essential Drugs

**Indications:** amnionitis; septic arthritis due to *Listeria monocytogenes*; bacteraemia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably urinary tract, neonatal, due to *Salmonella*, *Shigella*, *Oerskovia*, *Enterococcus*); brain abscess from ear and mastoid or due to *Listeria monocytogenes* or *Haemophilus*; bronchiectasis; bronchitis; acute chest infections; cholangitis and cholecystitis in normal host; infantile diarrhoea; bacterial dysentery; disseminated gonococcal and meningococcal disease; endocarditis treatment and prophylaxis; enteric fever treatment and carriers; acute epididymitis and epididymo-orchitis; acute epiglottitis in normal host; simple gastritis, duodenal ulcer, peptic ulcer; bacterial gastroenteritis; purulent conjunctivitis due to *Listeria monocytogenes*; severe uncomplicated gonorrhoea; hepatitis due to *Shigella*; hepatic abscess; hepatic granuloma due to *Listeria monocytogenes*; mild leptospirosis; listeriosis; Lyme disease (arthritis, Bell's palsy, mild cardiac disease); lymph gland infections due to *Brucella*; neonatal and post-neonatal pyogenic meningitis due to *Listeria monocytogenes*, *Pasteurella multocida*; listerial meningoencephalitis; myocarditis and pericarditis due to *Actinomyces*, *Haemophilus influenzae*, *Listeria monocytogenes*; nasopharyngitis; osteomyelitis and osteochondritis due to *Listeria monocytogenes*, *Eikenella corrodens*; treatment and prophylaxis of otitis media; pancreatic abscess; peritonitis (suspected bowel origin, spontaneous, due to *Capnocytophaga*, *Listeria monocytogenes*); peritonsillar abscess in normal host; pertussis; pneumonia (moderate community acquired, severe *Haemophilus influenzae*); post-partum infections; severe acute prostatitis and seminal vesiculitis; prosthetic implants prophylaxis; severe acute pyelonephritis; rape prophylaxis; local and generalised sepsis (including due to *Enterococcus*, *Salmonella*); acute maxillary sinusitis; splenic abscess due to *Listeria monocytogenes*; surgical prophylaxis (ruptured, perforated or gangrenous viscus; postsplenectomy; joint); systemic infection prophylaxis in agammaglobulinemia; acute tracheitis; typhoid carriers; non-gonococcal urethritis; urinary tract infections; streptococcal vaginitis

**Side Effects:** sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; skin reactions (especially in glandular fever; increased incidence of rash when combined with allopurinol), nausea, vomiting, diarrhoea, enterocolitis, pseudomembranous colitis, superinfection, hearing loss; safe in therapeutic amounts during pregnancy; modify dosage interval in renal dysfunction (rarely, seizures, interstitial nephritis, sodium overload, hypokalemia) and in dialysis; probenecid increases levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect; safety in pregnancy not established; safe in breastfeeding but monitor infant for diarrhoea

**Contraindications:** penicillin hypersensitivity

**AMOXICILLIN (AMOXICILLIN):** moderate spectrum,  $\beta$ -lactamase sensitive aminopenicillin; oral dosage schedule 3 times daily; more readily absorbed after oral administration than ampicillin (not affected by food) but parenterally equivalent; mean peak serum concentration 7.7 mg/L after 0.8 mole oral dose; 66% urinary recovery; 3.5% bronchial penetration 2-3 h after 1 g oral dose; intraperitoneal penetration 84%; protein binding 15%; mode of elimination renal; moderate cost; greater activity than benzylpenicillin against some Gram negative organisms; agent of choice against *Enterococcus*; oral amoxicillin preferred to oral ampicillin except in treatment of shigellosis; in WHO Model List of Essential Drugs

**Indications:** as for ampicillin; also purulent conjunctivitis due to *Neisseria* in remote areas; acute otitis media in remote areas; meningitis due to *Haemophilus influenzae* and *Listeria monocytogenes*; mild to moderate community acquired pneumonia in adult > 60 y or with coexisting illness and in child 3 mo - 10 y; acute sinusitis; gonorrhoeal vaginitis ( $\beta$ -lactamase negative)

**Side Effects:** low risk of serious adverse reactions and skin rash (increased risk of rash in patients receiving allopurinol); moderate risk of gastrointestinal adverse effects; pseudomembranous colitis; allergic reactions; adjustment of dosage interval in renal failure (rarely, seizures) and in dialysis; safe in pregnancy; probenecid increases plasma levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

**AMINOCILLIN PIVOXIL:** moderate spectrum penicillin; binds chiefly to PBP2; kills only growing organisms; not affected by type I  $\beta$ -lactamase; low inducer of type I  $\beta$ -lactamase; spectrum includes *Escherichia coli* (MIC 0.13 mg/L)

**Indications:** bacterial dysentery

**APALCILLIN:** moderate spectrum penicillin; spectrum includes  $\beta$ -lactamase negative *Haemophilus influenzae* (MIC

? 0.5 mg/L, ?-lactamase negative *Neisseria gonorrhoeae* (? 0.5 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Proteus mirabilis* (? 0.5 mg/L), *Streptococcus agalactiae* (? 0.5 mg/L), *Streptococcus pneumoniae* (? 0.02-1 mg/L), *Streptococcus pyogenes* (? 0.02-0.5 mg/L)

**BACAMPICILLIN:** moderate spectrum penicillin; mean peak serum concentration 8.2 mg/L after 0.8 mole oral dose; 55% urinary recovery

**FORAMINDOCILLIN:** moderate spectrum penicillin; spectrum includes *Escherichia coli* (0.12-0.5 mg/L), *Haemophilus influenzae* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.25-0.5 mg/L), *Klebsiella pneumoniae* (0.25-0.5 mg/L), *Proteus mirabilis* (0.25-0.5 mg/L)

**HETACILLIN:** moderate spectrum penicillin; activity equal to ampicillin

**Side Effects:** safety not established in pregnancy

**MECILLINAM:** moderate spectrum penicillin; serum protein binding 5%; spectrum includes Group IIf (MIC 0.5-1 mg/L)

**PIVAMPICILLIN:** moderate spectrum penicillin; mean peak serum concentration 7.1 mg/L after 0.8 mole oral dose; 70% urinary recovery

**Indications:** bacterial gastroenteritis

**PIVEMECILLINAM**

**Indications:** bacterial gastroenteritis

**TALAMPICILLIN:** moderate spectrum penicillin; mean peak serum concentration 5.3 mg/L after 0.8 mole oral dose; 75% urinary recovery; intraperitoneal penetration 48%; protein binding 85%

**TEMOCILLIN:** moderate spectrum penicillin; spectrum includes *Haemophilus influenzae* (MIC 0.25-0.5 mg/L), *Neisseria gonorrhoeae* (0.5-1 mg/L), *Neisseria meningitidis* (0.12 mg/L)

**CARBENICILLIN:** extended spectrum (broad spectrum and *Pseudomonas aeruginosa*), very acid stable penicillin; orally ineffective; implicated in emergence of multiple drug resistance during therapy; less active than ampicillin against *Neisseria meningitidis*, non-?-lactamase-producing *Staphylococcus aureus* and streptococci; more active than ampicillin against *Proteus*; spectrum includes *Actinomyces* (100% susceptible), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), *Erysipelothrix* (100% susceptible), Group IIf (MIC 0.13-0.25 mg/L), ?-lactamase negative *Haemophilus influenzae* (0.5 mg/L), *Hafnia alvei* (100% susceptible), *Moraxella* (? 0.06-0.25 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Proteus mirabilis* (1 mg/L), *Streptococcus pneumoniae* (0.25 mg/L), *Streptococcus pyogenes* (0.25-1 mg/L); no inoculum effect with aerobes, shows inoculum effect with anaerobes; incompatible with chloramphenicol, erythromycin, gentamicin, lincomycin, streptomycin, tetracycline

**Indications:** anaerobic cellulitis, endocarditis, meningitis, otitis externa, pneumonia, septicemia, urinary tract infection; replaced by ticarcillin

**Side Effects:** pain at injection site, platelet dysfunction, sodium overload; leucopenia, eosinophilia, drug fever and rash with total dose > 750 g; safety not established during pregnancy; modify dosage in renal dysfunction (platelet inhibition); further dose required after haemodialysis

**TICARCILLIN:** broad spectrum and antipseudomonal (high doses required); serum protein binding 40%; no postantibiotic effect; implicated in emergence of multiple drug resistance during therapy; no inoculum effect; mode of elimination renal; more expensive than most other penicillins; spectrum includes *Actinomyces* (100% susceptible), *Alcaligenes denitificans* (MIC 0.5-1 mg/L), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), Group IIf

(? 0.06-0.13 mg/L), ?-lactamase negative *Haemophilus influenzae* (0.5 mg/L), ?-lactamase negative *Neisseria gonorrhoeae* (0.5-1 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Peptostreptococcus asaccharolyticus* (? 1 mg/L), *Peptostreptococcus prevoti* (? 1 mg/L), *Propionibacterium acnes* (? 1mg/L), *Streptococcus pneumoniae* (0.25-1 mg/L), *Streptococcus pyogenes* (0.25-1 mg/L); *Staphylococcus aureus* 85% acquired resistance due to ?-lactamase, *Klebsiella* 98% intrinsic resistance due to ?-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 48% resistant due to ?-lactamase, *Proteus mirabilis* 18% resistant due to ?-lactamase, *Pseudomonas aeruginosa* 13% resistant

**Indications:** septic arthritis due to *Pseudomonas aeruginosa* in immunocompromised; cellulitis due to aerobic Gram negatives; purulent conjunctivitis due to *Pseudomonas aeruginosa*; endocarditis due to Gram negative bacilli; otitis externa; nosocomial otitis media; *Pseudomonas aeruginosa* infections; rhabdomyolysis

**Side Effects:** modify dose in renal dysfunction (platelet inhibition; rarely, seizures, interstitial nephritis, sodium overload, hypokalemia); further dose required after haemodialysis; probably safe in pregnancy

**PIPERACILLIN:** broad spectrum and antipseudomonal (high doses required) ureidopenicillin; binds chiefly to PBP3; kills only growing organisms; more active against enterococci than ticarcillin; spectrum includes *Actinomyces* (100% susceptible), *Aeromonas hydrophila* (100% susceptible), *Alcaligenes denitrificans* (MIC 0.25-1 mg/L), anaerobic cocci (100% susceptible at < 1 mg/L), *Arachnia* (100% susceptible), *Bordetella bronchiseptica* (0.5-1 mg/L), *Clostridium* (100% susceptible), Group IIf

(? 0.06 mg/L), *Hafnia alvei* (100% susceptible), *Moraxella catarrhalis* (< 0.015-1 mg/L), penicillinase negative *Neisseria gonorrhoeae* (0.06 mg/L), *Neisseria meningitidis* (? 0.5 mg/L), *Streptococcus agalactiae* (? 0.5 mg/L), *Streptococcus pneumoniae* (1 mg/L), *Streptococcus pyogenes* (? 0.02-0.15 mg/L), *Streptococcus viridans* (0.5 mg/L); *Staphylococcus aureus* 85% acquired resistance due to ?-lactamase, *Klebsiella* 98% intrinsic resistance due to ?-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 48% resistance due to ?-lactamase, *Proteus mirabilis* 18% resistance due to ?-lactamase, *Pseudomonas aeruginosa* 9% resistance; implicated in emergence of multiple drug resistance during therapy; may show inoculum effect; in WHO Model List of Essential Drugs; more expensive than most other penicillins

**Indications:** bacteraemia and septicemia (due to *Pseudomonas pseudomallei*, *Pseudomonas aeruginosa*, *Yersinia enterocolitica*, *Campylobacter fetus subsp fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*); cervical fascial space infections in immunocompromised; purulent conjunctivitis due to *Pseudomonas aeruginosa*; malignant otitis externa due to *Pseudomonas aeruginosa*; perianal and perirectal abscess in patients with malignant disease; peritonsillar abscess in immunocompromised; endomyometritis and endometritis; febrile neutropenic patients

**Side Effects:** leucopenia, drug fever, thrombocytopenia, eosinophilia, urticarial rash, pruritis, hepatic damage; rare reports of haemolytic anaemia in patients with CSF; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; dose interval adjustment required in renal failure and in dialysis; increased duration of neuromuscular blockade with vecuronium; reduces methotrexate clearance with possible increase in toxicity

**AZLOCILLIN:** broad spectrum and antipseudomonal ureidopenicillin; more active than ticarcillin against *Pseudomonas* in vitro; spectrum includes *Alcaligenes denitrificans* (MIC 0.13-0.25 mg/L), *Bordetella bronchiseptica* (0.5-1 mg/L), Group IIf

(? 0.06 mg/L), *Moraxella* (? 0.06-0.5 mg/L), *Neisseria meningitidis* (? 0.5 mg/L), *Proteus mirabilis* (< 1 mg/L), *Streptococcus agalactiae* (? 0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.125 mg/L), *Streptococcus pneumoniae*

(? 0.02-1 mg/L), *Streptococcus pyogenes* (? 0.02-0.5 mg/L); *Staphylococcus aureus* 90% acquired resistance due to ?-lactamase, *Klebsiella* 98% intrinsic resistance due to ?-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 45% resistant due to ?-lactamase, 14% *Proteus mirabilis* resistant due to ?-lactamase; reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

**Indications:** bacteraemia and septicemia due to *Pseudomonas aeruginosa*; endocarditis due to *Pseudomonas aeruginosa*; neonatal and postneonatal pyogenic meningitis due to *Pseudomonas aeruginosa*; myocarditis and pericarditis due to *Pseudomonas aeruginosa*

**Side Effects:** leucopenia, drug fever, thrombocytopenia, eosinophilia, rash, hepatic damage; dose adjustment needed in renal failure and dialysis

**MEZLOCILLIN:** broad spectrum and antipseudomonal ureidopenicillin; binds chiefly to PBP3; roughly equivalent to ticarcillin in vitro; spectrum includes *Actinomyces* (100% susceptible), *Aeromonas hydrophila* (100% susceptible), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), ?-lactamase negative *Haemophilus influenzae*

(? 0.5 mg/L), *Hafnia alvei* (100% susceptible), ?-lactamase negative *Neisseria gonorrhoeae* (0.08 mg/L), *Neisseria meningitidis* (? 0.5 mg/L), *Proteus mirabilis* (? 1 mg/L), *Streptococcus agalactiae* (? 0.5 mg/L), *Streptococcus canis*

(100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (< 0.02 mg/L), *Streptococcus pyogenes* (? 0.02-0.5 mg/L); implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

**Indications:** large bowel surgical prophylaxis

**Side Effects:** leucopenia, drug fever, thrombocytopenia, eosinophilia, rash, hepatic damage

**CLAVULANIC ACID:** Class 2  $\beta$ -lactamase inhibitor; used in combination with amoxicillin to treat  $\beta$ -lactamase-producing *Neisseria gonorrhoeae* and *Haemophilus influenzae*; also inhibits  $\beta$ -lactamases produced by *Escherichia coli*, *Klebsiella*, *Proteus mirabilis*, *Proteus vulgaris*, *Moraxella catarrhalis*, *Bacteroides*, *Staphylococcus aureus*; combination with ticarcillin also available; binds chiefly to PBP2; serum protein binding 20%

**AMOXICILLIN-CLAVULANATE (AUGMENTIN):** broad spectrum; expensive; oral dose schedule 3 times daily; take immediately before or with first mouthful of food; spectrum includes anaerobes (100% susceptible), *Campylobacter fetus* (0.25-1 mg/L), *Capnocytophaga canimorsus* (95% susceptible), *Eikenella corrodens* (100% susceptible), *Enterococcus* (100% susceptible), *Haemophilus influenzae* (< 5% resistance in Australia), *Listeria monocytogenes* (100% susceptible at 0.25 mg/L), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria meningitidis* (100% susceptible at 0.12 mg/L), *Pasteurella multocida* (100% susceptible), *Pseudomonas stutzeri* (100% susceptible), *Shigella* (100% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible at 1 mg/L), *Staphylococcus intermedius* (100% susceptible), *Streptococcus agalactiae* (100% susceptible at 0.12 mg/L), *Streptococcus bovis* (100% susceptible at 0.12 mg/L), *Streptococcus pneumoniae* (100% susceptible at 1 mg/L), *Streptococcus pyogenes* (100% susceptible at ? 0.06 mg/L); *Enterobacter*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia*, *Serratia* 92% intrinsic resistance due to  $\beta$ -lactamase (possibly all resistant in clinical practice); *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* 100% intrinsic resistance; in Australia, *Escherichia coli* 27% resistance due to  $\beta$ -lactamase, *Klebsiella pneumoniae* 11% resistant, *Proteus mirabilis* 9% resistant due to  $\beta$ -lactamase; in WHO Model List of Essential Drugs; more expensive than amoxicillin

**Indications:** should be reserved for treatment of organisms in which resistance to amoxicillin is due to enzyme which clavulanic acid can inhibit; abortifacient and puerperal infections; septic arthritis (unknown organism in < 5 years old) *Haemophilus influenzae*, *Eikenella corrodens*; bacteraemia and septicemia due to *Burkholderia pseudomallei*, *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*; bronchitis; cat, dog and human bite and clenched fist injury infections; less severe cellulitis due to *Haemophilus influenzae*; chancroid; cholecystitis; chorioamnionitis; acute cystitis in adults; diverticulitis; acute epididymitis and epididymoorchitis; epiglottitis in normal host; chronic mastitis and breast abscess; postneonatal pyogenic meningitis due to *Moraxella catarrhalis*; osteomyelitis and osteochondritis due to *Staphylococcus aureus*; otitis media; parotitis and submandibular sialadenitis due to *Burkholderia pseudomallei*; pneumonia (resistant organism or slow response in mild to moderate community acquired in adult > 60 y or with coexisting illness or in child 3 mo -10 y, mild *Haemophilus influenzae*, *Moraxella catarrhalis*, mild anaerobic, mild nosocomial with no specific risk factors); *Haemophilus influenzae* pneumonitis; postpartum fever and endometritis; preseptal cellulitis in < 4 y old; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; mild acute pyelonephritis; acute maxillary sinusitis; tooth abscess unresponsive to treatment; acute tracheitis; less severe ulcers in diabetics; *Haemophilus* and other non-gonococcal urethritis; suppurative wound infections

**Side Effects:** low risk of serious adverse reactions and skin rash; very high risk of gastrointestinal adverse effects (diarrhoea more frequent than with amoxicillin); hepatotoxicity more frequent than with amoxicillin; can cause cholestasis; probably safe in pregnancy; dose adjustment required in renal failure and in dialysis; unpredictable enhanced warfarin effect

**Contraindications:** avoid in breastfeeding (insufficient data; monitor infant for diarrhoea)

**TICARCILLIN-CLAVULANATE (TIMENTIN):** broad spectrum and antipseudomonal; parenteral; spectrum includes *Actinomyces* (100% susceptible), *Bacteroides* (99-100% susceptible at 128 mg/L), *Clostridium* (100% susceptible), *Fusobacterium* (97% susceptible), *Peptostreptococcus* (100% susceptible), *Propionibacterium acnes* (MIC ? 1 mg/L), *Proteus mirabilis* (100%), *Stenotrophomonas maltophilia* (98% of hospital isolates); more expensive than most other penicillins

**Indications:** should be reserved for treatment of organisms in which resistance to ticarcillin is due to enzyme which clavulanic acid can inhibit; bacteraemia and septicemia (focus probably decubitus or ischaemic ulcer or diabetic

foot ulcer, febrile neutropenic patients without renal impairment/not on nephrotoxic drugs, *Pseudomonas aeruginosa* suspected); severe bite and clenched fist injuries; hepatic abscess; treatment and prophylaxis of mixed aerobic and anaerobic infections; pancreatic abscess; parametritis and pelvic inflammatory disease due to coliforms; peritonitis of suspected bowel origin; pneumonia (mild to moderate community acquired with risk factors, severe nosocomial); surgical prophylaxis (total hip replacement); severe ulcers in diabetics

**Side Effects:** dose adjustment required in renal failure and dialysis; safety in pregnancy and breastfeeding not established (monitor infant for diarrhoea if breastfeeding)

**SULBACTAM:**  $\beta$ -lactamase inhibitor (same range of organisms as clavulanic acid); intraperitoneal penetration 92%; protein binding  $\approx$  20%; low inducer of type I  $\beta$ -lactamase

**Indications:** multiresistant *Acinetobacter baumannii* infections

**AMPICILLIN-SULBACTAM:** i.v.

**Indications:** chronic mastitis and breast abscess (organisms in which resistance to ampicillin is due to enzyme which sulbactam can inhibit); mixed Gram positive and anaerobic infections such as community acquired aspiration pneumonia, diabetic foot infections, decubitus infections, mild to moderate intraabdominal infections; i.v. drug of choice for empiric treatment of animal bites; prophylaxis for colorectal surgery; *Acinetobacter baumannii* bacteraemia

**TAZOBACTAM:**  $\beta$ -lactamase inhibitor (same range of organisms as clavulanic acid); apparently less likely than clavulanic acid or sulbactam to induce production of  $\beta$ -lactamases leading to failure of therapy of *Citrobacter*, *Enterobacter*, *Pseudomonas*, *Serratia*

**PIPERACILLIN-TAZOBACTAM:** broad spectrum and antipseudomonal; spectrum includes *Escherichia coli* (97% of hospital isolates), *Klebsiella oxytoca* (93% of hospital isolates), *Klebsiella pneumoniae* (96% of hospital isolates), *Proteus mirabilis* (100%), *Pseudomonas aeruginosa* (91% of hospital isolates); greater in vitro activity against enterococci and *Klebsiella* than ticarcillin-clavulanate but more expensive

**Indications:** similar to ticarcillin; bacteraemia, septicemia and septic shock (unidentified source in febrile neutropenic patients with no renal impairment and not on nephrotoxic drugs and with *Pseudomonas aeruginosa* suspected); nosocomial mixed aerobic/anaerobic infections, including pelvic and abdominal infections and pneumonia; empirical therapy in febrile neutropenic patient; treatment of ischaemic/diabetic foot

**Side Effects:** those of piperacillin; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; requires dosage interval adjustment in renal failure and in dialysis

**Contraindications:** avoid if breastfeeding (insufficient data)

**CARBAPENEMS:** very broad spectrum of potent antibacterial activity; postantibiotic effect; inactivated by metallo- $\beta$ -lactamases; produce relatively low amounts of endotoxins; used in mixed infections and neutropenic patients; widespread use has been linked with increasing prevalence of infections due to methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, multi-resistant Gram-negative organisms and *Clostridium difficile*; expensive and regarded as reserve agents

**Side Effects:** thrombophlebitis at injection site, nausea, diarrhoea, vomiting common; fever, rash, itch, paraesthesia, headache, dizziness, somnolence, confusion, tremor, encephalopathy, psychiatric disturbances, seizures, blood dyscrasias uncommon; pseudomembranous colitis, hepatitis, anaphylaxis, erythema multiforme, angioedema, Stevens-Johnson syndrome, tachycardia, renal toxicity rare; dose adjustment required in renal impairment

**THIENAMYCIN:** structure similar to clavulanic acid but has broad antibacterial activity (Enterobacteriaceae and *Pseudomonas* comparable to aminoglycosides, excellent activity against anaerobes including *Bacteroides fragilis* and most Gram positive cocci) as well as possessing potent  $\beta$ -lactamase inhibition; spectrum includes *Bacteroides fragilis* (100% susceptible), *Enterococcus faecalis* (MIC 1 mg/L), *Escherichia coli* (0.25 mg/L), *Staphylococcus aureus* ( $\approx$  0.06 mg/L)

**IMPENEM:** N-formimidoyl thienamycin; greater stability than thienamycin; kills non-growing organisms; inactivated by renal dipeptidase and therefore combined with dipeptidase inhibitor cilastatin; may show inoculum effect; activity against Gram negative bacilli and *Pseudomonas aeruginosa* equivalent to that of aminoglycosides, excellent activity against anaerobes and many Gram positive organisms; not active against methicillin resistant *Staphylococcus aureus*, *Enterococcus faecium*, *Stenotrophomonas*, *Mycoplasma*, *Chlamydia* and some species of *Pseudomonas*; relatively expensive; broadest spectrum of any  $\beta$ -lactam available; spectrum includes *Achromobacter* (100% susceptible),

*Acinetobacter* (98% of hospital isolates), *Actinomyces* (100% susceptible), *Aeromonas*, *Alcaligenes* (100% susceptible), *Bacteroides distasonis* (99% susceptible), *Bacteroides fragilis* (100% susceptible at 8 mg/L), *Bacteroides gracilis* (100% susceptible at 8 mg/L), *Bacteroides thetaiotaomicron* (99% susceptible), *Bordetella bronchiseptica* (100% susceptible), *Campylobacter* (100% susceptible), *Citrobacter* (100%), *Clostridium* (99-100% susceptible at < 1 mg/L), *Enterobacter aerogenes* (94% of hospital isolates), *Enterobacter cloacae* (100%), Enterobacteriaceae (< 5% resistance in Australia), *Escherichia coli* (0.1% resistant in Australia), *Eubacterium* (100% susceptible), *Fusobacterium* (90-95% susceptible at < 1 mg/L), *Gardnerella vaginalis* (100% susceptible), *Haemophilus influenzae* (0.5 mg/L), *Klebsiella oxytoca* (100% susceptible at < 1 mg/L), *Klebsiella pneumoniae* (0.4% resistant in Australia), *Legionella* (? 0.004-1 mg/L), *Listeria monocytogenes* (100% susceptible at < 1 mg/L), *Moraxella* (96% susceptible), *Morganella morganii* (100% susceptible), *Neisseria* (100% susceptible at < 1 mg/L), *Nocardia* (98% susceptible at < 1 mg/L), *Peptococcus* (100% susceptible at < 1 mg/L), *Peptostreptococcus* (100% susceptible at < 1 mg/L), *Prevotella melaninogenica* (99% susceptible), *Propionibacterium* (100% susceptible), *Proteus mirabilis* (18% resistant in Australia), *Proteus vulgaris* (100%), *Providencia stuartii* (100% susceptible), *Salmonella* (100% susceptible at < 1 mg/L), *Serratia liquefaciens* (100% susceptible), *Serratia marcescens* (100%), *Shigella* (100% susceptible at < 1 mg/L), methicillin susceptible *Staphylococcus aureus* (100% susceptible at < 1 mg/L), *Streptococcus agalactiae* (100% susceptible), *Streptococcus canis* (100% susceptible), *Streptococcus* group C (100% susceptible), *Streptococcus pneumoniae* (100% susceptible at < 1 mg/L), *Streptococcus pyogenes* (100% susceptible at < 1 mg/L), *Streptococcus viridans* (100% susceptible), *Veillonella* (100% susceptible), *Wolinella* (? 1 mg/L), *Yersinia* (100% susceptible); *Stenotrophomonas maltophilia* 100% intrinsic resistance due to ?-lactamase; methicillin resistant *Staphylococcus aureus*, *Enterococcus faecium*, some strains of *Burkholderia cepacia* and *Pseudomonas* (in Australia, 17% of *Pseudomonas aeruginosa*) resistant; expensive; in WHO Model List of Essential Drugs

**Indications:** restricted at present to complicated nosocomial infections and infections due to multiply resistant Gram negative bacilli; bacteraemia and septicemia (febrile neutropenic patients with renal impairment/on nephrotoxic drugs, neutrophil count 500-1000/? L, due to *Acinetobacter*, *Burkholderia pseudomallei*); bone and joint infections; cervical fascial space infection in immunocompromised; cervical parameningeal deep fascial space infections in immunocompromised; emphysematous gastritis; endocarditis due to *Acinetobacter*, *Alcaligenes*; gynaecological infections; intraabdominal infections; severe nosocomial pneumonia; postneonatal meningitis due to *Nocardia asteroides*, *Acinetobacter*; polymicrobial infections; skin and soft structure infections

**Side Effects:** CNS toxicity (seizures in 1%; increased risk with ganciclovir) in renal insufficiency (adjust dose appropriately and avoid daily dose of > 2 g), nausea and vomiting in 2%; dose adjustment required in dialysis; avoid cilastatin if glomerular filtration rate < 10 mL/min and in dialysis; safety in pregnancy not established; safe in breastfeeding

**MEROPENEM:** carbapenem resistant to renal dipeptidase; attains better levels in CSF than imipenem; spectrum includes *Aeromonas* (MIC ? 0.06-1 mg/L), *Bacteroides* (0.13-0.5 mg/L), *Bifidobacterium* (1 mg/L), *Burkholderia cepacia* (best MIC<sub>90</sub>), *Citrobacter* (? 0.06-0.13 mg/L), *Clostridium* (? 0.06-4 mg/L), *Enterobacter* (0.13-0.25 mg/L), *Escherichia coli* (? 0.06 mg/L), *Eubacterium* (0.03-0.13 mg/L), *Hafnia alvei* (0.06 mg/L), *Klebsiella* (0.03-0.25 mg/L), *Morganella morganii* (0.25 mg/L), *Pasteurella multocida* (0.13 mg/L), *Peptococcus* (0.03-0.25 mg/L), *Peptostreptococcus* (0.13-2 mg/L), *Plesiomonas shigelloides* (? 0.06 mg/L), *Propionibacterium* (0.25 mg/L), *Proteus* (0.13-0.5 mg/L), *Providencia* (0.13-0.5 mg/L), *Pseudomonas* (0.25-8 mg/L), *Salmonella* (? 0.06 mg/L), *Serratia* (0.13- 0.25 mg/L), *Shigella* (0.03-0.06 mg/L), methicillin susceptible *Staphylococcus* (0.25-4 mg/L), *Streptococcus* (? 0.01-8 mg/L), *Yersinia enterocolitica* (0.06 mg/L); *Stenotrophomonas maltophilia* 100% intrinsic resistance; expensive

**Indications:** could find place in therapy of seriously ill hospital patients, especially those with intra-abdominal infections, neutropenic cancer patients and intensive care unit patients with lower respiratory tract infections and hospital acquired meningitis

**Side Effects:** rare seizures (lower incidence than imipenem), nausea and vomiting in 1%; safety in pregnancy not established; caution in breastfeeding (monitor infant for diarrhoea)

**ERTAPENEM:** once a day injectable carbapenem; active against anaerobes, Gram positive and Gram negative aerobic bacteria and is resistant to some  $\beta$ -lactamases but does not cover *Acinetobacter*, *Pseudomonas*, penicillin resistant *Streptococcus pneumoniae*,  $\beta$ -lactamase positive *Haemophilus influenzae*

**Indications:** moderate to severe adult bacterial infections caused by gram positive and gram negative aerobic and anaerobic bacteria suspected or proven resistant to all other antibiotics or in patients unable to tolerate other antibiotics; initial empiric therapy of complicated intra-abdominal infections and acute pelvic infections including post-partum endomyometritis, septic abortion and post-surgical gynaecological infections

**Side Effects:** diarrhoea, infused vein complications, nausea, headache, vaginitis, vein inflammation, vomiting

**CEPHALOSPORINS:** inhibit transpeptidase thus preventing cross-linking of cell wall peptidoglycan; bactericidal; act only on proliferating bacteria; in high concentrations, penetrate into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces*, *Cardiobacterium hominis*, *Corynebacterium diphtheriae*; *Enterococcus* 100% intrinsic resistance, *Pseudomonas aeruginosa* 100% intrinsic resistance (except ceftazidime, cefepime, cefpirome), *Stenotrophomonas maltophilia* 100% intrinsic resistance (except ceftazidime), *Bacteroides fragilis* 100% intrinsic resistance (except cefoxitin and cefotetan); widespread use linked to increased prevalence of methicillin resistant staphylococci, vancomycin resistant enterococci, drug-resistant *Streptococcus pneumoniae*, multiresistant Gram negative organisms, and *Clostridium difficile*; no effect on opsonisation, decrease neutrophil chemotaxis, no effect on phagocytosis, no effect on bacterial adherence, increase capsule enzyme/toxin, decrease intracellular killing

**Indications:** intraabdominal infections; ischioanal abscess; otitis externa due to *Corynebacterium diphtheriae*, *Actinomyces israelii*; post-surgery peritonitis; localised staphylococcal skin lesions; surgical prophylaxis (total hip replacement); systemic infection in agammaglobulinemia, C1, 2, 3, 4, factor B deficiency, hyposplenism/splenectomy; tetanus

**Side Effects:** diarrhoea, nausea, rash, eosinophilia, drug fever, electrolyte disturbances, pain and inflammation at injection site, pseudomembranous colitis common; vomiting, headache, dizziness, oral and vaginal candidiasis uncommon; hypersensitivity reactions including anaphylactic shock (cross-hypersensitivity can occur in 3-6% of penicillin allergic subjects), interstitial nephritis, neurotoxicity, blood dyscrasias, bleeding, renal impairment, bone marrow suppression, haemolysis, megaloblastic marrow, superinfection, aseptic meningitis rare; probably all safe in therapeutic amounts during pregnancy; modify dose in renal failure (CNS toxicity); require further dose after haemodialysis; maximum permissible blood level 32 mg/L; probenecid increases plasma levels

**CEPHALOTHIN:** moderate spectrum parenteral first generation cephalosporin active against  $\beta$ -lactamase-producing staphylococci (highly susceptible) and some Enterobacteriaceae; streptococci highly susceptible but not active against *Enterococcus faecalis*, poor activity against *Haemophilus influenzae*, *Bacteroides fragilis*, *Serratia*, *Enterobacter*, *Pseudomonas*; not active against *Listeria monocytogenes*; spectrum includes *Erysipelothrix* (100% susceptible at  $\geq 1$  mg/L), *Helicobacter pylori*, *Neisseria meningitidis* (< 5% resistance in Australia), methicillin susceptible *Staphylococcus aureus* (MIC 0.06-0.5 mg/L), *Streptococcus pneumoniae* (0.25 mg/L), *Streptococcus pyogenes* (0.12 mg/L); *Enterobacter*, *Serratia*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia* 92% intrinsic resistance due to  $\beta$ -lactamase (probably all resistant in clinical practice); in Australia, *Escherichia coli* 32% resistant due to  $\beta$ -lactamase, *Klebsiella pneumoniae* 21% resistant due to  $\beta$ -lactamase, *Proteus mirabilis* 10% resistant due to  $\beta$ -lactamase; poorly absorbed; strongly hydrolysed by type I  $\beta$ -lactamase; moderate inducer of type I  $\beta$ -lactamase; serum levels increased and prolonged by probenecid; increased  $V_d$ , reduced clearance in elderly; minimal inoculum effect; CSF penetration 0 - > 50%; mode of elimination renal; incompatible with colistimethate, erythromycin, gentamicin, kanamycin, lincomycin, tetracycline

**Indications:** one of most important agents for prophylaxis in orthopaedic and vascular surgery where prostheses are being inserted; staphylococcal septic arthritis in penicillin hypersensitive patients; bacteraemia and septicemia (infection from female genital tract in penicillin hypersensitive, focus probably biliary or gastrointestinal in penicillin hypersensitive, focus probably open skin infection/cellulitis, focus decubitus or ischaemia or diabetic foot ulcer in penicillin hypersensitive, due to *Staphylococcus aureus*, due to *Streptococcus pyogenes* in penicillin hypersensitive, unidentified source); severe streptococcal and staphylococcal cellulitis in penicillin hypersensitive; compound fractures; severe erysipelas in penicillin hypersensitive; local and generalised sepsis (organism not known); osteomyelitis and osteochondritis due to *Staphylococcus aureus* in penicillin hypersensitive; pneumonia (Gram negative, staphylococcal, mild to moderate community acquired in adult); severe acute pyelonephritis; septicemia; surgical prophylaxis

(cardiovascular; vascular graft; breast; dialysis access; orthopaedic; head, neck and thoracic; gastrointestinal; colorectal; appendectomy; hysterectomy; termination of pregnancy; renal transplantation; liver transplantation; muscular, skeletal and soft tissue trauma; endoscopic procedures; caesarean section); staphylococcal toxic shock syndrome; severe ulcers in diabetics

**Side Effects:** positive direct Coomb's test (uncommonly, associated haemolytic anaemia with very large doses), pain and local reaction at injection site; hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; dose adjustment required in renal failure and in dialysis; avoid use in severe renal dysfunction (nephrotoxicity (interstitial nephritis), enhanced by aminoglycosides and large doses of ethacrynic acid or frusemide, particularly in elderly; may falsely elevate serum creatinine measurement by certain assays; rarely, seizures); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

**CEPHAPIRIN:** parenteral first generation cephalosporin; minimal to significant inoculum effect

**Side Effects:** hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

**CEPHRADINE:** first generation cephalosporin; can be given parenterally or orally; 15% bronchial penetration after 1 g oral dose; serum levels increased and prolonged by probenecid; reduced clearance in elderly; withdrawn from market in mid 1980s

**Side Effects:** gastrointestinal disturbances, hypersensitivity syndrome, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome

**CEPHALORIDINE:** moderate spectrum parenteral first generation cephalosporin; poorly absorbed; less serum bound; binds chiefly to PBP1a; kills only growing organisms; serum levels not increased or prolonged by probenecid; activity equal to cephalothin; significant inoculum effect; no longer used because of nephrotoxicity

**CEPHALEXIN:** moderate spectrum first generation cephalosporin; well absorbed; can be given orally; not affected by food; similar activity to cephalothin; spectrum includes *Moraxella catarrhalis* (100% susceptible),  $\beta$ -lactamase negative *Neisseria gonorrhoeae* (100% susceptible), *Neisseria meningitidis* (100% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible), *Staphylococcus intermedius* (95% susceptible); *Enterobacter*, *Serratia*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia*, 92% intrinsic resistance due to  $\beta$ -lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 7% resistant due to  $\beta$ -lactamase, *Klebsiella pneumoniae* 21% resistant due to  $\beta$ -lactamase, *Proteus mirabilis* 10% resistant due to  $\beta$ -lactamase; kills only growing organisms; serum levels increased and prolonged by probenecid; no significant change in absorption in elderly; mode of elimination renal (> 80%); half life 0.9 h;  $C_{max}$  18 mg/L; bioavailability > 90%; inexpensive

**Indications:** has found important role in urinary and skin/soft tissue infections; excellent substitute for penicillin in some infections in hypersensitive patients; biliary infections; bullous impetigo; less severe streptococcal cellulitis in penicillin hypersensitive; diverticulitis; prophylaxis of recurrent nonvenereal dysuria-frequency syndrome; mild acute epididymitis and epididymo-orchitis associated with urinary tract infection; less severe erysipelas in penicillin hypersensitive; severe impetigo; acute mastitis and breast abscess; aphthous mouth ulcers (compresses); nasal septal abscess; osteomyelitis and osteochondritis due to *Staphylococcus aureus*; pharyngitis; pneumonia; staphylococcal pyoderma treatment and prophylaxis; respiratory tract infections; staphylococcal local and generalised sepsis; acute sinusitis; less severe ulcers in diabetics; urinary tract infections (acute cystitis in adults, mild acute pyelonephritis); water-related infections in remote areas

**Side Effects:** hypersensitivity syndrome, fixed drug reaction, lupus erythematosus, pemphigus, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; vestibular ototoxicity and nephrotoxicity (interstitial nephritis) and, rarely, seizures in renal insufficiency (adjust dose appropriately); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; dose interval adjustment required in dialysis; very weak association with oral contraceptive failure

**CEFADROXIL:** oral first generation cephalosporin

**Side Effects:** hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome

**CEFPROZIL:** oral first generation cephalosporin; *Staphylococcus aureus* and *Streptococcus pyogenes* highly susceptible, *Escherichia coli* and *Proteus mirabilis* susceptible, *Klebsiella* moderately susceptible, *Pseudomonas aeruginosa* resistant; half life 1.3 h;  $C_{max}$  10.5 mg/L; bioavailability > 90%; renal excretion 61%

**Indications:** empirical use after amoxicillin/ampicillin failure in otitis media, sinusitis; completion of therapy with second generation cephalosporin

**Side Effects:** hypersensitivity syndrome, serum-sickness like illness, Stevens-Johnson syndrome

**CEPHALOGLYCIN:** moderate spectrum oral first generation cephalosporin; well absorbed; activity equal to cephalothin; no longer recommended

**CEPHAZOLIN:** parenteral first generation moderate spectrum cephalosporin; similar to cephalothin but more suitable for intramuscular use and longer half-life; spectrum includes Group IIf (MIC 0.13-0.25 mg/L), *Streptococcus canis* (100% susceptible at 1 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L); *Enterobacter*, *Serratia*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia*, 92% intrinsic resistance due to  $\beta$ -lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 13% resistant due to  $\beta$ -lactamase, *Klebsiella pneumoniae* 21% resistant due to  $\beta$ -lactamase, *Proteus mirabilis* 10% resistant due to  $\beta$ -lactamase; reduced clearance in elderly; no to moderate postantibiotic effect; significant inoculum effect

**Indications:** septic arthritis due to *Staphylococcus aureus* in penicillin hypersensitive patient; bacteraemia and septicemia (focus probably from skin/cellulitis, from female genital tract in penicillin hypersensitive, from decubitus or ischaemic ulcer or diabetic foot ulcer in penicillin hypersensitive, unidentified source, methicillin sensitive *Staphylococcus aureus* in penicillin hypersensitive, *Streptococcus pyogenes* in penicillin hypersensitive); cellulitis due to *Streptococcus pyogenes* or *Staphylococcus aureus* in penicillin hypersensitive; cholangitis and cholecystitis; compound fractures; endocarditis; severe erysipelas in penicillin hypersensitive; local and generalised sepsis (organism not known); osteomyelitis; pneumonia (mild to moderate community acquired); surgical prophylaxis (cardiovascular; vascular graft; breast; dialysis access; orthopaedic; head, neck and thoracic; gastrointestinal; colorectal; appendectomy; hysterectomy; termination of pregnancy; renal transplantation; liver transplantation; muscular, skeletal and soft tissue trauma; endoscopic procedures; caesarean section); severe ulcers in diabetics; suppurative wound infections (surgical or traumatic, Gram negative bacilli suspected or proven)

**Side Effects:** pain and local reaction at injection site, hypersensitivity syndrome, fixed drug reaction, lupus erythematosus, photosensitivity, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; modify dosage in renal dysfunction (coagulopathy) and in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

**LORACARBEF:** first generation oral cephalosporin; *Streptococcus pyogenes* highly susceptible, *Escherichia coli*, *Proteus mirabilis* and *Staphylococcus aureus* susceptible, *Klebsiella* moderately susceptible, *Pseudomonas aeruginosa* resistant

**Side Effects:** serum sickness-like illness

**CEFACLOR:** first generation moderate spectrum and *Haemophilus* active oral cephalosporin; not affected by food; similar activity to cephalothin and cephalexin but active against *Haemophilus influenzae* (< 5% resistance in Australia); spectrum also includes  $\beta$ -lactamase negative *Neisseria gonorrhoeae* (100% susceptible), *Neisseria meningitidis* (100% susceptible at 0.12 mg/L), *Shigella* (100% susceptible), *Staphylococcus aureus*, *Streptococcus agalactiae* (0.5 mg/L), *Streptococcus bovis* (100% susceptible at 0.25 mg/L), *Streptococcus pneumoniae*, *Streptococcus pyogenes* (100% susceptible at 0.5 mg/L); significant inoculum effect; half life 0.6 h;  $C_{max}$  16.5 mg/L; bioavailability > 90%; renal excretion 75%; very expensive

**Indications:** has found role in treatment of acute cystitis in children, respiratory tract infection (bronchitis, acute bacterial otitis media, mild to moderate community acquired pneumonia due to resistant organism or slow response in adult > 60 y or with coexisting illness or in child 3 mo - 10 y with penicillin hypersensitivity, acute sinusitis), water-related infections in children and remote areas

**Side Effects:** hypersensitivity syndrome, serum sickness-like reaction; moderate risk of serious adverse reactions and gastrointestinal adverse effects, low risk of skin rash (pustulosis, Stevens-Johnson syndrome); requires dose adjustment in renal failure and dialysis; probably safe in pregnancy

**CEPHAMANDOLE:** parenteral second generation moderate spectrum and *Haemophilus* active cephalosporin; more stable to some Gram negative  $\beta$ -lactamases and more active against *Haemophilus influenzae* than first generation; similar activity against Gram positives to first generation; spectrum includes *Aeromonas hydrophila*, Group IIf (MIC 0.25-0.5 mg/L), *Moraxella* (? 0.06-1 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L),

*Yersinia enterocolitica* (100% susceptible); resistance (and cross-resistance to other  $\beta$ -lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; no to moderate postantibiotic effect; may show inoculum effect; CSF penetration 2-9%; mode of elimination renal; more expensive than first generation

**Indications:** limited role in therapy; bacteraemia and septicemia due to *Anaerobiospirillum succiniciproducens*; severe *Haemophilus influenzae* pneumonia

**Side Effects:** hypoprothrombinemia, haemorrhage, hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy in renal insufficiency (administer vitamin K supplement), rarely seizures and interstitial nephritis (modify dose interval); requires dose adjustment in dialysis; cephamandole-induced hypoprothrombinemia may enhance anticoagulant effect of warfarin and other oral anticoagulants; probably safe in pregnancy

**CEFOXITIN:** cephamycin but usually included in second generation cephalosporins; moderate spectrum and anaerobes; parenteral; less active than first generation against Gram positives, particularly *Staphylococcus aureus*; greater activity than cephamandole against *Bacteroides fragilis* (60-70% susceptible; cefoxitin and cefotetan only cephalosporins active against this species); spectrum includes *Actinomyces* (95-100% susceptible), *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Arachnia* (95-100% susceptible), *Bacteroides gracilis* (100% susceptible), *Bacteroides uniformis* (100% susceptible), *Capnocytophaga canimorsus* (95% susceptible), *Eikenella corrodens* (95% susceptible), *Fusobacterium* (99% susceptible), Group IVe (MIC 0.13 mg/L), *Moraxella catarrhalis* (< 0.06-0.25 mg/L), *Neisseria meningitidis* (0.12 mg/L), *Pasteurella multocida* (95% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible), *Streptococcus agalactiae* (100% susceptible), *Streptococcus canis* (1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Streptococcus viridans* (100% susceptible); 25% bronchial penetration 2-3 h after 2 g i.v. dose; intraperitoneal penetration 85%; CSF penetration 1-35%; increased  $V_d$  in elderly; protein binding 70% (reduced in elderly); implicated in emergence of multiple drug resistance during therapy; no significant inoculum effect; mode of elimination renal; more expensive than first generation

**Indications:** limited role in therapy; has been used as prophylactic antibiotic for colorectal, appendectomy, hysterectomy, termination of pregnancy, liver transplantation surgery and for treatment of septic arthritis due to *Neisseria*, cervical fascial space infections in normal patients, clostridial abortional and puerperal infection, disseminated gonococcal and meningococcal disease, pelvic inflammatory disease and associated acute peritonitis, peritonitis suspected associated with IUD, salpingitis and other gynecologic and obstetric infections, mycobacterial local and generalised sepsis; metronidazole provides superior cover against most anaerobes

**Side Effects:** hypersensitivity syndrome, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy (administer vitamin K supplement) and nephrotoxicity (interstitial nephritis; adjust dose interval appropriately, monitor renal function; may falsely elevate serum creatinine measurement by certain assays) and, rarely, seizures in renal insufficiency; dose adjustment required in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

**CEFOTETAN:** parenteral second generation cephalosporin; moderate spectrum and anaerobes; less active than first generation against Gram positives, especially *Staphylococcus aureus*; similar activity to cefoxitin but longer half life; spectrum includes *Actinomyces* (95% susceptible), *Clostridium* (95% susceptible), *Enterobacter agglomerans* (MIC 0.12 mg/L), *Haemophilus influenzae* (0.5 mg/L), *Neisseria gonorrhoeae* (0.25 mg/L), *Neisseria meningitidis* (0.06 mg/L), *Peptostreptococcus* (100% susceptible), *Proteus mirabilis* (0.5-1 mg/L), *Providencia rettgeri* (0.25 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Streptococcus pyogenes* (1mg/L); covers 68% of *Bacteroides fragilis* group (cefotetan and cefoxitin only cephalosporins active against this group); intraperitoneal penetration 56%; protein binding 89%; implicated in emergence of multiple resistance during therapy; may show inoculum effect; more expensive than first generation

**Indications:** limited role in therapy; epiglottitis in immunocompromised; prophylaxis and treatment of mixed aerobic and anaerobic infections, especially those arising from gastrointestinal and genital tracts; septicemia; surgical prophylaxis (colorectal, appendectomy, hysterectomy, termination of pregnancy, liver transplantation)

**Side Effects:** hypoprothrombinemia, haemorrhage, hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; disulfiram-like reaction with alcohol possible; dose interval adjustment required in renal failure and in dialysis; probably safe in pregnancy; cefotetan-induced hypoprothrombinemia may enhance anticoagulant effect of warfarin and other oral anticoagulants

**CEFUROXIME:** parenteral second generation cephalosporin; spectrum includes Group II<sub>f</sub> (MIC 0.5-1 mg/L), *Haemophilus influenzae* (0.2 mg/L), *Helicobacter pylori* (4 mg/L), *Moraxella catarrhalis* (2 mg/L), *Neisseria gonorrhoeae* (0.06 mg/L), *Proteus mirabilis* (1 mg/L), *Peptococcus* (2 mg/L), *Shigella* (4 mg/L), methicillin susceptible *Staphylococcus* (2 mg/L), *Streptococcus agalactiae* (? 0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (0.06-4 mg/L), *Streptococcus pyogenes* (0.03 mg/L); *Bacteroides*, *Clostridium difficile*, *Proteus vulgaris*, *Pseudomonas aeruginosa* resistant; no significant change in  $V_d$  but clearance reduced in elderly; implicated in emergence of multiple drug resistance; may show inoculum effect; CSF penetration 12-14%

**Indications:** bronchitis; epiglottitis and bacterial tracheitis in immunocompromised; large bowel and cardiothoracic surgical prophylaxis; beta-lactamase producing *Haemophilus influenzae* infections; *Staphylococcus aureus* or *Haemophilus influenzae* in 3 mo - 6 y.o.; cellulitis without evidence of trauma; sinusitis; septic arthritis

**Side Effects:** hypersensitivity syndrome, pemphigus, photosensitivity, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

**CEFUROXIME AXETIL:** oral dosing schedule twice a day (with or after food); spectrum includes *Haemophilus influenzae*, *Moraxella catarrhalis*, *Proteus mirabilis* (++) , *Staphylococcus aureus* (++) , *Streptococcus pneumoniae*, *Streptococcus pyogenes* (+++); very expensive

**Indications:** gonorrhoea; acute otitis media

**Side Effects:** low risk of serious adverse reactions, skin rash; moderate risk of gastrointestinal adverse effects

**CEFORANIDE:** parenteral second generation cephalosporin; implicated in emergence of multiple drug resistance

**CEFONICID:** parenteral second generation cephalosporin; strongly affected by type I  $\beta$ -lactamase; moderate inducer of type I  $\beta$ -lactamase; implicated in emergence of multiple drug resistance

**Side Effects:** hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

**CEFOTIAM:** spectrum includes *Streptococcus pneumoniae* (MIC < 0.12 mg/L), *Streptococcus pyogenes* (< 0.12 mg/L)

**Side Effects:** autoimmune neutropenia in infants

**CEFOTAXIME:** broad spectrum third generation cephalosporin; parenteral; 25% bronchial penetration 2-3 h after 1 g i.m. dose; intraperitoneal penetration 92%; CSF penetration 0-54%; protein binding 55%; reduced clearance in elderly; extended spectrum of activity covering majority of community-acquired enteric Gram negative bacilli; less active against Gram positive organisms than first and second generation; not active against *Enterococcus* or methicillin resistant *Staphylococcus aureus*; greater penetration into CSF than earlier cephalosporins; covers only 20-50% of *Pseudomonas* strains and 33% of *Bacteroides fragilis* group; spectrum includes *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Clostridium* (85% susceptible), *Escherichia coli* (0.1% resistant in Australia), *Fusobacterium* (90% susceptible), Group II<sub>f</sub> (0.13-0.5 mg/L), Group IV<sub>e</sub> (< 0.06-1 mg/L), *Haemophilus influenzae* (0.6% resistance in Australia), *Klebsiella oxytoca* (96% of hospital isolates), *Klebsiella pneumoniae* (6% resistance in Australia), *Legionella* (? 0.12-0.5 mg/L), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), other *Moraxella* (< 0.06-0.25 mg/L), penicillinase positive *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Neisseria meningitidis* (0.06 mg/L), *Proteus mirabilis* (0.5% resistant in Australia), *Salmonella* (< 0.003-0.6 mg/L), *Shigella* (0.03-0.06 mg/L), *Staphylococcus aureus* (98% susceptible), *Streptococcus agalactiae* (0.01-0.25 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (resistance not yet confirmed in Australia), *Streptococcus pyogenes* (< 1 mg/L), *Streptococcus viridans* (0.5 mg/L), *Yersinia* (0.06-0.25 mg/L); in Australia, *Enterobacter* 52% resistant due to  $\beta$ -lactamase; resistance (and cross-resistance to other  $\beta$ -lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; strongly affected by type I  $\beta$ -lactamase; slight inducer of type I  $\beta$ -lactamase; inactivated by plasma-mediated extended spectrum  $\beta$ -lactamases; may show inoculum effect; mode of elimination hepatic

**Indications:** many more times expensive than gentamicin and use should be restricted to broad Gram negative coverage in renally impaired patients and in intensive care areas (69-94% cure rate in Gram negative pneumonia, 87% cure rate in osteomyelitis, 90% cure rate in other serious infections); severe bite and clenched fist injuries; treatment of hospital acquired meningitis and meningitis due to enteric Gram negative bacilli, *Haemophilus influenzae*, *Neisseria* or *Streptococcus* in penicillin hypersensitive or relatively resistant *Streptococcus pneumoniae*; paediatric invasive *Haemophilus influenzae* type b infections; single dose therapy for gonorrhoea; septic arthritis due to unknown organism in < 5 year old; cholangitis and cholecystitis; fish spine injury and other water-related infections due to *Aeromonas* or

*Vibrio*; hepatic abscess; pancreatitis due to coliforms; pancreatic abscess; peritonitis of suspected bowel origin; pneumonia (severe community acquired, mild to moderate community acquired due to resistant organisms or slow response in child 3 w - 3 mo, mild to moderate nosocomial with no specific risk factors in penicillin hypersensitive with significant renal failure); complicated or severe acute sinusitis; Lyme disease, especially with rheumatologic, neurologic or cardiac involvement; also used for bacteraemia and septicemia (infection from genital tract in elderly or diminished renal function, infection from respiratory system, focus from biliary or gastrointestinal tract in elderly patients with diminished renal function or significantly elevated serum creatinine, focus probably urinary tract in penicillin hypersensitive, children < 5 y with facial or periorbital cellulitis, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer in elderly or diminished renal function, unidentified source in child, due to *Neisseria meningitidis*); brain and epidural abscess; severe cellulitis due to *Haemophilus influenzae*; cerebrospinal fluid shunt infection due to aerobic Gram negative bacilli; cervical fascial space infections in immunocompromised; purulent conjunctivitis due to penicillinase-producing *Neisseria gonorrhoeae*; acute cystitis due to *Klebsiella*; deep fascial space infections in immunocompromised; disseminated gonococcal and meningococcal disease; endocarditis due to *Haemophilus influenzae*, *Eikenella corrodens*, *Corynebacterium*, epiglottitis in normal host; penetrating eye injuries when clindamycin not available; sexually acquired pelvic sepsis and pelvic inflammatory disease in inpatient; perinatal generalised disease due to penicillinase-producing *Neisseria gonorrhoeae*, spontaneous peritonitis; peritonsillar abscess in immunocompromised; pneumonia (coliform, severe and moderate community acquired in patients with chronic lung disease, diabetics, alcoholics, nosocomial, aspiration, severe *Haemophilus influenzae*, *Acinetobacter*); preseptal and postseptal cellulitis; pulmonary abscess; severe acute pyelonephritis if aminoglycoside undesirable

**Side Effects:** local reactions in 5%, hypersensitivity, serum sickness-like illness, Stevens-Johnson syndrome, haematological effects, gastrointestinal effects (including pseudomembranous colitis), increases in serum transaminases, alkaline phosphatase, creatinine, blood urea; moderate to significant adjustment of dosage interval in renal failure (rarely, seizures and interstitial nephritis) and in dialysis; probably safe in pregnancy

**MOXALACTAM (LATAMOXEF):** third generation cephalosporin; parenteral; covers only about 20-50% of *Pseudomonas* strains but 73% of *Bacteroides fragilis* group; resistance (and cross-resistance to other  $\beta$ -lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; moderately affected by type I  $\beta$ -lactamase; low inducer of type I  $\beta$ -lactamase; intraperitoneal penetration 70%; CSF penetration 12%; protein binding 50%; increased  $V_d$ , reduced clearance in elderly; may show inoculum effect; withdrawn due to low usage because of uncommon, but important, tendency to cause bleeding in patients with poor nutritional state

**CEFOPERAZONE:** third generation cephalosporin; parenteral; covers 70-90% of *Pseudomonas* strains but only 4% of *Bacteroides fragilis* group; spectrum includes *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Haemophilus influenzae* (< 1 mg/L), *Hafnia alvei* (100% susceptible), *Neisseria gonorrhoeae* (< 1 mg/L), *Neisseria meningitidis* (0.008-0.12 mg/L), *Peptostreptococcus* (? 1 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Serratia marcescens* (0.06 mg/L), *Streptococcus agalactiae* (0.25 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia enterocolitica* (100% susceptible); considerably longer half life than other members of group except ceftriaxone; strongly affected by type I  $\beta$ -lactamase; no to moderate postantibiotic effect; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 3-6%

**Indications:** use should be restricted to treatment of Gram negative meningitis due to Enterobacteriaceae or of organisms resistant to first and second generation cephalosporins in which aminoglycoside therapy is not indicated; cure rate in Gram negative pneumonia 68-94%

**Side Effects:** coagulopathy (hypoprothrombinemia in 4-66% and haemorrhage in 0.5-8%), especially in renal insufficiency (administer vitamin K supplement), hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

**CEFTIZOXIME:** third generation cephalosporin; parenteral; covers only 34% of *Bacteroides fragilis* group; spectrum includes anaerobic cocci (100% susceptible), *Escherichia coli* (MIC < 1 mg/L), *Fusobacterium* (94% susceptible), *Klebsiella*

(< 1 mg/L), *Proteus mirabilis* (< 1 mg/L), *Shigella* (< 1 mg/L), *Streptococcus canis* (100% susceptible at ? 0.015 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L); implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 23%

**Indications:** appendicitis; cervical fascial space infections in immunocompromised; cranial parameningeal deep fascial space infections in immunocompromised; Gram negative pneumonia (66-100% cure rate); other serious Gram negative infections (89% cure rate)

**Side Effects:** erythema nodosum, serum sickness-like illness, Stevens-Johnson syndrome

**CEFTRIAXONE:** broad spectrum third generation cephalosporin; parenteral (i.m. or i.v. daily dose); considerably higher half life than other members of group except cefoperazone; almost identical spectrum to cefotaxime but different pharmacology; spectrum includes *Borrelia burgdorferi* (MIC 0.01-1 mg/L), *Clostridium perfringens* (? 1 mg/L), *Escherichia coli* (0.1% resistant in Australia), *Haemophilus influenzae* (0.6% resistant in Australia), *Klebsiella oxytoca* (94% of hospital isolates), *Klebsiella pneumoniae* (6% resistant in Australia), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (resistance not yet reported), *Neisseria meningitidis* (resistance not yet reported), *Peptostreptococcus*

(? 1 mg/L), *Proteus mirabilis* (100%), *Pseudomonas acidovorans* (0.5 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Salmonella* (0.01-0.19 mg/L), *Shigella* (< 1 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae*

(< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia* (0.06-0.12 mg/L); in Australia, *Enterobacter cloacae* 40% resistant; resistance (and cross-resistance to other ?-lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; covers only 26% of *Bacteroides fragilis* group; strongly affected by type I ?-lactamase; low inducer of type I ?-lactamase; inactivated by plasma-mediated extended spectrum ?-lactamases; no significant change in  $V_d$ , reduced protein binding in elderly; CSF penetration 2-7%; in WHO Model List of Essential Drugs

**Indications:** many times more expensive than gentamicin and use should be restricted; septic arthritis (due to *Neisseria*, *Haemophilus influenzae*, *Eikenella corrodens*; organism unknown, < 5 y); bacteraemia and septicemia (infection from female genital tract in elderly or diminished renal function, infection from respiratory system, focus probably biliary or gastrointestinal tract in elderly patients with diminished renal function or significantly elevated serum creatinine, focus probably urinary tract in penicillin hypersensitive, children < 5 y with facial or periorbital cellulitis, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer in elderly or diminished renal function, focus probably intravascular catheter in elderly or diminished renal function, unidentified source in child or remote areas, due to *Neisseria meningitidis*); severe cat and dog and human bite and clenched fist injury infections; chancroid; cholangitis and cholecystitis; purulent conjunctivitis due to penicillinase-producing *Neisseria gonorrhoeae*; disseminated gonococcal and meningococcal disease; bacterial dysentery; endocarditis due to *Escherichia coli*; enteric fever; sexually acquired acute epididymitis and epididymoorchitis; epiglottitis; penetrating eye injuries when clindamycin not available; fish spine injury and other water-related infections due to *Aeromonas* or *Vibrio*; gonorrhoea; hepatic abscess; Lyme disease (arthritis, meningoenzephalitis, heart block); meningitis (hospital acquired and due to enteric Gram negative bacilli or to *Neisseria* or *Streptococcus* in penicillin hypersensitive, relatively resistant *Streptococcus pneumoniae*, *Haemophilus influenzae*); meningococcal and *Haemophilus influenzae* type b meningitis prophylaxis in pregnant; osteomyelitis and osteochondritis; pancreatitis due to coliforms; pancreatic abscess; sexually acquired pelvic sepsis and pelvic inflammatory disease in inpatient; peritonitis (spontaneous, suspected bowel origin); peritonsillar abscess in immunocompromised; pneumonia (*Haemophilus influenzae*, coliform (66-94% cure rate), mild to moderate community acquired with risk factors or due to resistant organisms or slow response in child

3 w - 3 mo, moderate community acquired in patient with risk factors in remote areas, severe community acquired, mild to moderate nosocomial with no specific risk factors in penicillin hypersensitive with significant renal failure); other serious Gram negative infections (87% cure rate); preseptal and postseptal cellulitis; pulmonary abscess; severe acute pyelonephritis if aminoglycoside undesirable; rape prophylaxis; complicated or severe acute sinusitis; surgical prophylaxis; syphilis prophylaxis; gonococcal vaginitis (?-lactamase positive)

**Side Effects:** hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy in renal insufficiency (administer vitamin K supplement); reversible pseudolithiasis or biliary sludge

formation; hyperprothrombinemia and enhanced anticoagulant effect of warfarin and other oral anticoagulants; dose adjustment not required in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea  
**CEFSULODIN:** third generation cephalosporin; binds chiefly to PBP1a; specific activity against *Pseudomonas aeruginosa* and Gram positive cocci other than *Enterococcus* but little activity against Enterobacteriaceae; implicated in emergence of multiple resistance during therapy

**CEFMENOXIME:** third generation cephalosporin; covers only 18% of *Bacteroides fragilis* group; spectrum includes *Citrobacter diversus* (MIC 0.12 mg/L), *Enterobacter aerogenes* (0.25-1 mg/L), *Escherichia coli* (0.06-0.13 mg/L), *Klebsiella oxytoca* (0.12-1 mg/L), *Klebsiella pneumoniae* (< 0.12 mg/L), *Proteus mirabilis* (= 0.01 mg/L), *Providencia stuartii* (0.06-1 mg/L), *Salmonella* (? 0.12 mg/L), *Streptococcus pneumoniae* (0.01-0.06 mg/L), *Streptococcus pyogenes* (0.01-0.03 mg/L), *Yersinia* (0.06-0.25 mg/L); no significant effect on  $V_d$ , reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; no inoculum effect; CSF penetration 6-19%

**CEFAZAFLUR:** minimal inoculum effect; spectrum includes Group III (MIC 0.5 mg/L)

**CEFBUPERAZONE:** spectrum includes *Citrobacter diversus* (MIC 0.12-0.25 mg/L), *Klebsiella oxytoca* (0.25-1 mg/L), *Klebsiella pneumoniae* (0.25-0.5 mg/L)

**CEFIXIME:** oral third generation cephalosporin; oral dosing schedule 4 times a day; expensive; spectrum similar to parenteral third generation cephalosporins; includes *Citrobacter diversus* (100% susceptible at ? 0.5 mg/L), *Escherichia coli* (MIC 0.25-32 mg/L), *Haemophilus influenzae* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.54 mg/L), *Klebsiella pneumoniae* (0.25 - > 64 mg/L), *Moraxella catarrhalis* (0.25-0.5 mg/L), *Neisseria gonorrhoeae* (0.015 mg/L), *Neisseria meningitidis* (100% susceptible at ? 0.06 mg/L), *Proteus mirabilis* (100% susceptible at ? 0.2 mg/L), *Proteus vulgaris* (0.015-0.25 mg/L), *Providencia rettgeri* (100% susceptible at 0.5 mg/L), *Providencia stuartii* (100% susceptible at ? 0.25 mg/L), *Pseudomonas acidovorans* (0.5 mg/L), *Salmonella* (1 mg/L), *Streptococcus agalactiae* (0.5 mg/L), penicillin-susceptible *Streptococcus pneumoniae*

(0.5 mg/L), *Streptococcus pyogenes* (0.5 mg/L); anaerobes, *Enterococcus*, *Helicobacter pylori*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Shigella*, *Staphylococcus* 100% resistant

**Side Effects:** low risk of serious adverse reactions (hypersensitivity syndrome, serum sickness-like illness), skin rash (Stevens-Johnson syndrome); moderate risk of gastrointestinal adverse effects

**CEPIRAMIDE:** spectrum includes *Klebsiella oxytoca* (MIC 0.1-0.5 mg/L), *Streptococcus pneumoniae* (0.02-0.25 mg/L), *Streptococcus pyogenes* (0.02-0.25 mg/L)

**CEFODIZIME:** spectrum includes *Escherichia coli* (MIC 1 mg/L), *Klebsiella oxytoca* (0.5 mg/L), *Serratia marcescens* (0.1-0.2 mg/L)

**Side Effects:** high risk of substantial renal function derangement on simultaneous infusion with vancomycin, especially in diabetics

**CEFETAMET PIVOXIL:** oral third generation cephalosporin (take with or after food); *Streptococcus pyogenes* and *Proteus mirabilis* highly susceptible, *Escherichia coli* and *Klebsiella* susceptible, *Staphylococcus aureus* and *Pseudomonas aeruginosa* resistant

**CEPODOXIME PROXETIL:** oral broad spectrum (similar to parenteral third generation) third generation cephalosporin (take with or after food (absorption increased)); increased pH (antacids,  $H_2$ -antagonists) reduces bioavailability; *Streptococcus pyogenes* and *Proteus mirabilis* highly susceptible, *Escherichia coli* and ?-lactamase-producing *Haemophilus influenzae* susceptible, *Klebsiella* moderately susceptible, *Staphylococcus aureus* and *Pseudomonas aeruginosa* resistant

**Indications:** upper and lower respiratory tract infections due to streptococci, *Haemophilus influenzae*, *Moraxella catarrhalis*; skin and soft tissue infections; urinary tract infections

**Side Effects:** diarrhoea, nausea, chest pain, hypotension, rash, pseudomembranous colitis, anaphylactic shock, hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; probably safe in pregnancy; requires dosage interval adjustment in renal failure and in dialysis

**CEFTIBUTEN:** oral (once daily) highly ?-lactamase stable third generation cephalosporin; spectrum includes *Escherichia coli* (MIC 0.25-12 mg/L), *Haemophilus influenzae* (0.03-0.5mg/L), *Helicobacter pylori* (8 mg/L), *Klebsiella oxytoca* (0.06 mg/L), *Klebsiella pneumoniae* (0.12 - >64 mg/L), *Moraxella catarrhalis* (2-4 mg/L), *Proteus vulgaris* (0.03 mg/L), *Neisseria gonorrhoeae* (0.015-0.13 mg/L), *Salmonella* (0.06 mg/L), *Serratia marcescens* (4-8 mg/L), *Shigella* (0.25

mg/L), *Streptococcus pyogenes* (0.5 mg/L); *Pseudomonas aeruginosa*, anaerobes and Gram positives other than *Streptococcus pyogenes* and some strains of penicillin-susceptible *Streptococcus pneumoniae* resistant

**Side Effects:** diarrhoea (infrequent, usually mild), hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

**CEFPIROME:** broad spectrum and antipseudomonal third generation parenteral cephalosporin; spectrum includes *Escherichia coli* (MIC 0.03-0.12 mg/L), *Haemophilus influenzae* (0.06 mg/L), *Klebsiella* (0.03-0.25 mg/L), *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Proteus mirabilis* (0.01-0.12 mg/L), *Pseudomonas aeruginosa*, *Salmonella* (0.06-0.12 mg/L), *Shigella* (0.01-0.03 mg/L), methicillin susceptible *Staphylococcus aureus* (0.5-1 mg/L), *Streptococcus agalactiae* (0.01-0.06 mg/L), *Streptococcus pneumoniae* (0.01-0.25 mg/L), *Streptococcus pyogenes* (0.02-0.25 mg/L), *Yersinia* (? 0.25 mg/L)

**Side Effects:** local phlebitis, thrombophlebitis and pain, hypersensitivity, gastrointestinal (including pseudomembranous colitis), increased liver enzyme serum levels, rare cholestatic jaundice, increased serum creatinine, haematological effects, headache, dizziness, haemorrhage, ecchymosis, altered rhythm, dyspnoea, malaise, superinfection; safety in pregnancy not established; requires dose adjustment in renal failure and in dialysis

**CEFTAZIDIME:** broad spectrum and antipseudomonal parenteral third generation cephalosporin; stability to most  $\beta$ -lactamases (but susceptible to extended spectrum  $\beta$ -lactamases and resistance due to chromosomal  $\beta$ -lactamases may develop during therapy) and ease of use attractive features; less active against Gram positive organisms than cefepime and cefpirome; covers 96% of Enterobacteriaceae, 86% of nonenteric Gram negative bacilli (including 70-90% of *Pseudomonas* strains), 67% of staphylococci and 93% of nonenterococcal streptococci but < 1% of *Enterococcus*; spectrum includes *Burkholderia cepacia*, *Escherichia coli* (99% of hospital isolates), *Haemophilus influenzae* (0.06-0.125 mg/L), *Klebsiella oxytoca* (98% of hospital isolates), *Klebsiella pneumoniae* (94% of hospital isolates), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (0.01-0.06 mg/L), *Proteus mirabilis* (100%), *Pseudomonas aeruginosa* (10% resistance in Australia), *Salmonella* (0.06-0.5 mg/L), *Streptococcus agalactiae* (0.25-0.5 mg/L), *Streptococcus canis* (0.125 mg/L), *Streptococcus pneumoniae* (0.12-0.5 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia* (0.12-0.5 mg/L); only cephalosporin active against *Stenotrophomonas maltophilia* (92% of hospital isolates); in Australia, *Enterobacter cloacae* 61% resistant; serum protein binding 17%; reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 14%; in WHO Model List of Essential Drugs

**Indications:** many times more expensive than gentamicin and use should be restricted to infections (including bacteraemia and septicemia) in febrile neutropenic patients (Gram negative pneumonia cure rate 66-94%, other serious Gram negative infections 84% cure rate); melioidosis (including bacteraemia and septicemia); severe community acquired pneumonia in adult with bronchiectasis or cystic fibrosis; severe nosocomial pneumonia; *Klebsiella pneumoniae* pneumonia; *Pseudomonas* infection (including bacteraemia and septicemia) in penicillin hypersensitive patient or patient at increased risk for aminoglycoside toxicity; endophthalmitis; perianal and perirectal abscess and cellulitis in patients with malignant disease; *Pseudomonas aeruginosa* meningitis

**Side Effects:** occasional urticarial rash, bullous pemphigoid, pemphigus, photosensitivity, Stevens-Johnson syndrome, local reaction, hypersensitivity, serum sickness-like illness, gastrointestinal (including pseudomembranous colitis), headache, dizziness, neurological sequelae in patients with renal impairment, candidiasis, rise in liver enzymes; dose adjustment required in renal failure and dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

**CEFEPIME:** broad spectrum and antipseudomonal parenteral 'fourth generation' cephalosporin; similar activity to cefotaxime but improved coverage of *Pseudomonas aeruginosa*, *Enterobacter*, *Serratia* and methicillin resistant *Staphylococcus aureus*; spectrum includes *Escherichia coli* (0.03-0.12 mg/L), *Haemophilus influenzae* (0.01-0.12 mg/L), *Klebsiella* (0.01-0.12 mg/L), *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Proteus mirabilis* (0.03-0.06 mg/L), *Salmonella* (0.03-0.2 mg/L), *Shigella* (0.01-0.06 mg/L), *Streptococcus agalactiae* (0.01-0.06 mg/L), *Streptococcus pneumoniae* (0.01-0.06 mg/L); more active against Gram positives than ceftazidime; susceptible to extended spectrum  $\beta$ -lactamases and chromosomal cephalosporinases

**Indications:** treatment of severe community- or hospital-acquired infections that are documented or suspected to involve resistant aerobic Gram negative bacteria, including Enterobacteriaceae, *Haemophilus influenzae* and *Pseudomonas*; empiric therapy for febrile neutropenia

**Side Effects:** hypersensitivity syndrome, Stevens-Johnson syndrome; probably safe in pregnancy; dose adjustment required in renal impairment

**CEFditoren:** oral third generation aminothiazolyl cephalosporin active against *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, methicillin susceptible *Staphylococcus aureus*; not active against *Bacteroides fragilis*, *Chlamyphila pneumoniae*, *Legionella*, *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*

**Indications:** acute exacerbation of chronic bronchitis, pharyngitis/tonsillitis, uncomplicated skin and skin structure infections

**Side Effects:** diarrhoea, nausea, vomiting, headache, dyspepsia

**Contraindications:** hypersensitivity to penicillins, cephalosporins, milk protein; carnitine deficiency

### MONOBACTAMS

**AZtreonam:** monobactam; binds chiefly to PBP3; kills only growing organisms; inhibits class I cephalosporins; relatively inactive against Gram positive organisms (only 1% of staphylococci, 0.1% of *Enterococcus* and 4% of other streptococci susceptible) and anaerobes but highly active against majority of aerobic Gram negative bacteria including  $\beta$ -lactamase-producing *Haemophilus influenzae* (MIC 0.016-0.25 mg/L), Enterobacteriaceae (97% susceptible) and nonenteric Gram negative bacilli (68% susceptible, including *Pseudomonas* resistant to aminoglycosides); spectrum includes *Escherichia coli* (99% of hospital isolates), *Haemophilus influenzae*, *Klebsiella oxytoca* (94% of hospital isolates), *Klebsiella pneumoniae* (93% of hospital isolates), *Morganella morganii* (100%), *Neisseria meningitidis*, *Proteus mirabilis* (100%), *Pseudomonas fluorescens*, *Salmonella* (? 0.12 mg/L); no significant change in  $V_d$ , protein binding or clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

**Indications:** shows promise as an aminoglycoside substitute but high cost has restricted use to people with severe penicillin hypersensitivity or at increased risk for aminoglycoside toxicity; superior efficacy to aminoglycosides in treating bacteraemia involving aerobic Gram negatives; Gram negative bacterial meningitis (86% cure rate); neonatal sepsis; *Klebsiella pneumoniae* pneumonia; *Haemophilus influenzae* pulmonary infection in cystic fibrosis

**Side Effects:** rash (common), phlebitis and thrombophlebitis at injection site (common), rare reduction in platelet count and anaemia, rare jaundice and hepatitis, gastrointestinal effects (diarrhoea, nausea, vomiting common; gastrointestinal bleeding, abdominal cramps and bloating uncommon; pseudomembranous colitis rare), abnormal taste (common), elevated transaminases (transient common, significant rare), eosinophilia (common), headache (uncommon), dizziness (uncommon), mild local reactions, oral ulceration (uncommon), anaphylaxis (rare), angioedema (rare), bronchospasm (rare), shock (rare), neutropenia (rare), prolonged bleeding time (rare); probably safe in pregnancy; dose adjustment required in renal failure and dialysis; can be given to people with severe penicillin hypersensitivity as there is little cross sensitisation; theoretical possibility of enhanced warfarin effect

**CARumonam:** monobactam; 98% of Enterobacteriaceae and 75% of nonenteric Gram negative bacilli susceptible, but only 1% of staphylococci, 0.3% of *Enterococcus* and 8% of streptococci; spectrum includes *Citrobacter diversus* (MIC ? 0.12 mg/L), *Enterobacter aerogenes* (0.12-0.5 mg/L), *Escherichia coli* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.12-0.5 mg/L), *Klebsiella pneumoniae* (0.12-0.25 mg/L), *Morganella morganii* (? 0.12 mg/L), *Proteus mirabilis* (? 0.01 mg/L), *Salmonella* (? 0.12 mg/L), *Yersinia* (0.25-1 mg/L)

**BACTRACIN:** polypeptide mixture; inhibits dephosphorylation of lipid pyrophosphate thus impairing regeneration of lipid carrier; bactericidal; acts only on proliferating bacteria; active against Gram positive bacteria; diminishes phagocytosis

**Indications:** hordeolum (topical), skin infections (topical), *Clostridium difficile*-associated diarrhoea (oral)

**Side Effects:** allergic contact dermatitis

**GLYCOPEPTIDES:** active against wide range of Gram positive organisms; Gram negatives not susceptible

**Indications:** treatment and prophylaxis of methicillin resistant staphylococcal infection, severe infections with susceptible organisms in penicillin hypersensitive

**Side Effects:** itch, fever, chills, eosinophilia, pain, erythema, thrombophlebitis, nephrotoxicity uncommon; anaphylaxis, superinfection, thrombocytopenia, leucopenia, neutropenia, tinnitus, dizziness, ototoxicity, toxic epidermal necrolysis rare

**VANCOMYCIN (VANCOCIN):** glycopeptide; parenteral (i.v. infusion over at least an hour) and oral (treatment of pseudomembranous colitis only; relationship of dose to food doesn't matter); inhibits peptidoglycan synthetase and polymerisation of linear peptide; kills non-growing organisms; increased  $V_d$ . no significant change in protein binding, reduced clearance in elderly; moderate postantibiotic effect; bactericidal; active against Gram positive bacteria, including *Bacillus*

(< 5% resistance in Australia), *Corynebacterium* (resistance not yet reported), *Micrococcus* (< 5% resistance in Australia), methicillin resistant staphylococci (*S.aureus* resistance reported from Japan and Slovak Republic; not yet confirmed in Australia; coagulase negative staphylococci < 5% resistance in Australia), *Streptococcus* (*S.mitis* resistance reported from USA and Europe); in Australia, *Enterococcus faecalis* 0.7% resistant, *Enterococcus faecium* 29% resistant; in USA, *Enterococcus* 14% resistant; kills bacteria phagocytosed by granulocytes; minimal inoculum effect; decreased bactericidal and bacteriostatic effect under anaerobic conditions; not active against Gram negative organisms; mode of elimination renal; in WHO Model List of Essential Drugs

**Indications:** increasing role in treatment of serious Gram positive infections (predominantly organisms resistant to  $\beta$ -lactams, methicillin resistant *Staphylococcus* or penicillin hypersensitive patients); reactive arthritis due to *Clostridium difficile*; septic arthritis due to methicillin resistant *Staphylococcus aureus*; bacteraemia and septicemia (focus probably intravascular catheter; febrile neutropenic patients with *Staphylococcus* suspected, hospital acquired or vascular catheter infection or febrile after 3 d; due to methicillin resistant *Staphylococcus aureus*, *Bacillus*, *Stomatococcus mucilaginosus*, *Corynebacterium jeikeium*, *Corynebacterium striatum*, *Corynebacterium urealyticum*, *Enterococcus*); severe streptococcal and staphylococcal cellulitis in penicillin hypersensitive; cerebrospinal fluid shunt infections due to *Staphylococcus*, *Enterococcus*, diphtheroids, *Propionibacterium*; cranial parameningeal deep fascial space infections following cranial surgery in immunocompromised; acute cystitis due to *Corynebacterium urealyticum*; endocarditis prophylaxis and treatment in penicillin hypersensitive; endophthalmitis; penetrating eye injuries; hospital acquired meningitis; postneonatal pyogenic meningitis due to penicillin resistant *Streptococcus pneumoniae*, *Staphylococcus*; mycotic aneurism; myocarditis and pericarditis due to *Staphylococcus aureus*; osteomyelitis and osteochondritis due to methicillin resistant *Staphylococcus aureus*; progressive perianal and perirectal abscess and cellulitis in patients with malignant disease; peritonitis (continuous ambulatory peritoneal dialysis, *Stomatococcus mucilaginosus*); pneumonia (methicillin resistant *Staphylococcus aureus*, *Corynebacterium pseudodiphtheriticum*, severe community acquired in children < 10 y or with MRSA suspected or proven, mild to moderate nosocomial in patient with diabetes, coma or head injury and MRSA suspected or proven); prosthetic implants prophylaxis; pseudomembranous colitis and antibiotic-associated diarrhoea due to *Clostridium difficile* and unresponsive to metronidazole (oral); acute pyelonephritis with Gram positive cause in penicillin hypersensitive patient; septicemia; localised skin lesions due to methicillin resistant *Staphylococcus aureus*, *Corynebacterium jeikeium*, *Corynebacterium urealyticum*, *Corynebacterium striatum*, splenic abscess due to *Clostridium difficile*; surgical prophylaxis (cardiac surgery, arterial reconstructive surgery of abdominal aorta or lower limb, breast, dialysis access, craniotomy); systemic infections in granulocytopenia (breakthrough bacteraemia, catheter-associated infection); toxic shock syndrome due to methicillin resistant *Staphylococcus aureus*; vascular graft infection

**Side Effects:** nephrotoxicity (particularly with concomitant aminoglycoside, aciclovir, amphotericin, cyclosporin, frusemide, cefodizime, cidofovir), ototoxicity, 'red man' syndrome (rare infusion rate-dependent induction of histamine-mediated effects; prior administration of hydroxyzine gives protection, while diphenhydramine aborts it), bullous pemphigoid, hypersensitivity syndrome, lupus erythematosus, pustulosis, Stevens-Johnson syndrome, vasculitis, immune thrombocytopenia; delayed onset neutropenia in renal insufficiency; increased risk of neutropenia with zidovudine; uncommon mild gastrointestinal tract disturbances with oral; cholestyramine may bind to oral and reduce antibacterial activity; modify dosage interval, monitor serum levels (even in haemodialysis patients), monitor renal function in renal dysfunction; safety in pregnancy not established; safe in breastfeeding; dose interval adjustment required in continuous venovenous and arteriovenous haemodialysis; toxic level > 10 mg/L trough, > 40 mg/L peak (monitor routinely at least once during a course of therapy); incompatible with benzylpenicillin, chloramphenicol, heparin, hydrocortisone, methicillin, novobiocin

**TEICOPLANIN:** glycopeptide related to vancomycin; similar spectrum to vancomycin but different pharmacology and, possibly, lower toxicity; i.m. and i.v. (slow injection or infusion)

**Indications:** as for vancomycin; endocarditis prophylaxis (bronchoscopy with rigid bronchoscope, dental procedures inducing gingival or mucosal bleeding, surgical procedures breaking respiratory mucosa, tonsillectomy and/or adenoidectomy in patients penicillin hypersensitive, on long-term penicillin or having taken  $\beta$ -lactam antibiotic more than once in previous month; cystoscopy, gall bladder surgery, oesophageal dilatation, sclerotherapy for oesophageal varices, surgical procedures breaking intestinal or genital mucosa, urethral catheterisation or urinary tract surgery in presence of urinary tract infection, urethral dilatation, vaginal delivery in presence of infection, vaginal hysterectomy in penicillin hypersensitive)

**Side Effects:** fever, rashes, nausea, vomiting, rigours, pruritis, diarrhoea, red man syndrome; modify dosage interval in renal failure and in continuous venovenous and arteriovenous haemodialysis (monitor levels to determine precise dosage requirements); safety in pregnancy and breastfeeding not established

**SYNERCID:** quinupristin + dalbapristin; i.v. streptogramin; active against Gram positive cocci including glycopeptide resistant enterococci (but poor activity against *Enterococcus faecalis*) and staphylococci

**Indications:** bloodstream infections with vancomycin resistant *Enterococcus faecium*, skin and skin structure infections due to methicillin susceptible *Staphylococcus aureus* or *Streptococcus pyogenes*

**Side Effects:** inflammation at infusion site in 42%, pain at infusion site in 40%, erythema and irritation at injection site common, arthralgia in 4-8%, nausea in 3-5%, myalgia in 1-5%; elevated transaminases, rash, vomiting, diarrhoea, headache, raised bilirubin common; fever, anaphylaxis, chest pain, pseudomembranous colitis, pancreatitis, peripheral oedema, hypotension, gout, confusion, paraesthesia, dizziness, hypertonia, insomnia, anxiety, leg cramps, dyspnoea, pleural effusion, urticaria, tachycardia, jaundice, hepatitis, pharyngitis, oral candidiasis, stomatitis, anaemia, thrombocytopenia, eosinophilia, raised blood urea and creatinine uncommon; interacts with P450 3A4 substrates (midazolam, nifedipine; increased risk of QT prolongation); increases risk of toxicity with cyclosporin, protease inhibitors, erythromycin; safety in pregnancy and breastfeeding not established

**PRISTINAMYCIN:** oral streptogramin active against Gram-positive bacteria, *Neisseria*, *Mycoplasma*, *Ureaplasma*, *Chlamydia*, *Haemophilus influenzae*

**COUMERMYCIN:** bis-hydroxycoumarin; activity includes *Staphylococcus* (MIC ? 0.002-0.25 mg/L)

**COLISTIN AND COLISTIMETHATE:** binds and disrupts membrane phospholipids by detergent action; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and kills bacteria phagocytosed by granulocytes; active against Gram negative bacteria; spectrum includes *Bordetella bronchiseptica* (MIC 0.13-0.5 mg/L), Group IVe (0.03-0.25 mg/L), *Enterobacter aerogenes*, *Escherichia coli*, *Haemophilus influenzae* (0.25-0.5 mg/L), *Klebsiella* (0.5 mg/L), *Pseudomonas aeruginosa*; colistin sulphate topical only; colistimethate sodium injectable produg of colistin

**Indications:** primarily used to treat *Pseudomonas* infection (especially topically in 'swimmer's ear'); now rarely used systemically

**Side Effects:** systemic: respiratory arrest, nephrotoxicity, paraesthesia, hearing loss; modify dosage in renal dysfunction; maximum permissible blood level 5 mg/L; incompatible with cephalothin, erythromycin, hydrocortisone, lincomycin; potential for enhancement of neuromuscular blockade by aminoglycosides and curariform muscle relaxants; safety in pregnancy not established; caution in breastfeeding, monitor infant for diarrhoea

**POLYMYXIN B:** binds and disrupts phospholipids by detergent action; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and kills bacteria phagocytosed by granulocytes; active against Gram negative bacteria

**Indications:** now rarely used systemically, except for multiresistant *Acinetobacter baumannii*; bacterial blepharitis (topical); more severe purulent conjunctivitis (topical); endotoxemia; keratitis and iritis due to Gram negative bacilli (topical); otitis media prophylaxis (topical); folliculitis and paronychia due to *Pseudomonas aeruginosa*; ? useful in preventing septic shock in Gram negative bacteraemia and septicemia

**Side Effects:** hypersensitivity reactions, gastrointestinal disturbances, skin reactions, dizziness, hearing loss, paresthesias, neuromuscular blockade, respiratory paralysis, nephrotoxicity, pain at injection site, visual disturbances,

CNS toxicity in renal insufficiency (avoid use if possible or adjust dose appropriately); maximum permissible blood level 5 mg/L

**QUINOLONES:** bactericidal; anaerobes 100% intrinsic resistance

**NALIDIXIC ACID:** oral (relationship of dose to food doesn't matter) quinolone (quinoline carboxylic acid derivative); interferes with DNA template-RNA polymerase complex; active only against facultative Gram negative bacilli; spectrum includes *Aeromonas* (MIC 0.5 mg/L), *Campylobacter jejuni* (100% susceptible), *Haemophilus influenzae* (0.5 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Plesiomonas* (0.5 mg/L), but use virtually restricted to urinary tract infections; in WHO Model List of Essential Drugs as complementary drug for treatment of resistant shigellosis; mode of elimination renal

**Indications:** occasionally used in treatment of bacterial dysentery and urinary tract infection but several less toxic alternatives now available

**Side Effects:** gastrointestinal disturbances (nausea, vomiting, diarrhoea), skin reactions, photosensitivity, headache, precipitates convulsions in those predisposed, visual disturbances (glare reaction), bone marrow suppression, vestibular symptoms; avoid in renal dysfunction (CNS toxicity, seizures, ineffective in marked renal failure) and in dialysis; safe in pregnancy; may potentiate warfarin activity

**4-QUINOLONES:** includes fluoroquinolones; analogues of nalidixic acid with broader antibacterial activity, increased bactericidal effect, improved oral absorption and longer half lives; inhibit DNA synthesis by binding DNA gyrases; similar spectrum to aminoglycosides; only oral agents for treatment of *Pseudomonas*; also active against staphylococci (including methicillin resistant *Staphylococcus aureus*), borderline activity against *Streptococcus* and *Enterococcus*; close relation of MIC and MBC, with minor inoculum effect for most organisms; prolonged postantibiotic effect on staphylococci, Enterobacteriaceae and *Pseudomonas*; do not select resistant mutants of plasmid type; do not distort intestinal flora with respect to streptococci and anaerobic species; frequency of mutational resistance  $\approx 10^{-11}$ ; resistance has occurred where widely used in infections caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, enteric Gram-negative bacilli, *Campylobacter* and *Neisseria gonorrhoeae*; generally do not select high level cross-resistant isolates to  $\beta$ -lactamases or aminoglycosides; kill bacteria phagocytosed by granulocytes; decreased bactericidal effect under anaerobic conditions; spectrum includes *Eikenella corrodens* (100% susceptible), *Neisseria gonorrhoeae* (2% low level and 2% high level resistance in Australia; 82% resistance in China, 69% high level resistance in the Philippines), *Pasteurella multocida* (95% susceptible), *Staphylococcus aureus*; anaerobes 100% intrinsic resistance; expensive

**Indications:** should be reserved for treatment of infections resistant to cheaper agents or where oral agent is essential

**Side Effects:** elevation of hepatic enzymes in 1.8-2.5%; nausea, vomiting, diarrhoea, abdominal pain, dyspepsia in 1-5%; skin effects (rash, itch) in 0.5-2%; eosinophilia in 0.2-2%; azotemia in 0.2-1.3%; dizziness, confusion, headache, insomnia in 0.1-0.3% (more likely in older patients); arthralgia, arthritis, myalgia, tendonitis, crystaluria, interstitial nephritis, depression, QT interval prolongation uncommon; blood dyscrasias, hypoglycaemia, psychotic reactions, convulsions, phototoxicity, colitis, anaphylaxis, elevated liver enzymes, hepatitis rare; arthropathies in young animals; possible CNS toxicity, nephropathy, ocular toxicity, Achilles tendon disorders (especially in elderly taking corticosteroids); may antagonise polymyxin, chloramphenicol, erythromycin, rifampicin; aluminium, calcium, magnesium antacids, Asian dandelion, fennel seed, iron and zinc preparations, sucralfate, didanosine buffered preparations reduce plasma levels (space 2-6 h apart); phenytoin levels may be decreased, giving epileptogenic potential; increased anticoagulant effects with oral anticoagulants (rare but unpredictable); can markedly increase theophylline plasma levels

**Contraindications:** safety in pregnancy not established; use with caution in nursing mothers and children < 14 y

**ACROSOXACIN:** 4-quinolone

**Indications:** oral treatment of uncomplicated gonorrhoea

**CINOXACIN:** 4-quinolone; spectrum includes *Haemophilus influenzae* (MIC 1 mg/L)

**ENOXACIN:** 4-quinolone; oral (not affected by food); 40-78% penetration into blister fluid, 58-100% penetration into sputum and bronchial secretions, 35-50% penetration into bone, 18-21% penetration into prostatic tissue; spectrum includes aerobic Gram negative bacilli (MIC<sub>90</sub> 1 mg/L), *Aeromonas* (100% susceptible), *Bacillus* (1 mg/L), *Bacteroides*

*ureolyticus* (0.25 mg/L), *Bordetella pertussis* (0.25-0.5 mg/L), *Citrobacter amalonaticus* (97% susceptible at 0.25 mg/L), *Citrobacter diversus* (100% susceptible at 0.5 mg/L), *Citrobacter freundii* (98% susceptible at 0.5 mg/L), *Citrobacter koseri* (0.5 mg/L), *Enterobacter aerogenes* (94% susceptible at 0.5 mg/L), *Enterobacter agglomerans* (94% susceptible at 0.5 mg/L), *Enterobacter cloacae* (0.8-1 mg/L), *Enterobacter sakazakii* (100% susceptible at 0.5 mg/L), Enterobacteriaceae (0.5-1 mg/L), *Escherichia coli* (0.5 mg/L), *Haemophilus influenzae* (? 0.004-0.5 mg/L), *Haemophilus paraprophilus* (0.06 mg/L), *Haemophilus parainfluenzae* (0.5 mg/L), *Hafnia alvei* (100% susceptible), *Legionella*, *Morganella morganii* (100% susceptible at 0.5 mg/L), various species of *Mycobacterium*, *Neisseria gonorrhoeae* (? 0.06-0.12 mg/L), *Neisseria meningitidis* (100% susceptible at < 0.12 mg/L), *Plesiomonas* (0.125-0.5 mg/L), *Proteus* (0.5-1 mg/L), *Pseudomonas acidovorans* (1 mg/L), *Pseudomonas aeruginosa*, *Salmonella* (0.5 mg/L), *Serratia* (0.5 mg/L), *Shigella* (0.2-0.5 mg/L), *Staphylococcus haemolyticus* (1 mg/L), *Vibrio parahaemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.25 mg/L); poor activity against streptococci, none against anaerobes

**Indications:** complicated urinary tract infection

**Side Effects:** nausea/vomiting in 6%, headache in 2%, dizziness in 2%, diarrhoea in 1%, abdominal pain in 1%, dyspepsia/flatulence in 1%, insomnia in 1%; mineral antacids, didanosine, H<sub>2</sub>-antagonists, proton pump inhibitors, sucralfate reduce bioavailability; probenecid may reduce urinary excretion; may radically increase theophylline plasma levels; also interacts with caffeine, some non-steroidal anti-inflammatory drugs (has resulted in seizures); safety in pregnancy not established

**Contraindications:** avoid if breastfeeding

**OXOLINIC ACID:** 4-quinolone

**Indications:** used primarily in treatment of urinary infections

**CIPROFLOXACIN:** oral (take ½ to 1 h before food) and parenteral fluoroquinolone; achieves good serum, tissue and urine concentrations; serum protein binding 30%; no inoculum effect; 43-80% penetration into blister fluid, 17-235% penetration into sputum and bronchial secretions, 32-417% penetration into prostatic secretions, 3-146% penetration into CSF, 6-23% penetration into aqueous humour, 28-460% penetration into bone, 94-300% penetration into prostatic tissue, 200-700% penetration into cells; active against Gram negative bacilli (aerobic Gram negative bacilli MIC<sub>90</sub> 0.25 mg/L; *Aeromonas*

(< 5% resistance in Australia), *Bacteroides ureolyticus* (0.06 mg/L), *Bordetella parapertussis* (< 0.06 mg/L), *Bordetella pertussis* (0.12 mg/L), *Brucella melitensis* (0.5-0.8 mg/L), *Burkholderia cepacia*, *Capnocytophaga* (0.06-0.12 mg/L), *Citrobacter* (most active antibiotic; *Citrobacter diversus* 0.03-0.06 mg/L, *Citrobacter freundii* 0.015-0.25 mg/L), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (5% resistant in Australia), *Escherichia coli* (0.3% resistant in Australia), *Haemophilus ducreyi* (< 0.06 mg/L), *Haemophilus influenzae* (0.008-0.03 mg/L), *Haemophilus parainfluenzae* (100% susceptible at 0.06 mg/L), *Haemophilus paraprophilus* (? 0.03 mg/L), *Klebsiella oxytoca* (100%), *Klebsiella pneumoniae* (0.5 mg/L), *Legionella* (0.125 mg/L), *Morganella morganii* (0.03 mg/L), various species of *Mycobacterium*, *Plesiomonas* (< 5% resistance in Australia), indole positive *Proteus*, *Proteus mirabilis* (0.4% resistant in Australia), *Providencia*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens* (0.5-1 mg/L), *Pseudomonas pickettii* (0.12-0.25 mg/L), *Pseudomonas stutzeri* (0.5 mg/L), *Rhodococcus* (1 mg/L), *Salmonella* (< 5% resistance in Australia), *Serratia* (*Serratia marcescens* 0.125-1 mg/L), *Shigella*

(< 5% resistance in Australia), *Vibrio* (< 5% resistance in Australia), *Wolinella* (? 1 mg/L), *Yersinia enterocolitica* (0.03 mg/L), some Gram positive cocci (generally rather poor activity against streptococci; *Peptostreptococcus* MIC 0.5 mg/L, coagulase negative staphylococci 0.25-1 mg/L, *Streptococcus avium* 1 mg/L), Gram negative cocci (*Moraxella catarrhalis* 0.03-0.5 mg/L, *Neisseria gonorrhoeae* MIC 0.002-0.03 mg/L (4% less susceptible or resistant in Australia), *Neisseria meningitidis* (< 5% resistance in Australia), *Bacillus* (0.12-1 mg/L), various species of *Mycobacterium* (*Mycobacterium avium-intracellulare*, *Mycobacterium tuberculosis* 0.5-1 mg/L, *Mycobacterium ulcerans* 0.5 mg/L); resistance seen in *Staphylococcus aureus* (12% overall in Australia, 60% in methicillin resistant strains), *Pseudomonas aeruginosa* (13% in Australia), enteric Gram negative bacilli (*Klebsiella pneumoniae* 4% resistant in Australia), *Campylobacter*; poor activity against streptococci, none against anaerobes; constant use can induce resistance; expensive; in WHO model List of Essential Drugs as complementary drug when drugs in main list are known to be ineffective or inappropriate for given individual (tablet)

**Indications:** should be reserved for treatment of infections resistant to cheaper agents or where an oral agent is desirable and alternatives are parenteral; septic arthritis due to *Mycoplasma hominis*; bacteraemia and septicemia due to *Alcaligenes xylosoxidans*, *Campylobacter*, *Acinetobacter*; cat scratch disease; chancroid; cranial parameningeal deep fascial space infections (otogenic, following cranial surgery in normal patient); bacterial dysentery and gastroenteritis in immunocompromised; endocarditis due to *Legionella*; sexually acquired epididymitis and epididymo-orchitis; fish spine injury and other water-related infections due to *Vibrio*; bacterial gastroenteritis; gonorrhoea; joint and bone infections; lung abscess; postneonatal pyogenic meningitis due to *Acinetobacter*; meningococcal meningitis prophylaxis; *Mycobacterium avium-intracellulare* infection; pelvic sepsis and pelvic inflammatory disease due to *Neisseria gonorrhoeae*; perichondritis of pinna; pneumonia (due to *Klebsiella pneumoniae*, *Acinetobacter*; severe nosocomial); chronic prostatitis and seminal vesiculitis; *Pseudomonas aeruginosa* pulmonary infection in cystic fibrosis; respiratory tract infections in immunocompromised; *Salmonella* enteric fever (98% cure rate), enterocolitis (86% cure rate), chronic carriage (88% cure rate) and bacteraemia/metastatic infection (95% cure rate); local and generalised sepsis, cellulitis and pyoderma, malignant otitis externa due to *Pseudomonas*, *Aeromonas hydrophila* skin infections; acute skin ulcers due to *Flavobacterium meningosepticum*, moderate to severe traveller's diarrhoea; gonococcal vaginitis (?-lactamase positive)

**Side Effects:** nausea, vomiting, diarrhoea and abdominal pain in up to 10%; anxiety, nervousness, insomnia, euphoria, tremor in 1-4%; seizures reported; possible tendinopathy in adults and arthropathy in children and adults; sunlight sensitivity rash; peripheral neuropathy; red man syndrome with i.v. infusion; safety in pregnancy not established; monitor infant for diarrhoea in breastfeeding; dose adjustment required in renal failure and dialysis; antacids, didanosine, H<sub>2</sub>-antagonists, iron and zinc preparations and sucralfate reduce bioavailability; probenecid may reduce urinary excretion; increases theophylline plasma levels and unpredictably enhances warfarin activity; also interacts with caffeine

**NORFLOXACIN:** oral fluoroquinolone (take ½ to 1 h before food); no inoculum effect against aerobes, shows inoculum effect against anaerobes; 67% penetration into blister fluid, 90-120% penetration into prostatic tissue, 700-1400% penetration into cells; orally absorbed; spectrum includes *Aeromonas* (100% susceptible), *Bacillus* (1 mg/L), *Bacteroides ureolyticus*

(0.25 mg/L), *Bordetella pertussis* (0.25 mg/L), *Citrobacter amalonaticus* (100% susceptible), *Citrobacter diversus* (100% susceptible at > 0.06 mg/L), *Citrobacter freundii* (99% susceptible), *Citrobacter koseri* (0.06 mg/L), *Enterobacter* (0.25 mg/L), Enterobacteriaceae (0.25-0.5 mg/L), *Haemophilus influenzae* (100% susceptible at 0.12 mg/L), *Haemophilus parainfluenzae* (100% susceptible), *Haemophilus paraprophilus* (0.03 mg/L), *Hafnia alvei* (100% susceptible), *Klebsiella* (0.25 mg/L), *Moraxella* (1mg/L), *Moraxella catarrhalis* (100% susceptible at 0.12 mg/L), *Morganella morganii* (100% susceptible at 0.5 mg/L), *Mycobacterium fortuitum* (0.8 mg/L), *Neisseria gonorrhoeae* (100% susceptible at < 0.12 mg/L), *Neisseria meningitidis* (100% susceptible at < 0.12 mg/L), *Pasteurella multocida* (0.1 mg/L), *Pleisomonas* (0.06-0.5 mg/L), *Proteus mirabilis* (0.4% resistant in Australia), *Proteus vulgaris* (100% susceptible at 0.5 mg/L), *Providencia rettgeri* (0.25 mg/L), *Salmonella* (0.06-0.5 mg/L), *Serratia* (0.5 mg/L), *Shigella* (0.03-0.5 mg/L), coagulase negative staphylococci (100% susceptible at 1 mg/L), *Vibrio parahaemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.1-0.5 mg/L); in Australia, *Pseudomonas aeruginosa* 8% resistant, *Enterobacter cloacae* 1% resistant, *Escherichia coli* 0.3% resistant, *Klebsiella pneumoniae* 7% resistant

**Indications:** urinary tract (acute cystitis, especially complicated infections with mixed infections or with resistant organisms) and gastrointestinal (*Salmonella* enteric fever cure rate 89%, enterocolitis cure rate 80%, chronic carriage cure rate 78%; bacterial dysentery; cholera; bacterial gastroenteritis; moderate to severe traveller's diarrhoea; prophylaxis of traveller's diarrhoea in high risk host) infections; mild epididymitis and epididymo-orchitis associated with urinary tract infection; gonorrhoea; less severe acute and chronic prostatitis and seminal vesiculitis

**Side Effects:** nausea in 3%, headache in 3%, dizziness in 2%, fatigue, rash, abdominal pain, dyspepsia, somnolence, depression, insomnia, constipation, flatulence, heartburn in ? 1%, eosinophilia in 2%, elevation of ALT and AST in 2%, increased alkaline phosphatase in 1%, decreased white blood cell or neutrophil count in 1 %; tendinopathy; safety in pregnancy not established; caution in breastfeeding (monitor infant for diarrhoea); dose interval adjustment required in mild to moderate renal failure, not in dialysis; avoid in severe renal failure; antacids, didanosine, H<sub>2</sub>-antagonists and

sucralfate reduce bioavailability; probenecid may reduce urinary excretion; may increase plasma levels and effects of theophylline and warfarin

**OFLOXACIN:** oral and parenteral fluoroquinolone; 49% penetration into blister fluid, 39-115% penetration into sputum and bronchial secretions, 42-71% penetration into CSF, 2-48% penetration into aqueous humour, 61% penetration into bone, 170-317% penetration into prostatic tissue, 815% penetration into cells; spectrum includes *Acinetobacter calcoaceticus* (100% eradication), *Aeromonas* (100% susceptible at 0.5 mg/L), *Agrobacterium* (MIC 0.5 mg/L), *Bordetella* (100% susceptible at 0.5 mg/L), *Brucella* (0.03 mg/L), *Campylobacter* (100% susceptible at 2 mg/L), *Capnocytophaga* (100% susceptible at 0.5 mg/L), *Chlamydia* (100% susceptible at 2 mg/L, 97% eradication), *Corynebacterium* (100% susceptible at 1 mg/L), *Escherichia coli* (100% susceptible at 2 mg/L, 97% eradication), *Haemophilus ducreyi* (100% susceptible at 2 mg/L), *Haemophilus influenzae* (100% susceptible at 0.12 mg/L, 98% eradication), *Haemophilus parainfluenzae* (100% susceptible at 0.25 mg/L, 100% eradication), *Haemophilus paraprofilus* (0.03 mg/L), *Hafnia alvei* (100% susceptible at 0.25 mg/L), *Klebsiella* (100% susceptible at 1 mg/L, 98% eradication), *Legionella* (100% susceptible at 0.5 mg/L), *Moraxella catarrhalis* (100% susceptible at 0.5 mg/L, 100% eradication), *Morganella morganii* (100% susceptible at 0.5 mg/L), *Mycobacterium fortuitum* (100% susceptible at 2 mg/L), *Mycobacterium kansasii* (100% susceptible at 1 mg/L), *Mycobacterium xenopi* (100% susceptible at 2 mg/L), *Neisseria* (100% susceptible at 0.06 mg/L, 99-100% eradication), *Plesiomonas shigelloides* (0.015 mg/L), *Salmonella* (100% susceptible at 0.12 mg/L), *Shigella* (100% susceptible at 0.5 mg/L), *Staphylococcus aureus* (100% susceptible at 2 mg/L, 93% eradication), coagulase negative staphylococci (100% susceptible at 2 mg/L, 80-97% eradication), *Vibrio* (100% susceptible at 0.5 mg/L), *Yersinia* (100% susceptible at 0.25 mg/L); *Gardnerella vaginalis*, *Listeria*, *Nocardia*, *Mycobacterium avium-intracellulare*, *Mycobacterium chelonae*, *Mycobacterium scrofulaceum*, *Bacteroides*, anaerobic Gram positive cocci always resistant

**Indications:** in Australia, available as eye drops only; bacterial gastroenteritis; pseudomonal osteomyelitis (71% cure rate); prostatitis (85% cure rate); respiratory tract infections (67% cure rate); *Salmonella* enteric fever (100% cure rate), enterocolitis (100% cure rate), chronic carriage (100% cure rate) and bacteraemia/metastatic infection (100% cure rate); sexually transmitted infections (81% cure rate); skin infections (81% cure rate); moderate to severe traveller's diarrhoea; urinary tract infection (95% cure rate); conjunctivitis (topical)

**Side Effects:** tendinopathy, insomnia, headache; interacts with mineral antacids; dose adjustment required in renal failure and in dialysis; safety in pregnancy not established

**PEFLOXACIN:** fluoroquinolone; 59-60% penetration into blister fluid, 83-89% penetration into sputum and bronchial secretions, 9-66% penetration into CSF, 17-42% penetration into aqueous humour, 44-167% penetration into bone, 19-290% penetration into cells; spectrum includes *Acinetobacter* (MIC 1 mg/L), *Aeromonas hydrophila* (0.06 mg/L), *Agrobacterium* (0.25 mg/L), *Bacteroides ureolyticus* (0.12 mg/L), *Campylobacter fetus* (0.125-1 mg/L), *Campylobacter jejuni* (0.125-1 mg/L), *Capnocytophaga* (0.5 mg/L), *Citrobacter diversus* (? 0.03-0.5 mg/L), *Citrobacter freundii* (1 mg/L), *Citrobacter koseri*

(0.06 mg/L), *Clostridium perfringens* (< 0.25-1 mg/L), *Enterobacter aerogenes* (0.06-0.5 mg/L), *Enterobacter cloacae* (? 0.03-1 mg/L), Enterobacteriaceae (0.25-0.5 mg/L), *Escherichia coli* (0.125-0.25 mg/L), *Haemophilus ducreyi* (< 0.06 mg/L), *Haemophilus influenzae* (< 0.015-0.06 mg/L), *Klebsiella oxytoca* (? 0.03-0.5 mg/L), *Klebsiella pneumoniae* (0.5 mg/L), *Moraxella catarrhalis* (0.015-0.25 mg/L), *Morganella morganii* (0.5 mg/L), *Mycobacterium tuberculosis* (0.5 mg/L), *Neisseria gonorrhoeae* (0.016 mg/L), *Neisseria meningitidis* (0.03 mg/L), *Plesiomonas shigelloides* (0.06 mg/L), *Proteus mirabilis*

(? 0.03-1 mg/L), *Proteus vulgaris* (0.25 mg/L), *Providencia* (0.25 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Salmonella* (0.25 mg/L), *Serratia marcescens* (1 mg/L), *Shigella* (0.06-0.12 mg/L), *Staphylococcus aureus* (0.125-1 mg/L), *Staphylococcus epidermidis* (0.25-1 mg/L), *Staphylococcus haemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.25 mg/L)

**Indications:** myocarditis and pericarditis due to *Yersinia enterocolitica*; *Salmonella* enteric fever (96% cure rate)

**Side Effects:** tendinopathy; interacts with antacids, cimetidine

**ROSOXACIN:** fluoroquinolone; spectrum includes *Bordetella pertussis* (MIC 0.025 mg/L), *Enterobacter cloacae* (0.8 mg/L), *Escherichia coli* (0.05 mg/L), *Haemophilus influenzae* (0.05 mg/L), *Klebsiella pneumoniae* (0.8 mg/L), *Neisseria gonorrhoeae* (0.025 mg/L), *Neisseria meningitidis* (< 0.0125 mg/L), *Pasteurella multocida* (0.05 mg/L), *Salmonella typhi* (0.4 mg/L), *Serratia marcescens* (0.4 mg/L), *Shigella dysenteriae* (0.2 mg/L), *Staphylococcus aureus* (0.4 mg/L)

**Indications:** chancroid

**Side Effects:** tendinopathy

**IRLOXACIN:** fluoroquinolone; spectrum includes *Bacillus* (MIC 0.06 mg/L), *Staphylococcus* (0.5 mg/L)

**AMIFLOXACIN:** fluoroquinolone; spectrum includes *Acinetobacter* (MIC 1 mg/L), *Citrobacter* (0.125-0.5 mg/L), *Corynebacterium jeikeium* (1 mg/L), *Enterobacter* (0.25 mg/L), *Escherichia coli* (0.125 mg/L), *Haemophilus influenzae* (? 0.004 mg/L), *Klebsiella* (1 mg/L), *Proteus* (0.25 mg/L), *Serratia marcescens* (0.5 mg/L), *Staphylococcus haemolyticus* (1 mg/L)

**DIFLOXACIN:** fluoroquinolone; spectrum includes *Acinetobacter* (MIC 0.12 mg/L), *Bacteroides ureolyticus* (0.5 mg/L), *Citrobacter freundii* (0.5 mg/L), *Citrobacter koseri* (0.12 mg/L), *Enterobacter aerogenes* (0.5 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Legionella* (? 0.06-1 mg/L), *Moraxella catarrhalis* (0.12 mg/L), *Neisseria gonorrhoeae* (0.016 mg/L), *Providencia rettgeri* (1 mg/L), *Staphylococcus aureus* (0.25 mg/L), *Staphylococcus epidermidis* (0.5 mg/L)

**FLEROXACIN:** fluoroquinolone; 62% penetration into blister fluid; spectrum includes *Aeromonas* (MIC ? 0.06 mg/L), *Escherichia coli* (< 0.06-1 mg/L), *Haemophilus influenzae* (0.03-0.06 mg/L), *Moraxella catarrhalis* (0.125-0.5 mg/L), *Plesiomonas shigelloides* (? 0.06 mg/L), *Salmonella* (0.25-0.5 mg/L), *Shigella* (? 0.06-0.125 mg/L), *Staphylococcus aureus* (0.25-0.5 mg/L), *Staphylococcus epidermidis* (0.5-1 mg/L), *Vibrio* (? 0.06-0.125 mg/L), *Yersinia frederiksenii* (0.25 mg/L), *Yersinia kristensenii* (? 0.06 mg/L), *Yersinia pseudotuberculosis* (0.125 mg/L)

**Indications:** *Salmonella* enteric fever (cure rate 100%)

**Side Effects:** tendinopathy; phototoxicity and photocarcinogenicity; interacts with mineral antacids; dose adjustment required in moderate to severe renal failure (glomerular filtration rate < 50 mL/min); dose required after intermittent haemodialysis

**LOMEFLOXACIN:** spectrum includes aerobic Gram negative bacilli (MIC<sub>90</sub> 1 mg/L; *Citrobacter* 0.5 mg/L, *Enterobacter* 0.5 mg/L, *Escherichia coli* 0.25 mg/L, *Haemophilus* 0.06 mg/L, *Klebsiella* 1 mg/L, *Morganella morganii* 0.25 mg/L, *Proteus* 0.25 mg/L, *Providencia* 1 mg/L, *Serratia* 0.5 mg/L), coagulase negative staphylococci (1 mg/L), *Neisseria* (0.112 mg/L), *Staphylococcus aureus* (1 mg/L)

**Side Effects:** phototoxicity and photocarcinogenicity; tendinopathy

**LEVOFLOXACIN:** optical isomer of ofloxacin; bioavailability 99%, T<sub>max</sub> 1.3 h, C<sub>max</sub> 5.1 mg/L, AUC 48 mg.hr/L, protein binding 24-38%, half life 7.6 h; higher activity against ofloxacin sensitive strains and safer; active against *Chlamydia pneumoniae* (MIC<sub>90</sub> 0.25 mg/L), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.12 mg/L), *Legionella pneumophila* (0.03 mg/L), *Moraxella catarrhalis* (0.06 mg/L), *Mycoplasma pneumoniae* (0.06 mg/L), methicillin susceptible *Staphylococcus aureus* (0.25 mg/L), *Streptococcus pneumoniae* (1 mg/L)

**Indications:** uncomplicated urinary tract infections in women, community acquired pneumonia

**Side Effects:** nausea in 1.3%, diarrhoea in 1%; tendinopathy

**TOSUFLOXACIN:** activity includes *Streptococcus pneumoniae* (MIC 0.39 mg/L, bacterial elimination 90%)

**Indications:** community-acquired pneumonia

**Side Effects:** tendinopathy

**SPARFLOXACIN:** activity includes *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Streptococcus pneumoniae* (MIC

0.78 mg/L, bacterial elimination 91%)

**Indications:** community-acquired pneumonia

**Side Effects:** tendinopathy

**GREPAFLOXACIN:** high lung tissue concentration, minimal urine concentration; activity includes *Streptococcus pneumoniae* (MIC 0.78 mg/L), *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*; withdrawn from market because of severe anaphylaxis, prolongation of QT interval, cardiotoxicity

**GATIFLOXACIN:** extended spectrum (8-methoxy) oral fluoroquinolone (once daily; timing to food does not matter); bioavailability 96%, T<sub>max</sub> 1 h, C<sub>max</sub> 3.8 h, AUC 33 mg.h/L; protein binding 20%, half life 7.8 h; increased activity against Gram positive bacteria (including streptococci), wide activity against Gram negative aerobes, anaerobes and agents of atypical pneumonia; not as active as ciprofloxacin against *Pseudomonas*, active against *Bacteroides fragilis*

(MIC<sub>90</sub> 1 mg/L), *Chlamydomphila pneumoniae* (0.06 mg/L), *Clostridium perfringens* (1 mg/L), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Fusobacterium nucleatum* (0.5 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.06 mg/L), *Legionella pneumophila* (0.016 mg/L), *Mycoplasma pneumoniae* (0.05 mg/L), methicillin susceptible *Staphylococcus aureus* (0.12 mg/L), *Streptococcus pneumoniae* (0.5 mg/L)

**Indications:** acute sinusitis caused by *Streptococcus pneumoniae* or *Haemophilus influenzae*; acute bacterial exacerbation of chronic bronchitis caused by *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Haemophilus parainfluenzae* or *Moraxella catarrhalis*; community acquired pneumonia caused by *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Moraxella catarrhalis*, *Legionella pneumophila*, *Chlamydomphila pneumoniae* or *Mycoplasma pneumoniae*; urinary tract infections caused by *Escherichia coli*, *Klebsiella pneumoniae* or *Proteus mirabilis*; pyelonephritis caused by *Escherichia coli*, uncomplicated skin and skin structure infections

**Side Effects:** prolongation of QT interval (increased risk with any drug capable of prolonging the QT interval), nausea, diarrhoea, headache, dizziness, tendinopathy, hypoglycaemia, vaginitis in 6%

**TROVAFLOXACIN:** active against a wide range of respiratory pathogens, especially *Streptococcus pneumoniae* (including penicillin resistant strains); half life ? 13 h; suspended in July 1999 because of hypoglycaemia, eosinophilia and liver toxicity

**PRUFLOXACIN:** active mainly against Gram negatives (especially *Pseudomonas aeruginosa*)

**PAZUFLOXACIN:** similar spectrum to ciprofloxacin

**Side Effects:** dizziness in 1/2300 only recorded adverse effect; probable tendinopathy

**MOXIFLOXACIN:** oral (once daily; timing to food does not matter) extended spectrum fluoroquinolone (8-methoxyquinolone); increased activity against Gram positive organisms (including streptococci), wide activity against Gram negative aerobes, anaerobes and agents of atypical pneumonia, but less activity against *Pseudomonas*; active against *Aeromonas*, *Bacteroides fragilis* (MIC<sub>90</sub> 0.5 mg/L), *Bordetella pertussis*, *Chlamydomphila pneumoniae* (0.03 mg/L), *Clostridium perfringens* (0.5 mg/L), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Fusobacterium nucleatum* (0.25 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.12 mg/L), *Legionella pneumophila* (0.015 mg/L), *Moraxella catarrhalis* (0.06 mg/L), *Mycobacterium tuberculosis* (0.12-0.5 mg/L), *Mycoplasma pneumoniae* (0.06-0.12 mg/L), *Neisseria gonorrhoeae*, methicillin susceptible *Staphylococcus aureus* (0.12 mg/L), *Streptococcus pneumoniae* (0.12 mg/L)

**Indications:** acute bacterial sinusitis, acute bacterial exacerbations of chronic bronchitis, community acquired pneumonia

**Side Effects:** mild to moderate nausea, diarrhoea; prolongation of QT interval (use with caution in patients receiving antiarrhythmia agents—quinidine, procainamide, amiodarone, sotalol); tendinopathy; dose adjustment unnecessary in renal dysfunction or mild to moderate hepatic dysfunction; safety in pregnancy not established

**Contraindications:** avoid in breastfeeding (insufficient data)

**ANSAMYCINS (RIFAMYCINS):** active against Gram positive organisms (including staphylococci) and *Mycobacterium*; rapid emergence of resistance dictates usage in combination with unrelated antimicrobials

**Side Effects:** gastrointestinal effects, orange discolouration of body fluids, staining of soft contact lenses common; allergic reactions, wheeze, flu-like syndrome, blood dyscrasias uncommon; pseudomembranous colitis, neurological symptoms, thrombophlebitis (i.v.) rare

**RIFAMPICIN (RIFAMPIN):** oral ansamycin (take ½ -1 h before food); inhibits DNA-dependent RNA polymerase; no significant change in V<sub>d</sub> or clearance in elderly; bactericidal; lethal for proliferating bacteria and bacteria in latent phase; in high concentrations, penetrates into mammalian cells; active against Gram positive and Gram negative bacteria and mycobacteria; spectrum includes *Bacillus anthracis* (MIC 0.6 mg/L), *Brucella* (0.06-1 mg/L), *Clostridium perfringens* (0.02 mg/L), *Corynebacterium*, *Coxiella burnetii*, *Haemophilus influenzae* (0.02 mg/L), *Legionella* (? 0.008-0.5 mg/L), *Listeria monocytogenes* (0.06 mg/L), *Mycobacterium avium* (0.02 mg/L), *Mycobacterium tuberculosis* (0.05 mg/L; spontaneous resistance 1:10<sup>8</sup> organisms; dosage 600 mg daily or twice weekly), *Neisseria gonorrhoeae* (0.02 mg/L), *Neisseria meningitidis* (< 5% resistance in Australia), *Rickettsia rickettsii*, *Rickettsia typhi*, *Streptococcus canis* (100% susceptible at 0.03 mg/L), *Streptococcus pneumoniae* (0.01 mg/L), *Streptococcus pyogenes* (0.02 mg/L); methicillin resistant *Staphylococcus aureus* 12% resistant in Australia; reduces bacterial adherence, increases neutrophil

penetration and intracellular killing; inhibits chemotactic activity of granulocytes; shows microbicidal activity against bacteria ingested by monocytes or macrophages; in WHO Model List of Essential Drugs as antileprosy drug and antituberculosis drug; mode of elimination hepatic, gastrointestinal; very potent inducer of hepatic P450 activity

**Indications:** mainly tuberculosis, *Mycobacterium avium* complex infections, methicillin resistant *Staphylococcus aureus* infections, prophylaxis in contacts of *Haemophilus influenzae* type b and meningococcal infections; anterior uveitis due to *Mycobacterium tuberculosis*; septic arthritis due to *Mycobacterium tuberculosis*, methicillin resistant *Staphylococcus aureus*, *Brucella*; bacteraemia and septicemia due to methicillin resistant *Staphylococcus aureus* (should never be used alone), *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*; bone marrow infections due to *Mycobacterium tuberculosis*, *Brucella*; tuberculous brain and epidural abscess; brucellosis in non-pregnant/nursing; cat scratch disease; staphylococcal cerebrospinal fluid shunt infections; cholangitis and cholecystitis; chorioretinitis due to *Mycobacterium tuberculosis*; purulent conjunctivitis due to *Haemophilus aegyptius*; treatment and prophylaxis of disseminated mycobacteriosis due to *Mycobacterium gordonae* in non-AIDS patients; endocarditis due to *Brucella*, *Flavobacterium meningosepticum*, *Stenotrophomonas maltophilia*, *Coxiella burnetii*, *Legionella*, methicillin resistant *Staphylococcus aureus*; granulomatous synovitis; hepatic granuloma due to *Mycobacterium tuberculosis*; hepatitis due to *Mycobacterium tuberculosis*, *Coxiella burnetii*, *Brucella*; leprosy in adults; lymph gland infections due to *Mycobacterium tuberculosis*; meningitis due to *Flavobacterium meningosepticum*, *Brucella*, *Mycobacterium tuberculosis*, penicillin resistant *Streptococcus pneumoniae*, *Haemophilus influenzae* and meningococcal meningitis carriers and prophylaxis; meningoencephalitis due to *Brucella*; mesenteric lymphadenitis due to *Mycobacterium tuberculosis*; tuberculous mouth ulcers; mycobacteriosis due to *Mycobacterium kansasii*; myocarditis and pericarditis due to *Actinomyces*, *Coxiella burnetii*; oesophagitis due to *Mycobacterium tuberculosis*; ornithosis; otitis media due to *Corynebacterium bovis*, *Mycobacterium tuberculosis*; peritonitis due to *Mycobacterium tuberculosis*; pneumonia and pneumonitis (tuberculous, moderately severe to severe due to *Legionella pneumophila*, diffuse interstitial due to *Rhodococcus equi*, due to *Mycobacterium szulgai*, *Mycobacterium xenopi*); less severe acute prostatitis and seminal vesiculitis and epididymitis and epididymoorchitis due to *Mycobacterium tuberculosis*; pulmonary abscess; pulmonary tuberculosis due to *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium kansasii*, *Mycobacterium xenopi*, *Mycobacterium szulgai*; acute Q fever; splenic abscess due to *Mycobacterium tuberculosis*; treatment and prophylaxis of tuberculosis; chronic ulcers due to *Mycobacterium marinum*, *Mycobacterium ulcerans*, *Arcanobacterium haemolyticum*, *Corynebacterium bovis*

**Side Effects:** > 600 mg dose ? 'flu syndrome' (fever, chills, headache, bone pain, dizziness); hypersensitivity syndrome (flushing, fever, redness of eyes and thrombocytopenia), shock, shortness of breath, haemolytic anaemia, renal failure, immune thrombocytopenia with high dosage intermittent therapy, hepatotoxicity (in 3% of children; more likely if combined with isoniazid; ? 1% of all patients; check liver function before commencing treatment), gastrointestinal disturbances, blurred vision, skin rashes; discolours urine, sputum, tears and sweat (and soft contact lenses) reddish-brown; single case report of hearing loss; dosage modification not required in renal dysfunction nor in dialysis; reduce dosage to 1/2 to 2/3 normal in liver dysfunction or avoid; accelerates metabolism of several other drugs, including oestrogen (high incidence of menstrual irregularities and pregnancy in patients on oral contraceptives); combination with pyrazinamide can cause potentially lethal hepatitis; can significantly reduce plasma concentrations and effects of alfentanil, atovaquone, caspofungin, chloramphenicol, clarithromycin, clozapine, codeine, cortisone, cyclosporin, dapsone, delavirdine, dexamethasone, diazepam, diclofenac, digitoxin, digoxin, diltiazem, disopyramide, efavirenz, fluconazole, fludrocortisone, fluvastatin, glibenclamide, haloperidol, hydrocortisone, itraconazole, ketoconazole (rifampicin levels may increase or decrease), losartan, methadone (producing symptoms of narcotic withdrawal in addicts on maintenance), metoprolol, mexiletine, midazolam, nifedipine, nitrazepam, oral contraceptives (likely to reduce effectiveness), paracetamol, phenytoin, prednisolone, quinidine, tacrolimus, terbinafine, theophylline, tolbutamide (may make diabetic control more difficult), triazolam, verapamil, warfarin (effect may persist 10-14 d after ceasing), human immunodeficiency virus-related protease inhibitors, voriconazole, zidovudine; plasma levels markedly reduced by phenobarbitone and phenytoin; plasma levels may be increased by cotrimoxazole, probenecid; clinically significant interactions also with glucocorticoids, quinidine sulphate, buspirone hydrochloride, zolpidem tartrate, simvastatin, propafenone hydrochloride, ondansetron hydrochloride, opiates; increases metabolism of enalapril causing increased

plasma levels of active metabolite (enalaprilat); phenobarbitone reduces bioavailability; monitor infant for jaundice if breastfeeding

**Contraindications:** pregnancy; treatment with protease inhibitors or nonnucleoside transcriptase inhibitors

#### **RIFAMIDE**

**Indications:** biliary infections; treatment and prophylaxis of *Mycobacterium avium* complex infections

**Side Effects:** hypersensitivity reactions, gastrointestinal disturbances, skin reactions, pain at injection site, yellow discolouration of skin, darkens urine

**RIFABUTIN:** oral ansamycin (relationship of dose to food doesn't matter)

**Indications:** treatment and prophylaxis of disseminated mycobacteriosis and pancreatitis due to *Mycobacterium avium-intracellulare*; disseminated mycobacteriosis due to *Mycobacterium malmoense*

**Side Effects:** rash, hepatitis, fever, thrombocytopenia, orange-coloured body fluids (secretions, urine, tears— may permanently discolour contact lenses); uveitis common; less potent inducer of P450 activity than rifampicin; may reduce plasma levels and effects of clarithromycin, dapsone, diazepam, itraconazole, ketoconazole, methadone, oral contraceptives (likely to reduce effectiveness), oral hypoglycemics, prednisolone, verapamil, warfarin, protease inhibitors (bioavailability of rifabutin increased), nonnucleoside reverse transcriptase inhibitors, digitalis, beta-blockers, anticonvulsives, theophylline; increase of plasma levels by clarithromycin or fluconazole may cause uveitis, severe arthralgias, leucopenia; significantly decreases bioavailability of indinavir; indinavir increases bioavailability; markedly decreases delavirdine effect (increased metabolism) while increasing rifabutin toxicity (decreased metabolism); dose adjustment not required in renal failure or in dialysis

**Contraindications:** pregnancy; avoid if breastfeeding (insufficient data); treatment with ritonavir, saquinavir hard-gel cap or delavirdine

**RIFAPENTINE:** oral ansamycin

**Indications:** treatment of pulmonary tuberculosis (once weekly dosing effective in continuation phase except in HIV/AIDS patients)

**Side Effects:** hyperuricaemia, elevated ALT and AST, neutropenia; reduces plasma concentrations and increases clearance of indinavir

**SULPHONAMIDES:** inhibit dihydropteroate synthetase, thereby producing competitive inhibition of para-aminobenzoic acid; bacteriostatic; mode of elimination renal; decreased bacteriostatic effect under anaerobic conditions

**Indications:** now have limited use; glanders; hepatitis due to *Burkholderia pseudomallei*, *Mycobacterium leprae*, *Nocardia*; meningitis due to *Nocardia asteroides*; lack of efficacy in treatment of *Shigella* or other intestinal infections

**Side Effects:** neonatal jaundice (< 2 mo, mother in late pregnancy), hypersensitivity reactions (rare anaphylactic shock), gastrointestinal disturbances (fever, nausea, vomiting, diarrhoea common), skin reactions (rash common), anorexia (common), Stevens-Johnson syndrome (rare), toxic epidermal necrolysis (rare), photosensitivity, headache (uncommon), drowsiness (uncommon), malaise, dizziness, tinnitus, vestibular symptoms, paresthesias, possible crystalluria (depends on solubility and urinary concentration), haematological complications (blood dyscrasias; uncommon), haemolytic anaemia in those with glucose-6-phosphate dehydrogenase deficit, megaloblastic anaemia (rare), pulmonary eosinophilia and infiltrates (rare), nephrotoxicity, erythema (rare), hepatitis (rare), aseptic meningitis (rare), ? precipitate polyarteritis nodosa; cause neutropenia by myelosuppression; short-acting safe in therapeutic amounts during pregnancy; further dose required after haemodialysis; likely enhanced warfarin effect (frequent monitoring of prothrombin time essential); very weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

**Contraindications:** avoid long-acting in renal dysfunction and pregnancy; avoid if breastfeeding G6PD deficient infant or premature infant or < 1 mo

**SULPHABENZAMIDE:** sulphonamide

#### **SULPHACETAMIDE**

**Indications:** mycobacterial keratitis and iritis

**Side Effects:** allergy, overgrowth of non-susceptible organisms

**Contraindications:** pregnancy

**SULPHADIAZINE:** oral (take with or after food); serum binding 56%; no significant change in protein binding in elderly; in WHO Model List of Essential Drugs

**Indications:** endocarditis due to *Flavobacterium meningosepticum*; postneonatal pyogenic meningitis due to *Flavobacterium meningosepticum*; nocardiosis; rheumatic fever prophylaxis; tenosynovitis; trachoma

**Side Effects:** moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias)

**Contraindications:** pregnancy

**SILVER SULPHADIAZINE:** anti-infective dermatological drug; in WHO Model List of Essential Drugs; staphylococci (including MRSA) and *Pseudomonas aeruginosa* susceptible

**Indications:** burns prophylaxis; folliculitis and rash due to *Pseudomonas aeruginosa*, *Yersinia*

**Side Effects:** sensitivity

**Contraindications:** pregnancy

#### **SULPHADIMIDINE**

**INDICATIONS:** infections with *Nocardia asteroides*; acute maxillary sinusitis; urethritis; lower urinary infections; in WHO Model List of Essential Drugs and in UNHCR Basic List of Essential Drugs

**Side Effects:** nausea, vomiting, rashes, blood disorders, allergic reactions; take blood counts in prolonged treatment, maintain adequate fluid intake; dose adjustment required in renal failure (monitor for myelosuppression)

**Contraindications:** pregnancy, children < 6 w, renal/hepatic failure, jaundice, blood disorders; caution in renal impairment, breast feeding

#### **SULPHAMETAPYRAZINE**

**Indications:** trachoma

**Side Effects:** rashes, dizziness, nausea

**Contraindications:** liver or kidney disease

**SULPHAMETHOXAZOLE:** impairs intracellular killing; oral (take with or after food)

**Indications:** lymphogranuloma venereum; mastoiditis prophylaxis; mycobacteriosis due to *Mycobacterium kansasii*; osteomyelitis and osteochondritis due to *Mycobacterium fortuitum*, *Nocardia asteroides*; mycobacterial local and generalised sepsis

**Side Effects:** moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias (monitor for myelosuppression)) and in dialysis; toxic level > 450 µmol/L

**Contraindications:** pregnancy

**SULPHATHIAZOLE:** sulphonamide

**SULPHIDOXIME:** sulphonamide

**SULPHISOXAZOLE:** delayed absorption, no significant change in  $V_d$ , reduced clearance in elderly

**Indications:** chancroid; *Mycobacterium chelonae* and *Mycobacterium fortuitum* infections; nocardiosis; otitis media prophylaxis; trachoma

**Side Effects:** rashes, dizziness, nausea, aseptic meningitis

**Contraindications:** liver or kidney disease; pregnancy

**SULPHAMETHIZOLE:** only readily accessible oral straight sulphonamide on market in Australia

**Indications:** urinary tract infections

**Side Effects:** infrequent nausea, vomiting, abdominal pain, anorexia, pancreatitis, malaise, headache, dizziness, fever, rare hypersensitivity, aseptic meningitis, extremely rare serious blood dyscrasias; moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias)

**Contraindications:** last month of pregnancy, lactation

#### **TRIPLE SULPHA**

**Indications:** cellulitis due to *Mycobacterium fortuitum*, pulmonary tuberculosis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*; bacterial vaginitis (topical)

**TRIMETHOPRIM:** inhibits enzyme dihydrofolate reductase; bacteriostatic; oral (take with or after food; daily dose); serum protein binding 50%; requires further dose after haemodialysis; impairs intracellular killing; spectrum includes *Haemophilus influenzae* (MIC 0.5 mg/L), *Listeria monocytogenes* (0.12 mg/L); *Moraxella catarrhalis* 98% intrinsic resistance (possibly all resistant in clinical practice), *Pseudomonas aeruginosa* 100% intrinsic resistance; in Australia, *Streptococcus pneumoniae* 52% resistant, *Escherichia coli* 22% resistant, *Enterobacter cloacae* 23% resistant, *Klebsiella pneumoniae* 26% resistant, *Proteus mirabilis* 28% resistant, *Staphylococcus aureus* 27% resistant overall (methicillin

susceptible strains 3%); in WHO Model List of Essential Drugs as complementary drug for use when drugs in main list are known to be ineffective or inappropriate for a given individual; mode of elimination renal

**Indications:** acute cystitis treatment and prophylaxis of recurrent; prophylaxis of recurrent nonvenereal dysuria-frequency syndrome; mild acute epididymitis and epididymo-orchitis associated with urinary tract infection; listerial meningitis; less severe acute and chronic prostatitis and seminal vesiculitis; mild acute pyelonephritis; prophylaxis of traveller's diarrhoea in high risk children

**Side Effects:** rash in 8%, sore mouth, aseptic meningitis, others as for sulphonamides but less common gastrointestinal and haematological effects; no adjustment of dosage in renal failure but monitor for blood dyscrasias; dose required after intermittent haemodialysis; safety in pregnancy not established; safe in breastfeeding; additional suppression of folate metabolism with pyrimethamine may result in megaloblastic anaemia, serious pancytopenia; less likely enhanced warfarin effect; increases plasma levels of digoxin, phenytoin; weak association with oral contraceptive failure

**COTRIMOXAZOLE:** trimethoprim + sulphamethoxazole; oral (twice a day, with or after food); optimum degree of antibacterial synergy may be lost with extremes of urinary pH (particularly acid pH); spectrum includes *Aeromonas hydrophila* (100% susceptible), *Alcaligenes*, *Brucella* (? 0.25-1 mg/L), *Citrobacter diversus* (88% susceptible), *Eikenella corrodens* (95% susceptible), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (12% resistant in Australia), *Enterococcus durans* (100% susceptible at 1 mg/L), *Enterococcus faecalis* (100% susceptible at 1 mg/L), *Enterococcus faecium* (100% susceptible at ? 0.06 mg/L), *Flavobacterium*, *Haemophilus influenzae* (not meningitis; 0.03-0.25 mg/L), *Haemophilus parainfluenzae*, *Haemophilus paraprophilus* (0.03-1 mg/L), *Klebsiella oxytoca* (100%), *Listeria monocytogenes* (100% susceptible at ? 0.06 mg/L; drug of choice), *Moraxella catarrhalis* (7% resistant in Australia), *Morganella morganii* (100% susceptible at 1 mg/L), *Neisseria gonorrhoeae*, *Neisseria meningitidis* (? 0.06-0.6 mg/L), *Nocardia* (drug of choice), *Pasteurella multocida* (95% susceptible), *Proteus mirabilis* (18% resistant in Australia), *Proteus vulgaris* (100% susceptible at 0.5 mg/L), *Pseudomonas pseudomallei*, *Salmonella* (100% susceptible), *Serratia* (88% susceptible), *Shigella* (100% susceptible), *Staphylococcus aureus* (26% resistance (mainly in methicillin resistant strains) in Australia), *Stenotrophomonas maltophilia* (98% of hospital isolates), *Streptococcus agalactiae* (0.12-0.25 mg/L), *Streptococcus bovis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (80% resistant in Australia), *Yersinia*; *Streptococcus pyogenes* resistant; *Pseudomonas aeruginosa* 100% intrinsic resistance; in Australia, *Escherichia coli* 19% resistant, *Klebsiella pneumoniae* 15% resistant; in WHO Model List of Essential Drugs; cheap

**Indications:** widespread use as broad spectrum agent, particularly in respiratory and urinary tract infections; should be restricted to few clinical situations where it is drug of choice (cat and dog bite infections; human bite and clenched fist infections; *Listeria monocytogenes* infection in penicillin hypersensitive; *Nocardia* infections; acute otitis media in remote areas); also used for reactive arthritis due to *Shigella*, *Salmonella*, *Yersinia*; bacteraemia and septicemia due to *Salmonella*, *Burkholderia pseudomallei*, *Alcaligenes xylosoxidans*, *Yersinia enterocolitica*, *Campylobacter fetus subsp fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*, *Stenotrophomonas maltophilia*, *Ochrobacterium anthropi*, *Oerskovia*; asymptomatic bacteriuria; bone marrow infection due to *Brucella*, *Salmonella typhi*; brain and epidural abscess due to *Brucella*; brucellosis in children < 8 y; cerebrospinal fluid shunt infections due to *Staphylococcus*, diphtheroids, *Propionibacterium*, cellulitis due to *Mycobacterium fortuitum*, chancroid; cholera; acute cystitis in children when trimethoprim syrup not available; disseminated mycobacteriosis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*, bacterial dysentery; dysuria-frequency syndrome due to Gram negative bacilli; endocarditis due to *Brucella*, *Stenotrophomonas maltophilia*, *Coxiella burnetii*; enteric fevers; acute epididymitis and epididymo-orchitis due to *Salmonella*; erysipelas-like condition due to *Yersinia enterocolitica*; glanders; gonorrhoea; granuloma inguinale; bacterial hepatic abscess; hepatic granuloma due to *Burkholderia pseudomallei*; hepatitis due to *Salmonella typhi*, *Shigella*, *Burkholderia pseudomallei*, *Brucella*, *Yersinia pseudotuberculosis*; melioidosis; meningoenzephalitis due to *Brucella*; mesenteric lymphadenitis due to *Yersinia*; mycetoma due to nocardiforms; orchitis due to *Salmonella*; osteomyelitis; otitis media due to *Haemophilus influenzae*, *Neisseria*; peritonitis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*; pharyngitis; pneumonia (mild *Haemophilus influenzae*, *Stenotrophomonas maltophilia*, *Acinetobacter*); *Burkholderia pseudomallei* pneumonitis; pseudotuberculosis; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; pulmonary tuberculosis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*, less severe acute prostatitis; prostatic abscess; acute respiratory infection in outpatients;

rhinoscleroma; rickettsioses; acute sinusitis; systemic infection prophylaxis in agammaglobulinemia, cell-mediated immunity disorders, granulocytopenia, microbial abnormality; tenosynovitis; moderate to severe traveller's diarrhoea; traveller's diarrhoea prophylaxis in high risk host; severe lower urinary tract infections; whooping cough, treatment of community-associated methicillin resistant *Staphylococcus aureus*

**Side Effects:** very high risk of serious adverse reactions (similar to sulphonamides), low risk of gastrointestinal adverse effects, moderate risk of skin rash; nausea and vomiting (7% in AIDS), skin reactions (10% in AIDS), headache, dizziness, haematological complications (folate metabolism may be impaired, especially in elderly; neutropenia 17% in AIDS; thrombocytopenia), pseudomembranous colitis, hypersensitivity reactions common, bone marrow suppression, megaloblastic marrow, azotemia, hepatitis, elevated levels of liver enzymes (20% in AIDS); nephrotoxicity, potential false increase in serum creatinine, hypoglycaemia in renal insufficiency (adjust dose appropriately, monitor renal function); acute hypotensive syndrome resembling septic shock in AIDS; may cause photosensitivity, hearing loss; possible additive antifolate effect with methotrexate, causing bone marrow depression, pancytopenia; aseptic meningitis; toxic level > 150 mg/L peak sulphamethoxazole, > 3 mg/L peak trimethoprim (monitor occasionally in renal impairment or with high doses); dose adjustment required in renal failure and in dialysis; take blood counts in prolonged treatment and in renal failure; maintain adequate fluid intake; decreases cyclosporin levels; potentiation of effect of warfarin likely by inhibiting metabolism; serious pancytopenia and megaloblastic anaemia from additional suppression of folate metabolism with pyrimethamine; plasma levels of rifampicin may be increased; weak association with oral contraceptive failure

**Contraindications:** pregnancy, children < 6 w, renal/hepatic failure, breast feeding (infant premature or < 1 mo); avoid in elderly

**NIBRISIN:** trimethoprim + sulphadiazine

**Indications:** bronchitis; pneumonia; sinusitis; tonsillitis

**AMINOGLYCOSIDES:** parenteral; act on 30S ribosome producing nonsense proteins from misreading of mRNA; bactericidal; activity depends on concentrations achieved over time; once-daily dosing as efficacious, cheaper and less likely to cause nephrotoxicity than more frequent dosing; *Stenotrophomonas maltophilia* 79% intrinsic resistance (possibly all resistant in clinical practice), anaerobes 100% intrinsic resistance, *Enterococcus* and *Streptococcus* 100% intrinsic resistance; induce postantibiotic effect even after brief periods of exposure; decreased antibacterial effect under anaerobic conditions; mode of elimination renal; decrease neutrophil chemotaxis, no effect on phagocytosis, reduce bacterial adherence, no effect on neutrophil penetration, decrease intracellular killing; no effective CNS penetration; produce relatively low amounts of endotoxins

**Indications:** cellulitis due to *Aeromonas hydrophila*; purulent conjunctivitis due to *Pseudomonas aeruginosa*; endocarditis due to *Escherichia coli*, *Corynebacterium*, infantile diarrhoea; infections with coliforms; intraabdominal infections; neonatal necrotising enterocolitis; bacterial parotitis and submandibular sialadenitis; initial treatment of serious Gram negative infections; systemic infections in granulocytopenia

**Side Effects:** neurotoxicity (common), gastrointestinal disturbances, skin reactions (sensitivity with topical use), neuromuscular blockade (rare respiratory depression; administer calcium and neostigmine for severe; increases effect of neuromuscular blockers and potentiates respiratory depression), nephrotoxicity (common; enhanced by aciclovir, amphotericin, cephalothin, bumetanide, ethacrynic acid, frusemide, vancomycin, NSAIDs, cyclosporin, cidofovir, capreomycin; prevented by polyaspartic acid), ototoxicity (vestibular and auditory; common; increased risk when combined with 'loop' diuretics (bumetanide, ethacrynic acid, frusemide), capreomycin), hypersensitivity (uncommon); inactivation by penicillins in renal insufficiency or if mixed together; relative contraindications: hearing impairment, old age, neuromuscular blockade, previous aminoglycoside exposure; increase nephrotoxicity of cyclosporine; in renal insufficiency, monitor renal function, avoid prolonged therapy and concurrent cephalothin (increased risk of nephrotoxicity, particularly in elderly), avoid other ototoxic drugs and neuromuscular blocking agents (potentiate respiratory suppression produced by these agents), avoid neomycin; further dose required after haemodialysis

**AMIKACIN:** aminoglycoside most resistant to enzymatic inactivation; at least 20 times as expensive as gentamicin; no significant change in clearance in elderly; low to moderate postantibiotic effect; no inoculum effect; spectrum includes *Aeromonas hydrophila* (100% susceptible), Enterobacteriaceae (< 5% resistance in Australia), Group IVe (MIC 0.25-1 mg/L), Group Ve (0.13-0.5 mg/L), *Mycobacterium chelonae*, *Yersinia enterocolitica* (100% susceptible); in Australia, *Pseudomonas aeruginosa* 13% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active

antibacterials, may occur by production of 6'-aminoglycoside acetyltransferase/2''-aminoglycoside phosphotransferase, 6'-aminoglycoside acetyltransferase or 3'-aminoglycoside phosphotransferase

**Indications:** must be reserved for treating infections due to microorganisms resistant to other aminoglycosides; bacteraemia and septicemia due to *Pseudomonas aeruginosa*; disseminated mycobacteriosis due to *Mycobacterium avium* in AIDS, *Mycobacterium chelonae* and *Mycobacterium fortuitum* in non-AIDS patients; endocarditis due to *Pseudomonas aeruginosa*, *Mycobacterium chelonae*, *Mycobacterium fortuitum*; meningitis due to *Pseudomonas aeruginosa*, *Nocardia asteroides*; mycetoma due to nocardiforms; mycobacteriosis due to *Mycobacterium kansasii*; peritonitis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*, *Klebsiella pneumoniae* pneumonia; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; mycobacterial local and generalised sepsis

**Side Effects:** less nephrotoxic than gentamicin or sisomicin but more audiotoxic than netilmicin; toxic level > 5 mg/L trough (monitor routinely at least once during a course of therapy); dose adjustment needed for renal failure and dialysis

**Contraindications:** pregnancy

**FRAMYCETIN (SOFRAMYCIN):** aminoglycoside

**Indications:** *Staphylococcus aureus* blepharitis (ointment); 'swimmer's ear' (topical); chronic discharging otitis media in remote communities

**Side Effects:** ototoxicity (cochlear function), intestinal malabsorption (continued use of oral)

**Contraindications:** use in ear when drum perforation known or suspected; pregnancy

**GENTAMICIN:** aminoglycoside of choice for most cases (? 95%) of hospital acquired aerobic Gram negative sepsis but more nephrotoxic than amikacin or tobramycin; cheaper than kanamycin; i.m. or i.v. twice daily or once daily (adults only) or single i.m. dose (urinary tract infection in children); 27% bronchial penetration 2-3 h after 0.2 mg/kg i.m. dose; 25-30% serum protein binding; no significant change in  $V_d$  in elderly; low to moderate postantibiotic effect; bactericidal; lethal for proliferating bacteria and for bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive and Gram negative bacteria— wide spectrum including *Aeromonas hydrophila* (100% susceptible), *Bacillus* (100% susceptible), *Brucella* (100% susceptible), *Campylobacter jejuni* (100% susceptible), *Citrobacter koseri* (100%), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (14% resistant in Australia), *Escherichia coli* (0.9% resistant in Australia), Group IVe (? 0.03-1 mg/L), Group Ve (? 0.03-0.13 mg/L), *Hafnia alvei*, *Helicobacter pylori*, *Klebsiella oxytoca* (98% of hospital isolates), *Listeria monocytogenes* (0.5-1 mg/L), *Morganella morganii* (100%), *Neisseria gonorrhoeae* (1 mg/L), *Proteus mirabilis* (2% resistant in Australia), *Pseudomonas fluorescens*

(? 0.03-1 mg/L), *Pseudomonas putida* (? 0.03-1 mg/L), *Pseudomonas putrefaciens* (0.13-0.5 mg/L), *Pseudomonas stutzeri* (0.13-1 mg/L), *Sarcina lutea* (100% susceptible), *Serratia marcescens* (100%), *Staphylococcus aureus* (0.5 mg/L); in Australia, *Pseudomonas aeruginosa* 17% resistant, *Klebsiella pneumoniae* 11% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may occur by production of 6'-aminoglycoside acetyltransferase/2''-aminoglycoside phosphotransferase (in Australia, *Enterococcus faecalis* 12% high level resistance, *Enterococcus faecium* 29% high level resistance); shows inoculum effect; in WHO Model List of Essential Drugs as drug requiring specific expertise, diagnostic precision, individualisation of dosage or special equipment for proper use, and for which adverse effects diminish benefit/risk ratio (indiscriminate use must be discouraged and dosage always calculated according to weight and renal clearance of patient)

**Indications:** after other antibiotics have failed; *Aeromonas hydrophila* infections; septic arthritis (hospital acquired, due to coliforms, *Pseudomonas aeruginosa*, *Serratia marcescens*); bacteraemia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably urinary tract, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer, focus probably intravascular catheter, unidentified source in adult or remote area, febrile neutropenic patient with no renal impairment/not on nephrotoxic drugs and *Pseudomonas aeruginosa* suspected, neonatal, due to *Shigella*, *Pseudomonas aeruginosa*, *Acinetobacter*, *Enterococcus*, *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*); brain and epidural abscess from ear and mastoid or due to *Haemophilus*, brucellosis; burn infections; cerebrospinal fluid shunt infections due to *Enterococcus*, *Streptococcus*, aerobic Gram negative bacilli; cholangitis and cholecystitis; compound fracture prophylaxis if wound soiling or severe tissue damage and/or devitalised tissue; acute cystitis in children; endocarditis prophylaxis

(dental procedures or upper respiratory tract interventions in high risk patients) and treatment; endometritis; endophthalmitis; severe acute epididymitis and epididymo-orchitis associated with urinary tract infection or due to *Pseudomonas aeruginosa*; penetrating eye injuries; folliculitis associated with spa; severe *Yersinia enterocolitica* gastroenteritis; granuloma inguinale; hepatic abscess; meningitis due to *Campylobacter fetus* subsp *fetus*; mycotic aneurism; nasal septal abscess; necrotising fasciitis; neonatal sepsis; osteomyelitis and osteochondritis (acute neonatal, due to *Aeromonas*); otitis media due to *Pseudomonas aeruginosa*, enteric Gram negative bacilli); pancreatic abscess; panophthalmitis due to *Pseudomonas aeruginosa*; parametritis; pelvic sepsis and pelvic inflammatory disease related to trauma; perinatal generalised disease due to penicillinase-producing *Neisseria gonorrhoeae*, coliforms; peritonitis (suspected bowel origin, spontaneous); pneumonia (intensive care; moderate nosocomial with no specific risk factors; severe community acquired; due to Gram negative bacilli, especially *Klebsiella pneumoniae*, *Acinetobacter*); severe acute prostatitis and seminal vesiculitis; *Pseudomonas aeruginosa* infections; severe acute pyelonephritis; salpingitis; local and generalised sepsis (including *Enterococcus*, *Aeromonas*); localised skin lesions due to Gram negative bacilli; surgical prophylaxis (cardiovascular; vascular graft; breast; dialysis access; gastrointestinal; colorectal; appendectomy; urinary tract; implant; perforated or gangrenous viscus; muscular, skeletal and soft tissue trauma; ophthalmic; joint; endoscopic procedures); symbiotic gangrene; staphylococcal toxic shock syndrome; tubo-ovarian abscess; catheter-associated urinary tract infection; vascular graft infection; water-related infections

**Side Effects:** headache, ototoxicity (mainly vestibular function), reversible nephrotoxicity, photosensitivity, Stevens-Johnson syndrome, vasculitis; causes neutropenia by myelosuppression; in renal insufficiency, contraindicated or dosage adjustment necessary; dose adjustment required in dialysis; toxic level > 2 mg/L trough (monitor routinely at least once during a course of therapy); incompatible with ampicillin, carbenicillin, heparin, cephalothin, colistimethate

**Contraindications:** pregnancy; caution in renal impairment

**KANAMYCIN:** aminoglycoside; not as active as, and more expensive than, gentamicin; may show inoculum effect; spectrum includes Group Ve (MIC 0.06-0.5 mg/L), *Moraxella* (? 0.03-1 mg/L), *Mycobacterium* (dosage 0.5-1 mg daily); enterococcal resistance, resulting in loss of synergy with cell wall active antibacterials, may occur by production of 6'-aminoglycoside acetyltransferase/2''-aminoglycoside phosphotransferase, 6'-aminoglycoside acetyltransferase or 3'-aminoglycoside phosphotransferase

**Indications:** none

**Side Effects:** systemic hypersensitivity reactions, paresthesias, headache, ototoxicity (mainly cochlear), pain at injection site, renal toxicity; maximum permissible blood level 20 mg/L; incompatible with ampicillin, cephalothin, heparin, lincomycin, methicillin, novobiocin

**NEOMYCIN:** aminoglycoside; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive and Gram negative bacteria and mycobacteria; spectrum includes *Klebsiella* (MIC 1 mg/L), *Moraxella* (0.5 mg/L), *Neisseria gonorrhoeae* (1 mg/L)

**Indications:** cholera carriers (oral); purulent conjunctivitis (topical); staphylococcal enterocolitis (oral); otitis media prophylaxis (topical); panophthalmitis due to *Pseudomonas aeruginosa* (topical); 'swimmer's ear' (topical); no proven value in the treatment of diarrhoea, associated with gastrointestinal toxicity and may prolong or exacerbate diarrhoea, promotes resistance to antimicrobial agents

**Side Effects:** most nephrotoxic and ototoxic (mainly cochlear function) of aminoglycosides, intestinal malabsorption with continued use of oral preparations, rashes (fixed drug reaction, Stevens-Johnson syndrome); less likely enhanced warfarin effect; topical use may induce sensitisation

**Contraindications:** avoid in renal dysfunction; pregnancy

**NEOMYCIN + BACITRACIN:** anti-infective dermatological drug; in WHO Model List of Essential Drugs

**Indications:** bacterial skin infections

**Side Effects:** high risk of skin allergy (no improvement suggests allergy to drug)

**NETILMICIN:** aminoglycoside; more resistant to inactivating enzyme than gentamicin and tobramycin but less resistant than amikacin; as expensive as tobramycin; spectrum includes Group IVe (MIC ? 0.03-0.25 mg/L), Group Ve (0.06-0.13 mg/L), *Moraxella* (? 0.03-0.5 mg/L), *Pseudomonas putrefaciens* (0.25-0.5 mg/L), *Pseudomonas stutzeri* (0.06-1 mg/L), *Streptococcus canis* (1 mg/L); enterococcal resistance, resulting in loss of synergism with cell wall active

antibacterials, may occur by production of 6'-aminoglycoside acetyltransferase/2''-aminoglycoside phosphotransferase or 6'-aminoglycoside acetyltransferase

**Indications:** endocarditis due to *Enterococcus*, *Streptococcus bovis* and other relatively resistant streptococci, *Neisseria mucosa*, *Rothia dentocariosa* in elderly

**Side Effects:** less ototoxic and nephrotoxic than gentamicin and tobramycin but more audiotoxic than amikacin; adjustment required in renal failure and in dialysis

**Contraindications:** pregnancy

**SISOMYCIN:** most active aminoglycoside in vitro against majority of Enterobacteriaceae; more efficacious in vivo than tobramycin but more nephrotoxic than amikacin; spectrum includes Group IIk (MIC 0.06-0.5 mg/L), Group IVe (? 0.03-1 mg/L), Group Ve (? 0.03-0.13 mg/L), *Moraxella* (? 0.03-0.25 mg/L), *Pseudomonas fluorescens* (0.06-0.5 mg/L), *Pseudomonas putida* (0.06-0.5 mg/L), *Pseudomonas putrefaciens* (0.13-0.5 mg/L), *Pseudomonas stutzeri* (0.06-0.5 mg/L)

**STREPTOMYCIN:** aminoglycoside; acts on initiation, codon recognition and translocation; bactericidal; active against bacteria irrespective of growth phase; in high concentrations, penetrates into mammalian cells; active against Gram positive and Gram negative bacteria and mycobacteria; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may result from production of streptomycin adenylyltransferase or ribosomally; 25-30% protein binding; in WHO Model List of Essential Drugs as antituberculous drug and in UNHCR Specialised List of Essential Drugs

**Indications:** use now limited to occasional selected cases of tuberculosis, other mycobacterial infections and enterococcal endocarditis (not registered for use in Australia)

**Side Effects:** systemic hypersensitivity reactions, peripheral neuropathy, ototoxicity (mainly vestibular function; hearing and balance problems), pain at injection site, blood dyscrasias, visual disturbances, nephrotoxicity, erythema nodosum, fixed drug reaction, lupus erythematosus, photosensitivity, pustulosis, Stevens-Johnson syndrome, vasculitis; causes neutropenia by myelosuppression; maximum permissible blood level 20 mg/L; incompatible with carbenicillin, erythromycin, heparin, novobiocin

**Contraindications:** pregnancy; avoid in breastfeeding (insufficient data); in renal insufficiency, contraindicated or dosage adjustments necessary

**TOBRAMYCIN:** aminoglycoside; i.v. and nebulised; once daily administration feasible; marginally more active than gentamicin against *Pseudomonas aeruginosa* (but not other Gram negative bacteria) in vitro but several times as expensive; not as efficacious in vivo as sisomicin; spectrum includes *Aeromonas hydrophila* (100% susceptible), *Citrobacter koseri* (100%), *Enterobacter aerogenes* (100%), *Enterobacter cloacae* (95% of hospital isolates), *Escherichia coli* (99% of hospital isolates), Group IVe (MIC 0.06-0.25 mg/L), Group Ve (? 0.03-0.25 mg/L), *Hafnia alvei* (100% susceptible), *Klebsiella oxytoca* (100%), *Morganella morganii* (100%), *Neisseria gonorrhoeae* (0.5 mg/L), *Proteus mirabilis* (97% of hospital isolates), *Proteus vulgaris* (100%), *Providencia*, *Pseudomonas aeruginosa* (5% resistant in Australia), *Pseudomonas stutzeri* (0.13-1 mg/L), *Staphylococcus aureus* (0.25 mg/L); in Australia, *Klebsiella pneumoniae* 6% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may result from production of 6'-aminoglycoside acetyltransferase/2''-aminoglycoside phosphotransferase or 6'-aminoglycoside acetyltransferase; no significant change in  $V_d$  in elderly; low to high postantibiotic effect

**Indications:** pseudomonal infections in cystic fibrosis patients; may have a role in treatment of suspected or proven *Pseudomonas* septic arthritis, bacteraemia and septicemia, purulent conjunctivitis (topical), acute cystitis, meningitis, myocarditis and pericarditis, osteomyelitis and osteochondritis, pneumonia, sepsis; septic arthritis due to coliforms, *Serratia marcescens*; bacteraemia and septicemia (focus probably urinary tract, febrile neutropenic patient with no renal impairment/not on nephrotoxic drugs and *Pseudomonas aeruginosa* suspected); cranial parameningeal deep fascial space infections following cranial surgery in normal patient; endocarditis due to Gram negative bacilli; emphysematous gastritis; keratitis and iritis due to Gram negative bacilli; myocarditis and pericarditis due to *Yersinia enterocolitica*; malignant otitis externa due to *Pseudomonas aeruginosa*; perianal and perirectal abscess and cellulitis in patients with malignant disease; peritonitis; pneumonia due to *Corynebacterium pseudodiphtheriticum*

**Side Effects:** less nephrotoxic than gentamicin but more nephrotoxic and audiotoxic than netilmicin (no ototoxicity or nephrotoxicity with nebulised form); muscle twitches, hypomagnesemia, hypersensitivity syndrome; moderate to significant

adjustment of dosage in renal failure (ototoxicity, nephrotoxicity; serum levels must be monitored (toxic level > 2 mg/L)); dose adjustment required in dialysis; safe in breastfeeding

**Contraindications:** pregnancy

**SPECTINOMYCIN:** aminocyclitol; in WHO Model List of Essential Drugs as drug with limited indications or narrow spectrum of activity; mode of elimination renal

**Indications:** active against a wide range of bacteria but clinical use restricted to treatment of uncomplicated gonorrhoea ( $\beta$ -lactamase positive; resistance not yet reported in Australia), chancroid, rape prophylaxis

**Side Effects:** gastrointestinal disturbances, skin reactions, pain at injection site, hypersensitivity syndrome; use single dose only in renal dysfunction and in dialysis; probably safe in pregnancy

**Contraindications:** avoid if breastfeeding (insufficient data)

**CHLORAMPHENICOL:** oral (take  $\frac{1}{2}$  - 1 h before food) and parenteral; acts on 50S ribosome to inhibit peptide bonding, acts on transpeptidation and translocation; low postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; penetrates well into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces* (good activity; 98-100% susceptible), anaerobic cocci (98-100% susceptible), *Arachnia* (98-100% susceptible), *Bacteroides* (100% susceptible), *Brucella*, *Chlamydia*, *Clostridium* (good activity; 100% susceptible), *Eubacterium* (good activity), *Fusobacterium* (good activity; 100% susceptible), *Haemophilus influenzae* (3% resistant in Australia), *Listeria*, *Moraxella catarrhalis* (MIC 0.25-0.5 mg/L), *Neisseria meningitidis* (< 5% resistance in Australia), *Rickettsia canada*, *Rickettsia rickettsii*, *Rickettsia tsutsugamushi*, *Rickettsia typhi*, *Salmonella*; in Australia, *Streptococcus pneumoniae*; no effect on opsonisation, reduces neutrophil chemotaxis, no effect on phagocytosis, no effect on capsule enzyme/toxin, increases neutrophil penetration, reduces intracellular killing; shows microbicidal activity against bacteria ingested by monocytes or macrophages; may show inoculum effect; in WHO Model List of Essential Drugs as drug for which adverse effects diminish benefit/risk ratio (oily suspension in complementary list for use in epidemics of meningococcal meningitis when the scale of the epidemic precludes any other form of therapy); mode of elimination hepatic and renal

**Indications:** potent, potentially toxic, broad spectrum antibiotic reserved for life-threatening situations; clostridial abortional and puerperal infections; septic arthritis due to *Haemophilus influenzae*, *Eikenella corrodens*, *Salmonella*; brain abscess; bacteraemia and septicemia (infection from respiratory tract in children, due to *Salmonella*); bacterial blepharitis (topical); bone marrow infection due to *Salmonella typhi*; brain abscess; cellulitis due to anaerobes, *Haemophilus influenzae*; cranial parameningeal deep fascial space infections (otogenic, rhinogenic, odontogenic in normal patient); dental infections; acute and chronic empyema; ear infections; enteric fever; acute epiglottitis in normal host; granuloma inguinale; hepatic abscess due to *Chromobacterium violaceum*; hepatic granuloma due to *Salmonella*; hepatitis due to *Salmonella typhi*, *Rickettsia*; intraabdominal abscess; mastoiditis (treatment failure); intracranial bacterial infections; intraocular infections; post-neonatal pyogenic meningitis; myocarditis and pericarditis due to *Actinomyces*, *Actinobacillus actinomycetemcomitans*, *Rickettsia rickettsii*; anaerobic osteomyelitis and osteochondritis; perinatal generalised disease due to coliforms; peritonitis; pertussis; pneumonia (*Chromobacterium violaceum*, other Gram negatives, intensive care); pneumonitis due to *Pseudomonas pseudomallei*; pulmonary gangrene; acute Q fever; louse-borne relapsing fever; acute respiratory infections in hospitalised patient; rickettsial haemorrhagic fever, rickettsioses; Rocky Mountain spotted fever; rickettsial localised skin lesions; acute skin ulcers due to *Chromobacterium violaceum*; splenic abscess due to *Salmonella*, *Escherichia coli*; ophthalmic surgery prophylaxis (topical); typhoid; endemic, epidemic and scrub typhus

**Side Effects:** headache, nausea, vomiting, haematological complications (leucopenia (neutropenia), thrombocytopenia, reversible dose-dependent bone marrow hypoplasia) common; stomatitis, glossitis, nausea, vomiting, diarrhoea, enterocolitis, pseudomembranous colitis, confusion, skin reactions (pemphigus, cutaneous porphyria, pustulosis, Stevens-Johnson syndrome, vasculitis) uncommon; rare (1 in 30 000 courses) irreversible dose-independent aplasia; possible increased risk with cimetidine), hyperbilirubinemia in newborn, circulatory collapse (grey baby syndrome) in newborn, optic neuritis, superinfection, hearing loss, anaphylaxis, neuropathy; toxic level 20 mg/L peak (monitor routinely in newborn); dosage modification not required in renal dysfunction but monitor peripheral blood count (marrow suppression); further dose not required after haemodialysis; reduce dose to  $\frac{1}{2}$  -  $\frac{1}{3}$  in liver dysfunction; avoid repeated courses and prolonged treatment; periodic blood counts required; may increase plasma levels and effects of oral hypoglycemics, phenytoin and warfarin (likely enhanced effect); plasma levels decreased to subtherapeutic amounts

by enzyme-inducing agents (eg., anticonvulsants, phenobarbitone, rifabutin, rifampicin); incompatible with erythromycin, hydrocortisone sodium succinate, novobiocin, polymyxin B, tetracycline, vancomycin; safe in pregnancy; very weak association with oral contraceptive failure

**Contraindications:** avoid if breast feeding (not topical); caution in neonates

**THIAMPHENICOL:** as for chloramphenicol but stated not to cause irreversible aplasia

**MACROLIDES:** inhibit protein synthesis by binding 50S ribosomal subunit; bacteriostatic; wide spectrum of activity, including Gram positive cocci, *Legionella*, *Bordetella*, *Corynebacterium*, Gram negative cocci, *Mycoplasma*, *Chlamydia* and Gram positive and Gram negative anaerobes; in Australia, *Moraxella catarrhalis* 3% resistant, *Staphylococcus aureus* 34% resistant overall (methicillin susceptible strains 13% resistant), *Streptococcus pneumoniae* 12% resistant, *Streptococcus pyogenes* 8% resistant

**Side Effects:** nausea, vomiting, diarrhoea, abdominal pain, cramps, headache, dyspnoea, cough, candidal infections common; rash, fixed drug eruptions, thrombophlebitis (i.v.), QT interval prolongation uncommon; anaphylaxis, acute respiratory distress, Stevens-Johnson syndrome, cholestatic hepatitis, psychiatric disturbances, hearing loss, pseudomembranous colitis, arrhythmias (i.v.) rare; increased risk of ergotism with ergot derivatives

**ERYTHROMYCIN:** macrolide; oral (twice daily) except for lactobionate; erythromycin base and erythromycin stearate ½ -1 h before food, estolate and ethylsuccinate does not matter; acts on 50S ribosome to inhibit peptide bonding, acts on transpeptidation and translocation; variable absorption; 41% bronchial penetration 2-3 h after 0.5 mg i.v. dose; serum protein binding 70%; moderate to high postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; spectrum includes *Actinomyces* (good activity), *Bacteroides*, *Bordetella*, *Borrelia burgdorferi* (MIC 0.01-1 mg/L), *Campylobacter jejuni* (95% susceptible), *Chlamydia trachomatis* (0.5 mg/L), *Clostridium perfringens* (good activity), *Corynebacterium diphtheriae* (resistance not yet confirmed in Australia), *Erysipelothrix* (100% susceptible at 0.25 mg/L), *Eubacterium* (good activity), *Haemophilus influenzae*, *Legionella* (? 0.06-0.5 mg/L), *Listeria monocytogenes* (0.25 mg/L), *Moraxella catarrhalis* (3% resistance in Australia), *Mycobacterium chelonae*, *Neisseria gonorrhoeae* (1 mg/L), *Mycoplasma*, *Rickettsia rickettsii*, *Rickettsia typhi*, *Staphylococcus aureus* (34% resistant in Australia); Enterobacteriaceae, *Pseudomonas* 100% intrinsic resistance; in Australia, *Streptococcus pyogenes* 8% resistant, *Streptococcus pneumoniae* 12% resistant; no effect on opsonisation, decreases chemotaxis, increases neutrophil penetration, reduces release of chemoattractants; minimal inoculum effect; in WHO Model List of Essential Drugs; mode of elimination hepatic

**Indications:** alternative to penicillin in hypersensitive patients; abortifacient and puerperal infections; actinomycosis; anthrax; reactive arthritis due to *Campylobacter*, *Chlamydia*; septic arthritis due to *Neisseria*, *Corynebacterium*; bacillary angiomatosis; bacillary peliosis; bacteraemia and septicemia (infection from respiratory system in adults); balanitis; bronchiectasis; acute mycoplasmal bronchiolitis and bronchopneumonia; diffuse panbronchiolitis (anti-inflammatory effect); cat scratch disease; cellulitis (mild streptococcal, staphylococcal or clostridial in penicillin hypersensitive); chancroid (drug of choice); chlamydial lymphogranuloma; cholangitis and cholecystitis; cholera; chondritis; bacterial croup; conjunctivitis (chlamydial treatment and prophylaxis; neonatal gonococcal prophylaxis); diphtheria treatment, prophylaxis and carriers; disseminated gonococcal and meningococcal disease; chlamydial dysuria-frequency syndrome; endocarditis due to *Legionella*, *Mycobacterium chelonae*, *Mycobacterium fortuitum*, *Campylobacter* enterocolitis; acute epiglottitis; erysipelas; erysipeloid; erythrasma; erythema chronicum migrans; furuncles; gingivitis and periodontitis in penicillin hypersensitive; gonorrhoea; granuloma inguinale (pregnant or breast-feeding); hepatitis due to *Campylobacter jejuni*, *Coxiella burnetii*, *Actinomyces*, hordeolum; severe impetigo with cellulitis; ischioanal abscess; laryngotracheitis; mastitis; myocarditis and pericarditis due to *Actinomyces*, *Campylobacter jejuni*, *Mycoplasma*, *Ureaplasma*; nasopharyngitis; ornithosis; otitis media due to *Corynebacterium bovis*; otitis externa due to *Corynebacterium diphtheriae*, *Actinomyces israelii*, *Staphylococcus aureus*; sexually acquired parametritis; pelvic sepsis and pelvic inflammatory disease; perichondritis; peritonsillar abscess; pertussis treatment and prophylaxis in close contacts; pharyngitis; pneumonia (mild community acquired in child 3 w - 3 mo, mild to moderate community acquired in adult < 60 years and with no coexisting illness and in child 3 mo - 10 y if *Mycoplasma pneumoniae* suspected, severe community acquired in adult, mild to moderate nosocomial in patient on high dose steroids, severe nosocomial, streptococcal, meningococcal, chlamydial; due to *Moraxella catarrhalis*, *Legionella pneumophila*; diffuse interstitial pneumonia and pneumonitis due to *Rhodococcus equi*); diffuse or interstitial pneumonitis in granulocytopenia;

postpartum fever and endometritis; proctitis due to *Campylobacter*, *Chlamydia trachomatis*; prostatitis and seminal vesiculitis; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; acute Q fever; rat bite fever; louse-borne relapsing fever; rape prophylaxis; rheumatic fever treatment and prophylaxis; scarlet fever; local and generalised sepsis due to *Staphylococcus aureus*, *Campylobacter fetus* subsp *fetus*; acute maxillary sinusitis; treatment and prophylaxis of localised skin infections due to *Streptococcus pyogenes*, *Neisseria*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Arcanobacterium haemolyticum*, *Corynebacterium bovis*; surgical prophylaxis (post-splenectomy in > 2 years old); granulomatous synovitis due to *Mycobacterium chelonae*; syphilis (penicillin hypersensitive pregnant); tenosynovitis due to *Mycobacterium nonchromogenicum*; tetanus; throat infections due to streptococci, *Corynebacterium*, *Arcanobacterium haemolyticum*; tooth abscess in penicillin hypersensitive; toxic shock syndrome due to *Campylobacter intestinalis*; trachoma; non-gonococcal urethritis; vaginitis due to *Chlamydia trachomatis*, *Mycoplasma hominis*

**Side Effects:** rare hypersensitivity reactions, frequent gastrointestinal disturbances (nausea, vomiting, diarrhoea after large doses; abdominal pain or nausea in 27% after infusion; pyloric stenosis in < 1 mo old), pseudomembranous colitis, uncommon skin reactions; pain, local reaction and phlebitis at injection site with 1 g doses (i.v. should be administered slowly to minimise local reactions and avoid arrhythmias); reversible jaundice with erythromycin estolate given for > 10-14 d; dizziness; CNS toxicity and rare ototoxicity following i.v. in renal insufficiency (avoid daily dose of > 2 g in severe renal insufficiency); increases risk of infantile hypertrophic pyloric stenosis in early infancy; dose adjustment not required in dialysis (except continuous venovenous or arteriovenous haemodialysis); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; risk of peripheral ischaemia with ergotamine; risk of cardiac arrhythmias with astemizole and terfenadine (which have resulted in deaths); may increase plasma levels and effects of amprenavir, buspirone, carbamazepine, cyclosporin, digoxin, theophylline (may cause toxicity), warfarin; ritonavir, amprenavir increase plasma levels; increased risk of QT prolongation with all drugs prolonging QT interval; synergicid may increase toxicity; incompatible with ampicillin, carbenicillin, cephalothin, chloramphenicol, cloxacillin, heparin, methicillin, novobiocin, streptomycin, tetracycline; very weak association with oral contraceptive failure

**Contraindications:** avoid estolate and propionate forms in liver dysfunction

**TRIACETYLOLEANDOMYCIN:** macrolide; substitute for erythromycin

**Side Effects:** reversible jaundice if given for > 10-14 d; increase in serum theophylline levels may result in toxicity; risk of peripheral ischaemia with ergotamine

**SPIRAMYCIN:** macrolide

**Indications:** gonorrhoea, non-specific urethritis

**Side Effects:** uncommon hypersensitivity and skin reactions, gastrointestinal disturbances; safe in pregnancy

**ROXITHROMYCIN:** macrolide; good oral bioavailability; usual dose 150 mg orally 12 hourly (1/2 -1 h before food); covers most common respiratory pathogens, including *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*, though some uncertainty about coverage of *Haemophilus influenzae*; and also Gram positive cocci, *Legionella*, *Corynebacterium*, Gram negative cocci, Gram positive and Gram negative anaerobes but not enteric Gram negative bacilli; more reliable absorption and longer half life than erythromycin but more expensive

**Indications:** has rapidly earned a place in treatment of respiratory tract infections (bronchitis, mycoplasmal and chlamydial pneumonia, acute streptococcal throat infections, mild to moderate community acquired pneumonia in adult > 60 years or with coexisting illness) in general practice; also bacterial balanitis; cat scratch disease; chlamydial lymphogranuloma; less severe erysipelas in penicillin hypersensitive; gingivitis and periodontitis in penicillin hypersensitive; granuloma inguinale in pregnant or breastfeeding; severe impetigo; sexually acquired parametritis, pelvic sepsis and pelvic inflammatory disease; postpartum fever and endometritis; post-splenectomy prophylaxis; tooth abscess in penicillin hypersensitive; vaginitis

**Side Effects:** causes less gastrointestinal upset than erythromycin; probably safe in pregnancy; safe in breastfeeding; may increase plasma levels and effects of ergot alkaloids, theophylline and warfarin; possibility of interaction with astemizole and terfenadine; dose adjustment not required in renal failure or in dialysis

**CLARITHROMYCIN:** only macrolide with microbiologically active metabolite; usual dose 250 mg orally 12 hourly (relationship of dose to food doesn't matter); activity similar to erythromycin + activity against *Mycobacterium avium*; concentration in alveolar macrophages ? 100X greater than in plasma or serum; considerably more expensive than erythromycin and roxithromycin

**Indications:** at present, use largely confined to treatment of non-tuberculous mycobacterial infections, especially *Mycobacterium avium* lung disease and disseminated infections in AIDS patients; also respiratory tract infection with *Legionella*, *Streptococcus pneumoniae*, *Haemophilus influenzae* if intolerant of erythromycin; simple gastritis, duodenal ulcer and peptic ulcer due to *Helicobacter pylori*

**Side Effects:** gastrointestinal intolerance; infusion site pain in 92%, phlebitis and inflammation, hypersensitivity syndrome, fixed drug reaction, pustulosis, vasculitis; increased risk of fatal bone marrow toxicity in combination with colchicine; potential to prolong QT interval; may increase plasma levels and effects of some antihistamines (astemizole, terfenadine; risk of cardiac arrhythmias, which have resulted in deaths), carbamazepine, cisapride (increased risk of QT prolongation), cyclosporin, digoxin, fluconazole, itraconazole, rifabutin (may cause uveitis), theophylline, warfarin; plasma levels reduced by rifabutin and rifampicin; lopinavir, ritonavir increase plasma levels; reduces bioavailability of zidovudine (space 2 h apart); delavirdine, ritonavir may increase toxicity; adjustment required in renal failure and in dialysis

**Contraindications:** safety in pregnancy not established; caution if breastfeeding (safety not established), monitor infant for diarrhoea

**AZITHROMYCIN:** oral macrolide (timing to food does not matter); good in vitro activity against a wider range of organisms than erythromycin, including greater activity against *Haemophilus influenzae*, but less active against Gram positives (though active against nontuberculous mycobacteria, including *Mycobacterium avium* complex); first agent shown to be effective in a single dose for uncomplicated *Chlamydia trachomatis* infections of genital tract; also covers *Neisseria gonorrhoeae*; good oral bioavailability and rapid and sustained uptake by tissues; concentration in alveolar macrophages ? 100X greater than in serum or plasma; once daily dosing and long half life; considerably more expensive than erythromycin but better gastrointestinal tolerability

**Indications:** cat scratch disease; cerebral toxoplasmosis in AIDS; chancroid; chlamydial conjunctivitis; chlamydial lymphogranuloma; granuloma inguinale; *Mycobacterium avium-intracellulare* prophylaxis and pulmonary tuberculosis; respiratory tract infection due to *Chlamydia*, *Haemophilus influenzae*, *Moraxella*, *Mycoplasma*, *Streptococcus pneumoniae* when erythromycin not tolerated; trachoma; uncomplicated urethritis and cervicitis due to *Chlamydia trachomatis*; vaginitis

**Side Effects:** gastrointestinal intolerance, reversible ototoxicity, hypersensitivity syndrome, fixed drug reaction, photosensitivity, pustulosis; bioavailability reduced by antacids and didanosine (space doses by 2-3 h); causes high plasma levels of astemizole and terfenadine, with risk of cardiac arrhythmias; ritonavir, saquinavir increase plasma levels; antacids reduce bioavailability (space 2-3 h apart); dose adjustment required in renal failure and in dialysis; less likely enhanced warfarin effect (safest of macrolides); probably safe in pregnancy

**Contraindications:** avoid in breastfeeding (insufficient data); infants < 6 kg

**ERYTHROMYCIN + SULPHISOXAZOLE:** moderately expensive; oral dosing schedule 4 times daily; spectrum includes *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*

**Indications:** acute otitis media

**Side Effects:** high risk of serious adverse reactions and gastrointestinal adverse effects, moderate risk of skin rash

**LINCOSAMIDES:** inhibit protein synthesis by binding 50S ribosomal subunit; active against Gram positive aerobes and most anaerobes

**Indications:** should be used as second choice in those who cannot tolerate conventional therapy

**Side Effects:** antimicrobial-associated diarrhoea, colitis, nausea, vomiting, abdominal cramps, abdominal pain, metallic taste (i.v.), itch, rash, contact dermatitis (topical) common; anaphylaxis, blood dyscrasias, polyarthritis, jaundice, hepatotoxicity (high doses), thrombophlebitis (i.v.), pain, induration, sterile abscess (i.m.), hypotension, cardiac arrest (rapid i.v.) rare

**CLINDAMYCIN:** lincosamide; oral (relationship of dose to food doesn't matter) and i.v. (administer slowly (may cause serious arrhythmias); considerably more expensive than lincomycin); also cream, lotion, gel; acts on 50S ribosome to inhibit peptide bonding; bactericidal; very good intracellular and tissue penetration (except CNS), including abscesses; 61% bronchial penetration after 0.3 g oral dose; very large postantibiotic effect; increases opsonisation, increases phagocytosis, reduces bacterial adherence, reduces capsule enzyme/toxin, increases neutrophil penetration, increases intracellular killing; kills bacteria phagocytosed by granulocytes; no inoculum effect; mode of elimination hepatic and

renal; active against Gram positive aerobes, including methicillin sensitive *Staphylococcus aureus*, and most anaerobes; spectrum includes *Actinomyces* (85-100% susceptible), anaerobic cocci (97% susceptible), *Arachnia* (85-100% susceptible), *Bacteroides* (good activity; 97-99% susceptible, including 81% of *Bacteroides fragilis* group but only 59% of *Bacteroides thetaiotaomicron*, *Bacteroides bivius* MIC < 0.25 mg/L), *Capnocytophaga canimorsus* (98% susceptible), *Clostridium* (good activity except *Clostridium difficile*; 88% susceptible at < 1 mg/L), *Erysipelothrix* (100% susceptible at 0.25 mg/L), *Flavobacterium odoratum* (0.13-1 mg/L), *Fusobacterium* (good activity except *F. varium*; 92% susceptible), Group IIf (? 0.03 mg/L), *Peptococcus* (< 1 mg/L), *Peptostreptococcus* (< 1 mg/L), *Prevotella melaninogenica* (? 0.25 mg/L), *Propionibacterium acnes*, *Staphylococcus aureus* (95% susceptible), *Streptococcus canis* (0.12 mg/L); Enterobacteriaceae 100% intrinsic resistance, *Enterococcus* 100% intrinsic resistance, *Pseudomonas* 100% intrinsic resistance; in WHO Model List of Essential Drugs as complementary drug when drugs in the main list are known to be ineffective or inappropriate for a given individual

**Indications:** should be used as second line agent in patients who cannot tolerate conventional therapy, especially for staphylococcal (including community-associated methicillin resistant *Staphylococcus aureus*) and streptococcal infections (including scarlet fever), lung, dental and peritonsillar abscesses; also abortifacient and puerperal infection; abdominal sepsis; moderate acne vulgaris and rosacea (topical); septic arthritis due to *Staphylococcus aureus* in penicillin hypersensitive; bacteraemia and septicemia (focus probably biliary or gastrointestinal tract or open skin infection/cellulitis; due to *Leuconostoc*, due to *Streptococcus pyogenes* in penicillin hypersensitive); brain and epidural abscess; burn infection due to *Flavobacterium meningosepticum*, cellulitis due to *Staphylococcus aureus* or *Streptococcus pyogenes* in severely penicillin hypersensitive; cervical fascial space infections in normal patients; anaerobic empyema; endocarditis treatment and prophylaxis; postpartum fever and endometritis; intraabdominal abscess; iridocyclitis due to *Bacillus*; myocarditis and pericarditis due to *Actinomyces*; necrotising fasciitis due to *Streptococcus pyogenes*; necrotising ulcerative gingivostomatitis in penicillin hypersensitive; osteomyelitis and osteochondritis (due to *Staphylococcus aureus* in penicillin hypersensitive, due to anaerobes); panophthalmitis due to *Bacillus cereus*; parametritis; anaerobic parotitis and submandibular sialadenitis; pelvic inflammatory disease and pelvic sepsis due to trauma; perianal and perirectal abscess and cellulitis in patients with malignant disease; anaerobic pleuropulmonary infections; pneumonia (mild to moderate nosocomial associated with aspiration or thoracoabdominal surgery); salpingitis; scarlet fever; local and generalised sepsis due to anaerobes, *Bacillus cereus*; severe infections in penicillin allergic patients; chronic sinusitis; localised skin lesions; acute skin ulcers due to *Flavobacterium meningosepticum*; soft tissue infection in anogenital region; symbiotic gangrene; systemic infection in granulocytopenia (severe oral mucositis or necrotising gingivitis, perianal tenderness); toxic epidermal necrolysis; staphylococcal toxic shock syndrome; tubo-ovarian abscess; vaginosis in pregnancy (topical)

**Side Effects:** uncommon hypersensitivity reactions, gastrointestinal disturbances (diarrhoea in 0.3-21%, pseudomembranous colitis in 2-10%), skin reactions (rashes, Stevens-Johnson syndrome, vasculitis) in 8%; tinnitus; hepatotoxicity in 1%; may increase and prolong neuromuscular blockade produced by neuromuscular blockers; may increase saquinavir levels; dosage modification not required in renal dysfunction or in dialysis; reduce dosage to 1/3 – 1/2 normal in liver dysfunction; safe in pregnancy; very weak association with oral contraceptive failure

**Contraindications:** avoid in patients over 60 and those with a history of cardiovascular disease or treatment with anticholinergics; safe in breastfeeding but monitor infant for diarrhoea

**LINCAMYCIN (LINCOCIN):** lincosamide; now only available as parenteral formulation (considerably cheaper than clindamycin); bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; mainly active against Gram positive bacteria; spectrum includes *Bacteroides*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*; increases opsonisation, chemotaxis, phagocytosis, reduces capsule enzyme/toxin, increases neutrophil penetration and intracellular killing

**Indications:** abdominal sepsis; empyema; endocarditis due to *Fusobacterium*, *Prevotella*; putrid lung abscess; osteomyelitis; acute lobar pneumonia; chronic Q fever; septicemia; severe infections in penicillin allergic patients; chronic sinusitis, soft tissue infection in anogenital region; colon and uterus surgical prophylaxis

**Side Effects:** uncommon hypersensitivity reactions, serum sickness-like illness, gastrointestinal disturbances (diarrhoea, pseudomembranous colitis), skin reactions (photosensitivity), ? cardiopulmonary arrest after rapid i.v. infusion; modify dosage interval in renal dysfunction; dose adjustment not required in dialysis (except in continuous

venovenous or arteriovenous haemodialysis); safe in pregnancy; caution in breastfeeding (monitor infant for diarrhoea); serum levels markedly decreased by kaolin-pectin suspension and cyclamate diet drink (give 2 h apart); incompatible with ampicillin, benzylpenicillin, carbenicillin, cephalothin, colistimethate, kanamycin, novobiocin

**TELITHROMYCIN:** ketolide; spectrum includes *Actinomyces* (MIC ? 0.015 mg/L), *Bordetella pertussis* (0.03 mg/L), *Bordetella parapertussis* (0.25 mg/L), *Chlamydia trachomatis* (0.12 mg/L), *Clostridium perfringens* (0.06-0.25 mg/L), *Helicobacter pylori* (0.5 mg/L), *Lactobacillus* (0.015-0.03 mg/L), *Legionella pneumophila* (0.004-0.12 mg/L), *Leuconostoc* (0.015-0.06 mg/L), *Listeria monocytogenes* (0.06-0.25 mg/L), *Moraxella catarrhalis* (0.008-0.25 mg/L), *Mycoplasma pneumoniae* (0.00025-0.015 mg/L), *Neisseria gonorrhoeae* (0.03-0.5 mg/L), *Neisseria meningitidis* (0.03-0.5), *Porphyromonas* (< 0.016-0.25 mg/L), methicillin sensitive *Staphylococcus aureus* (0.06-0.25 mg/L), methicillin sensitive coagulase negative *Staphylococcus* (0.25-0.5 mg/L), *Streptococcus agalactiae* (0.015-0.06 mg/L), *Streptococcus canis* (0.06 mg/L), *Streptococcus pneumoniae* (? 0.004-0.5 mg/L; including strains resistant to other antibiotics), *Streptococcus pyogenes* (0.008-1 mg/L), group C streptococci (0.06 mg/L), group F streptococci (0.03 mg/L), viridans group streptococci (? 0.004-0.25 mg/L), *Ureaplasma urealyticum* (0.03-0.06 mg/L)

**Indications:** community acquired pneumonia, acute exacerbation of chronic bronchitis, acute sinusitis

**Side Effects:** diarrhoea, nausea, exacerbation of myasthenia gravis

**TETRACYCLINE:** oral (take ½ -1 h before food) and parenteral; acts on 30S ribosome to inhibit binding of amino-acyl-tRNA, acts on codon recognition and translocation; usually bacteriostatic; no significant change in absorption in elderly; low to moderate postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; penetrates well into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces*, *Bacteroides*, *Borrelia recurrentis*, *Brucella* (MIC ? 0.13-0.25 mg/L), *Cardiobacterium hominis*, *Chlamydia*, coliforms, *Fusobacterium* (good activity except *F. varium*), *Haemophilus influenzae* (5% resistance in Australia), *Helicobacter pylori*, *Listeria monocytogenes* (0.5 mg/L), *Moraxella catarrhalis* (0.8% resistance in Australia), some nontuberculous *Mycobacteria*, *Mycoplasma*, *Pseudomonas vesicularis* (0.13-1 mg/L), *Rickettsia*, *Salmonella*, *Shigella*, some spirochaetes, *Yersinia*, *Serratia marcescens* 100% resistant, *Streptococcus agalactiae* 79% acquired resistance, *Proteus mirabilis* 98% intrinsic resistance (possibly all resistant in clinical practice); in Australia, *Streptococcus pneumoniae* 13% resistant, *Neisseria gonorrhoeae* 5% high level resistance, *Staphylococcus aureus* 5% methicillin susceptible strains resistant (23% overall); 36% protein binding; reduces bacterial adherence and intracellular killing, reduces release of chemoattractants, inhibits chemotactic activity of granulocytes, diminishes phagocytosis; no inoculum effect; mode of elimination renal, hepatic

**Indications:** reduced value due to emergence of resistant strains and development of other antimicrobial agents; moderate to severe acne vulgaris; actinomycosis; anthrax; reactive arthritis due to *Shigella*, *Salmonella*, *Yersinia*, *Chlamydia*; septic arthritis due to *Mycoplasma hominis*, *Ureaplasma urealyticum*; bacillary angiomatosis; bacillary peliosis; bartonellosis; bacterial blepharitis; boils; bronchiectasis and chronic bronchitis in patients > 8 y of age; brucellosis; carbuncles; cellulitis due to *Vibrio*; chancroid; cholera; purulent conjunctivitis (treatment of more severe; prophylaxis of chlamydial and neonatal gonococcal); bacterial dysentery; chlamydial dysuria-frequency syndrome; ehrlichiosis; endocarditis due to *Fusobacterium*, *Prevotella*, *Coxiella burnetii*; acute epididymitis and epididymo-orchitis; erythema chronicum migrans; erythema serpens; furuncles; gas gangrene in penicillin allergic patient; simple gastritis, duodenal ulcer and peptic ulcer; gonorrhoea (including acute throat infections); granuloma inguinale; hepatic abscess due to *Actinomyces*; hepatitis due to *Coxiella burnetii*, *Rickettsia*, *Actinomyces*, *Borrelia recurrentis*, *Yersinia pseudotuberculosis*; severe leptospirosis; Lyme disease; myocarditis and pericarditis due to *Actinomyces*, *Actinobacillus actinomycetemcomitans*, *Rickettsia rickettsii*, *Mycoplasma*, *Ureaplasma*; *Neisseria meningitidis* carriers; ornithosis; pyogenic osteomyelitis and osteochondritis due to *Vibrio vulnificus*; otitis externa due to *Actinomyces israelii*; treatment of sexual partners of patients with parametritis, pelvic sepsis, pelvic inflammatory disease; periodontal disease; peritonitis of suspected bowel origin; plague; community acquired pneumonia and pneumonia due to *Francisella tularensis*, *Vibrio vulnificus*; pneumonitis due to *Francisella tularensis*, chlamydial proctitis; prostatitis; pseudotuberculosis; Q fever; rape prophylaxis; rat bite fever; relapsing fever treatment and prophylaxis; acute respiratory illness due to *Mycoplasma pneumoniae*, *Coxiella burnetii*, rickettsioses, local and generalised sepsis due to *Vibrio*, *Clostridium botulinum*; acute maxillary sinusitis; localised skin lesions due to *Staphylococcus aureus*, *Rickettsia*;

acute skin ulcers due to *Francisella tularensis*; styne; surgical prophylaxis in ruptured, perforated or gangrenous viscus (lavage); sycosis barbae; syphilis in penicillin allergic patient; systemic infection prophylaxis in agammaglobulinemia; acute throat infections due to *Mycoplasma pneumoniae*, *Chlamydia*; tracheitis; trachoma treatment and prophylaxis; bacterial vaginitis; non-gonococcal venereal infections; water-related infections

**Side Effects:** allergic reactions (rare); disorders of gastrointestinal tract (nausea, vomiting, epigastric burning, diarrhoea common; oesophageal ulcers, enterocolitis, pseudomembranous colitis rare) and CNS (rare benign intracranial hypertension in newborn); rash, stomatitis, overgrowth of resistant organisms (eg., *Candida albicans*), photosensitivity uncommon; permanent discolouration of children's teeth and nails, bone deformity, reduced bone growth if given after 18<sup>th</sup> week of pregnancy or to children < 8 y; raises blood urea; hepatotoxicity (hepatitis, fatty liver degeneration) in pregnancy with large doses given parenterally; pain and local reaction at injection site; Fanconi-like syndrome with outdated products; nephrotoxicity; exacerbation of systemic lupus erythematosus (rare); worsening uraemia and acidosis in renal insufficiency (avoid; use doxycycline when a tetracycline is indicated); avoid in dialysis; maximum permissible blood level 20 mg/L; bioavailability decreased by most liquid antacids, tri-potassium and di-citrate bismuthate, calcium preparations, aluminium, sodium, magnesium, didanosine, iron haematinics (absorption of iron also markedly decreased), sucralfate, zinc sulphate, kaolin + pectin (space doses by 2-3 h); activity of warfarin may be increased; incompatible with ampicillin, carbenicillin, cephalothin, chloramphenicol, cloxacillin, erythromycin, heparin, methicillin, novobiocin, penicillin, polymyxin B; weak association with oral contraceptive failure

**Contraindications:** renal failure; pregnancy after 18<sup>th</sup> week; avoid if breastfeeding (7-10 d course probably safe); children < 8 y

**CHLORTETRACYCLINE:** oral preparation no longer available

**DEMECLOCYCLINE:** tetracycline; give on empty stomach

**Side Effects:** greater risk of photosensitivity than with other tetracyclines

**DOXYCYCLINE:** oral tetracycline (take after food with full glass of water and remain upright for at least 30 min; once daily dosing); best pharmacology of tetracyclines (with minocycline) makes it preferred tetracycline in most situations; 35% bronchial penetration 2-3 h after 0.1 g oral dose; no significant change in  $V_d$  in elderly; 70% protein binding; spectrum includes *Acinetobacter calcoaceticus* var *Iwoffii* (MIC 0.06-1 mg/L), *Bordetella bronchiseptica* (0.06-0.25 mg/L), *Chlamydia*, Group IVc (0.13-0.5 mg/L), Group Va (0.25-1 mg/L), *Mycoplasma hominis*, *Pseudomonas vesicularis* (? 0.03-0.25 mg/L); in WHO Model List of Essential Drugs; mode of elimination renal and hepatic, non-renal in patients with renal failure

**Indications:** moderate to severe acne; reactive arthritis due to *Chlamydia*, septic arthritis due to *Brucella*, *Mycoplasma hominis*, *Ureaplasma urealyticum*; bacillary angiomatosis; bacillary peliosis; bronchiectasis in patients > 8 y; chronic bronchitis in patients > 8 y; brucellosis; cat and dog and human bite and clenched fist injury infections in penicillin hypersensitive nonpregnant adults; cat scratch disease; mycoplasmal cellulitis; chlamydial lymphogranuloma; acute cholecystitis; cholera; chlamydial conjunctivitis in nonpregnant adults; bacterial dysentery; chlamydial dysuria-frequency syndrome; ehrlichiosis; encephalitis due to *Chlamydia*, *Mycoplasma*, *Rickettsia*; endocarditis due to *Brucella*, endometritis; sexually acquired acute epididymitis and epididymo-orchitis; gonorrhoea; granuloma inguinale; severe leptospirosis; Lyme disease (arthritis, Bell's palsy, mild cardiac disease); melioidosis; meningitis due to *Brucella*; meningoencephalitis due to *Coxiella burnetii*, *Mycoplasma*, chlamydial; orchitis; ornithosis; acute bacterial otitis media; osteomyelitis and osteochondritis due to *Brucella*; parametritis; pelvic inflammatory disease; sexually acquired pelvic sepsis; perihepatitis; peritonitis suspected associated with pelvic inflammatory disease; pneumonia (mild to moderate community acquired in adult, mycoplasmal, chlamydial, *Legionella pneumophila*); chlamydial proctitis; prostatitis and seminal vesiculitis; acute Q fever; rape prophylaxis; rickettsioses treatment and prophylaxis; salpingitis; syphilis in penicillin hypersensitive nonpregnant; tick-borne relapsing fever; trachoma in nonpregnant adult; traveller's diarrhoea prophylaxis in high risk host; non-gonococcal or post-gonococcal urethritis, cervicitis due to *Chlamydia*, *Trichomonas*, vaginitis due to *Chlamydia trachomatis*, *Mycoplasma hominis*

**Side Effects:** nausea, vomiting, diarrhoea, allergic reactions (rare), oesophagitis (wash down well and remain upright at least 30 minutes after administration), photosensitivity, vaginal thrush; does not raise blood urea; does not require dosage modification in renal dysfunction or in dialysis; bioavailability decreased by antacids, iron and calcium preparations but not by zinc sulphate; plasma levels may be reduced by carbamazepine, phenobarbitone and phenytoin; weak association with oral contraceptive failure

**Contraindications:** > 18 w pregnant; use in breastfeeding only if = 10 d course and alternative drugs not appropriate; children < 8 y (though less permanent discolouration of children's teeth and nails than with tetracycline)

**METHACYCLINE:** oral tetracycline (take ½ - 1 h before food); bioavailability reduced by antacids, didanosine, iron and calcium preparations (space doses by 2-3 h)

**MINOCYCLINE:** oral tetracycline (take with or after food); best pharmacology of tetracyclines (with doxycycline); mode of elimination renal, hepatic; active against some strains of tetracycline-resistant bacteria, including strains of staphylococci; spectrum includes *Acinetobacter calcoaceticus var lwoffii* (MIC 0.06-1 mg/L), *Borrelia burgdorferi* (0.09-0.25 mg/L), *Bordetella bronchiseptica* (0.13-1 mg/L), *Comamonas terrigena* (0.06-4 mg/L), Group IIk (= 0.03-1 mg/L), Group IVc (0.25-1 mg/L), *Moraxella* (0.25-1 mg/L), *Nocardia*, *Pseudomonas diminuta* (0.13-2 mg/L), *Pseudomonas vesicularis* (? 0.03-0.5 mg/L)

**Indications:** severe acne not responding to other tetracyclines; bacillary angiomatosis; bacillary peliosis; fish spine injuries and other water-related infections due to *Vibrio*; meningitis due to *Acinetobacter*, *Nocardia asteroides*, nocardiosis; pneumonitis due to *Mycoplasma pneumoniae*, *Nocardia asteroides*, less severe acute prostatitis and seminal vesiculitis; nongonococcal urethritis

**Side Effects:** as for tetracycline but higher incidence of vestibular adverse effects; also benign intracranial hypertension (risk increased with etretinate, isotretinoin), skin pigmentation; dose adjustment not necessary in renal failure or in dialysis; weak association with oral contraceptive failure; bioavailability reduced by antacids, didanosine, iron and calcium preparations (space doses by 2-3 h)

**Contraindications:** pregnancy after first 18 w

**TIGECYCLINE:** glycylglycine derivative of minocycline; active against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Streptococcus pyogenes*, *Acinetobacter baumannii*, most Enterobacteriaceae, *Bacteroides*, *Clostridium perfringens*, not active against *Pseudomonas aeruginosa*, *Proteus*

**OXYTETRACYCLINE:** oral preparation no longer available

**Indications:** bronchitis prophylaxis; endocarditis due to *Brucella*, hepatitis due to *Leptospira*; leptospirosis

**Side Effects:** less permanent discolouration of children's teeth and nails than with tetracycline

**Contraindications:** avoid in renal failure (azotemia, nephrotoxicity) and pregnancy

**NITROFURANTOIN:** nitrofurantoin; exact mechanism of action uncertain; may have several bacterial enzyme targets and directly damage DNA; oral (take with or after food (absorption enhanced)); activity reduced in alkaline urine; in WHO Model List of Essential Drugs as complementary drug when drugs in main use or known to be ineffective or inappropriate for a given individual and for which adverse effects diminish benefit/risk ratio; mode of elimination renal; *Serratia marcescens* 100% resistant, *Proteus mirabilis* 95% intrinsic resistance (possibly all resistant in clinical practice)

**Indications:** used occasionally for urinary tract infection (acute cystitis) and prevention of recurrent urinary tract infection

**Side Effects:** hypersensitivity reactions (allergic skin reactions common), gastrointestinal disturbances (nausea, vomiting common; abdominal pain, diarrhoea uncommon), ascending peripheral polyneuropathy with high blood levels or in presence of renal failure, haemolytic anaemia (mainly in those with glucose-6-phosphate dehydrogenase deficit); severe acute or chronic pulmonary reactions (pneumonitis, fibrosis), nephrotoxicity, chronic active hepatitis, acute hepatocellular or cholestatic reaction rare; avoid in moderate to severe renal dysfunction (glomerular filtration rate < 50 mL/min) and in dialysis; safe in pregnancy

**Contraindications:** avoid if breastfeeding premature infant, < 1 mo old or with G6PD deficiency

**HEXAMINE (METHENAMINE) MANDELATE AND HIPPURATE:** concentrates in urine, where it is converted to formaldehyde (active agent); requires acidification and long dwell time; oral (not affected by food)

**Indications:** used occasionally for urinary tract infection and prevention of recurrent acute cystitis

**Side Effects:** gastrointestinal and skin reactions; dose adjustment not required in dialysis (except in continuous venovenous and arteriovenous haemodialysis); activity decreased by urinary alkalinisers (eg, acetazolamide, sodium bicarbonate); safe in pregnancy

**Contraindications:** avoid in severe renal failure (glomerular filtration rate < 10 mL/min; ineffective; seizures) and in dialysis; avoid in breastfeeding (insufficient data)

**NITROIMIDAZOLES:** spectrum of activity encompasses Gram negative and Gram positive anaerobes

**Side Effects:** nausea, diarrhoea, metallic taste, thrombophlebitis (i.v.) common; rash, itch, dizziness, vomiting, glossitis, stomatitis, paraesthesia uncommon; colitis, pancreatitis, hepatitis, anaphylaxis, optic neuritis, peripheral neuropathy, seizures rare

**METRONIDAZOLE:** nitroimidazole; exact mechanism of action uncertain but disrupts DNA; bactericidal; oral (twice daily; take with or after food; benzylmetronidazole, ½ -1 h before food), suppositories and i.v.; good absorption; no significant change in absorption, reduced clearance in elderly; no effect on chemotaxis or intracellular killing; in WHO List of Model Drugs; mode of elimination hepatic and renal; spectrum includes anaerobic cocci (98-99% susceptible), anaerobic Gram negative bacilli (*Bacteroides* good activity; *Bacteroides fragilis* < 5% resistance; *Fusobacterium* good activity, 100% susceptible at

< 1 mg/L), anaerobic Gram positive bacilli (*Clostridium* good activity, 99% susceptible; *Clostridium difficile* 100% susceptible at < 1 mg/L)

**Indications:** anaerobic infections; reactive arthritis due to *Clostridium difficile*; bacteraemia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer); brain abscess from frontal sinus or due to anaerobes; cat and dog and human bite and clenched fist injury infections in penicillin hypersensitive; anaerobic cellulitis; cervical fascial space infections in normal patient; clostridial myositis/myonecrosis (gas gangrene); cranial parameningeal deep fascial space infections (otogenic, rhinogenic, odontogenic in normal patient); *Clostridium difficile* diarrhoea and pseudomembranous colitis (drug of choice); endocarditis due to *Fusobacterium*, *Prevotella*; endometritis; *Bacteroides* enterocolitis; severe gingivitis and periodontitis; hepatic abscess; intraabdominal infections, ischiorectal abscess; postneonatal pyogenic meningitis due to *Bacteroides*; necrotising enterocolitis due to *Clostridium perfringens*; necrotising fasciitis; gastritis/ulcers due to *Helicobacter pylori*; necrotising ulcerative gingivostomatitis; anaerobic otitis externa; parametritis; pelvic inflammatory disease and pelvic sepsis; perinatal generalised disease due to anaerobes other than *Peptostreptococcus* and *Clostridium*; periodontitis; acute peritonitis associated with appendix etc; moderate to severe anaerobic pleuropulmonary infections; mild to moderate nosocomial pneumonia associated with aspiration or thoraco-abdominal surgery; pulmonary abscess; rape prophylaxis; salpingitis; local and generalised sepsis due to *Clostridium botulinum* or unknown organisms; splenic abscess due to *Clostridium difficile*; surgical prophylaxis (normal labour; colorectal; appendectomy; hysterectomy; termination of pregnancy; lower limb amputation; ruptured, perforated or gangrenous viscus; muscular, skeletal and soft tissue trauma); symbiotic gangrene; systemic infections in granulocytopenia (severe oral mucositis or necrotising gingivitis, perianal tenderness); severe tooth abscess; tropical ulcer; ulcers in diabetics; treatment failure in nongonococcal urethritis; vaginitis; vaginosis; Vincent's angina

**Side Effects:** peripheral neuropathy, acute pancreatitis; nausea, drowsiness, headache, rashes, dizziness, vestibular symptoms, ataxia, transient epileptiform seizures with high doses; moderate to significant adjustment of dosage needed in renal failure (vestibular toxicity may occur); dose adjustment required in dialysis; safety in pregnancy not established; marked potentiation of warfarin; may increase plasma levels and effects of cyclosporin, phenytoin, lithium; 'antabuse' syndrome may occur with alcohol; decreased plasma levels with phenobarbitone, cholestyramine, aluminium hydroxide, antacid; weak association with oral contraceptive failure; safety of systemic in pregnancy not established

**Contraindications:** patients with history of blood disease, patients with acute central nervous system disease; avoid high single dose systemic therapy in breastfeeding

**TINIDAZOLE:** oral only (take with or after food); longer half life than metronidazole and can be administered less frequently or as a single dose; spectrum includes anaerobic Gram negative bacilli, anaerobic Gram positive bacilli and cocci

**Indications:** sexually acquired pelvic sepsis in outpatient; surgical prophylaxis (hysterectomy, termination of pregnancy); vaginitis; vaginosis

**Side Effects:** lassitude, dizziness, bitter taste, nausea, rarely vomiting, diarrhoea, constipation, thirst, sweating, itching; safety in pregnancy not established; disulfiram-like reaction may occur with alcohol; dosage modification not required in renal failure; dose required after intermittent haemodialysis; safety in pregnancy not established

**Contraindications:** avoid if breastfeeding

## **NIMORAZOLE**

**Indications:** vaginosis

**Contraindications:** pregnancy

**NOVOBIOCIN:** bacteriostatic and bactericidal in high concentrations; acts only on proliferating bacteria; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive bacteria; 99% protein binding

**Indications:** none

**Side Effects:** hypersensitivity reactions, gastrointestinal disturbances, skin reactions, pain at injection site, blood dyscrasias, haemolytic anaemia (mainly in those with glucose-6-phosphate dehydrogenase deficit), hyperbilirubinemia in newborn, yellow discolouration of skin and sclera; maximum permissible blood level 15 mg/L

**Contraindications:** pregnancy

**SODIUM FUSIDATE:** oral (take with or after food); bacteriostatic and possibly bactericidal in high concentrations; very active against *Staphylococcus aureus* but resistance develops rapidly; in Australia, methicillin resistant *Staphylococcus aureus* 4% resistant; protein binding 97%

**Indications:** infections with methicillin resistant *Staphylococcus aureus* (should never be used alone); staphylococcal brain and epidural abscess; *Staphylococcus aureus* pulmonary infection in cystic fibrosis

**Side Effects:** gastrointestinal disturbances (epigastric discomfort, nausea), thrombophlebitis common; headache uncommon; granulocytopenia, thrombocytopenia, elevated transaminases, jaundice (i.v.), skin reactions (rash) rare; rhabdomyolysis and elevated creatine kinase when combined with statins; dose adjustment not required in renal failure or in dialysis

**Contraindications:** pregnancy; caution in breastfeeding (insufficient data)

**MUPIROCIN:** reversibly inhibits isoleucyl tRNA synthetase; active against broad range of Gram positive bacteria, including methicillin resistant *Staphylococcus aureus* (but high level resistance readily selected by prolonged or widespread use); moderately active against *Haemophilus influenzae* and *Neisseria gonorrhoeae*, deleted from WHO Model List of Essential Drugs because expensive and other drugs listed considered adequate

**Indications:** elimination of nasal carriage of *Staphylococcus aureus* (calcium dihydrate salt in soft paraffin base); impetigo (ointment of free base in polyethylene glycol); probably safe in pregnancy; safe in breastfeeding

**Side Effects:** local adverse reactions in 2%

## **FURAZOLIDONE**

**Indications:** cholera

**Side Effects:** tinnitus, hearing loss, vestibular symptoms

**OXAZOLIDINONES:** new class of agents; inhibit formation of initiation complex; active against Gram positive bacteria (including methicillin resistant *Staphylococcus aureus*, vancomycin resistant *Enterococcus*, resistant *Streptococcus pneumoniae*) and some anaerobic Gram negative bacteria (including *Bacteroides fragilis*)

**LINEZOLID:** first member of oxazolidinone class; injections, tablets, oral suspension (timing to food does not matter); inhibits protein synthesis by specifically binding to 50S ribosomal subunit; 100% bioavailability after oral dosing; effective against Gram positive organisms, including methicillin resistant *Staphylococcus aureus*, coagulase negative staphylococci, vancomycin resistant enterococci and penicillin resistant *Streptococcus pneumoniae*; expensive

**Indications:** reserved for multi-drug-resistant infections (should be commenced in hospital); infections with vancomycin resistant *Enterococcus* (including cases with concurrent bacteraemia; 2% develop resistance during therapy); pneumonia caused by *Staphylococcus aureus* or *Streptococcus pneumoniae* (including cases with concurrent bacteraemia); skin and skin structure infections caused by *Staphylococcus aureus*, *Streptococcus pyogenes* or *Streptococcus agalactiae*

**Side Effects:** diarrhoea in 8%, headache in 7%, nausea in 6%, vomiting in 4%, tongue discolouration in 3%, thrombocytopenia in 3%, dermatological reactions in 3%, reduced haemoglobin/haematocrit in 0.8%, leucopenia in 0.8%, allergy in 0.3%; abdominal pain, taste disturbance, raised liver enzymes, candidiasis, peripheral neuropathy common; thrombocytopenia, hypertension, eosinophilia, neutropenia, rash, pruritis, urticaria, thrombophlebitis, dizziness, hypaesthesia, insomnia, paraesthesia, blurred vision, pancreatitis uncommon; allergy, myelosuppression, pancytopenia, pseudomembranous colitis rare; monitor platelets if > 2 w of therapy; pure red blood cell aplasia reported; monoamine oxidase inhibitory activity can increase blood pressure if used with pseudoephedrine, phenylpropranolamine, dopamine,

adrenaline, tyramine-containing foods and serotonergic drugs; serotonin syndrome on coadministration with serotonergic drugs; safety in pregnancy not established

**Contraindications:** avoid in breastfeeding

**EPEREZOLID:** oxazolidinone similar to linezolid

**CAPREOMYCIN:** antitubercular

**Indications:** *Mycobacterium* infections (dosage 1 g daily or twice weekly; used infrequently)

**Side Effects:** ototoxicity, nephrotoxicity, pain on injection, symptomless eosinophilia, drug fever, skin rash, myelosuppression; single case report of hearing loss; possible cumulative nephrotoxicity and ototoxicity with aminoglycosides, high dose aspirin, frusemide, methoxyflurane; may increase neuromuscular blockade with neuromuscular blocking drugs

**Contraindications:** pregnancy, avoid in breastfeeding (insufficient data)

**CYCLOSERINE:** bacteriostatic; acts only on proliferating bacteria; penetrates well into mammalian cells; active against *Mycobacterium*, oral (not affected by food)

**Indications:** *Mycobacterium* infections (dosage 750 mg daily; used infrequently)

**Side Effects:** CNS reactions (headache, somnolence, mental disturbances, convulsions; seizures controlled by 100 mg pyridoxine daily; CNS toxicity increased by ethionamide, alcohol (increased risk of epileptic episodes), isoniazid); further dose required after haemodialysis; avoid use if possible in renal insufficiency (when indicated, adjust dose appropriately and monitor serum levels); maximum permissible blood level 25 mg/L; not recommended in pregnancy (safety not established); caution in breastfeeding (insufficient data)

**ETHAMBUTOL:** oral (relationship of dose to food doesn't matter) antitubercular and antileprotic; in WHO Model List of Essential Drugs; mode of elimination renal; bacteriostatic; impairs mycobacterial cell wall synthesis

**Indications:** *Mycobacterium* infections, tuberculous pneumonia (dosage 15-25 mg/kg daily)

**Side Effects:** retrobulbar neuritis (decreased visual acuity and red-green colour discrimination, central scotomata; very rare if dose  $\leq$  15 mg/kg/d,  $\approx$  5% if 25 mg/kg/d), peripheral neuritis with numbness and tingling of extremities (uncommon if normal renal function and dosage strictly observed), joint pain, gastrointestinal disturbances, malaise, headache, allergic reactions, rare anaphylaxis, hyperuricemia; modify dosage interval in renal dysfunction and in dialysis; safe in pregnancy and breastfeeding

**Contraindications:** children  $<$  6 y; elderly patients; monitor breastfed infant for jaundice

**ETHIONAMIDE**

**Indications:** multibacillary leprosy when clofazimine totally unacceptable; *Mycobacterium* infections (dosage 0.75-1 g daily); tuberculosis prophylaxis

**Side Effects:** anorexia, nausea, vomiting, metallic taste, ganglionic blockade reactions (postural hypotension, depression), hepatotoxicity (especially in diabetics), severe allergic skin rash, purpura, gynecomastia, impotence, amenorrhoea, rare neurotoxicity

**ISONIAZID (ISONICOTINIC ACID HYDRAZIDE, INAH, INH):** oral (relationship of dose to food doesn't matter) antitubercular; no significant change in  $V_d$  or clearance in elderly; in WHO Model List of Essential Drugs; mode of elimination hepatic (renal); bactericidal; interferes with lipid and nucleic acid biosynthesis

**Indications:** hepatic granuloma; infections with *Mycobacterium tuberculosis* (spontaneous resistance 1:10<sup>6</sup> organisms; dosage 300 mg daily or 15 mg/kg twice weekly), *Mycobacterium bovis*, *Mycobacterium kansasii*, *Mycobacterium szulgai*, *Mycobacterium xenopi*, *Mycobacterium avium-intracellulare*, *Mycobacterium leprae*, *Mycobacterium marinum*, *Mycobacterium goodnae*, *Mycobacterium malmoeense*; tuberculosis prophylaxis; tuberculous pneumonia

**Side Effects:** peripheral neuritis (minimised with cotreatment with pyridoxine 25 mg orally daily), optic neuritis, hepatotoxicity ( $\approx$  0.3% in persons  $<$  35 y,  $\approx$  2% in persons  $>$  50 y; daily alcohol ingestion may be associated with higher incidence (and reduced effect of isoniazid)), pellagra-like syndrome, mental abnormalities, convulsions, epigastric distress, rare hypersensitivity, skin rash, nausea, mild abnormalities in liver function, subtle mood changes, single case reports of tinnitus and vestibular symptoms; decrease daily dose to 200 mg in severe renal insufficiency, administer routine pyridoxine supplement, monitor drug levels, treat toxicity with high dose pyridoxine and haemodialysis; reduce dose to  $\frac{1}{2}$  -  $\frac{1}{3}$  normal in liver dysfunction; dose adjustment required in dialysis; serum half life increased by para-aminosalicylic acid (particularly in rapid inactivators; reduced doses probably needed); additive effect on rifampicin

reduction of plasma concentration of ketoconazole; marked increase in plasma level of carbamazepine, diazepam, phenytoin and disulfiram in some slow acetylators; may decrease plasma levels and effects of itraconazole, ketoconazole; decreased absorption by aluminium hydroxide gel; very weak association with oral contraceptive failure; safe in pregnancy

**Contraindications:** liver disease caused by other drugs; avoid if breastfeeding (if used, monitor infant for hepatitis, vision changes, fatigue, weakness, malaise, anorexia, nausea, vomiting and give pyridoxine to mother and infant)

**RIFAMPICIN + ISONIAZID:** in WHO Model List of Essential Drugs (essential that all combination tablets containing rifampicin shown to have adequate bioavailability)

**Indications:** infections due to *Mycobacterium tuberculosis*

**Contraindications:** pregnancy

**ISONIAZID + THIOACETAZONE:** in WHO Model List of Essential Drugs as complementary drug when drugs in main list cannot be made available and as drug for which adverse effects diminish benefit/risk ratio

**Indications:** tuberculosis

**Side Effects:** hypersensitivity, gastrointestinal symptoms, jaundice, peripheral neuritis; frequency of adverse reactions to thioacetazone appears much higher in tuberculosis patients infected with HIV than in those who are HIV negative

**Contraindications:** jaundice, liver disease caused by other drugs

#### **PARA-AMINOSALICYLIC ACID (PAS)**

**Indications:** infections with *Mycobacterium* (dosage 15-25 g daily)

**Side Effects:** gastrointestinal disturbances (nausea, gastric irritation, diarrhoea; extremely common), hypersensitivity (fever, rash, headache, sore throat), hepatotoxicity, blood dyscrasias, haemolytic anaemia, allergic pulmonary reactions, bleeding tendencies, goitre, rare hypokalemia; serum levels increased by probenecid; increased risk of mutual toxicity when combined with salicylates (more likely in large doses); avoid in renal dysfunction

**PYRAZINAMIDE:** oral (relationship of dose to food doesn't matter) antitubercular; in WHO Model List of Essential Drugs; bactericidal; mechanism of action uncertain

**Indications:** treatment and prophylaxis of *Mycobacterium* infections (dosage 20-35 mg/kg/d) including tuberculous pneumonia

**Side Effects:** nausea and flushing common; less commonly, hepatotoxicity (large doses for prolonged periods; potentially lethal in combination with rifampicin), hyperuricemia, acute gout (rare; increased risk with allopurinol, colchicine, probenecid, sulfin pyrazone), non-gouty polyarthralgia, anorexia, vomiting, dysuria, malaise, fever, cutaneous hypersensitivity; rash; decreases cyclosporin levels; avoid in moderate to severe renal failure (glomerular filtration rate < 50 mL/min) and in dialysis

**Contraindications:** jaundice; avoid if pregnant (can be given after first trimester) or breastfeeding (insufficient data)

#### **VIOMYCIN**

**Indications:** mycobacterial bone marrow infections; mycobacterial hepatic granuloma; pulmonary tuberculosis and hepatitis due to *Mycobacterium avium-intracellulare*

**CLOFAZIMINE:** oral (take with or after food (absorption enhanced)) antileprotic and antitubercular; in WHO Model List of Essential Drugs

**Indications:** disseminated mycobacteriosis due to *Mycobacterium mageritense*, multibacillary leprosy; treatment of *Mycobacterium avium-intracellulare* infection

**Side Effects:** red-brown pigmentation of skin and, to lesser degree, conjunctiva, urine, sweat and sputum (may clear slowly when discontinued), nausea and diarrhoea with high dosage (crystals deposited in walls of small bowel and mesenteric lymph nodes), intestinal obstruction (occasional, dose-related), decreased sweating and tearing, giddiness, headache, blue-black discolouration of lesions, generalised retinal degeneration, corneal opacification

**Contraindications:** hepatic and renal impairment, pregnancy; avoid in breastfeeding if possible (may cause skin discolouration in infants)

**DAPSONE:** sulphone; oral (take with or after food) antileprotic; in WHO Model List of Essential Drugs

**Indications:** leprosy (including hepatitis); chronic mycobacterial ulcers

**Side Effects:** vomiting, nausea, anorexia, skin rashes, headache, insomnia, giddiness, tachycardia, haemolytic anaemia (more severe in those with glucose-6-phosphate dehydrogenase deficit), agranulocytosis, leucopenia, hepatitis, methaemoglobinemia (usually with high dosages), exfoliative dermatitis, peripheral neuropathy, cholestatic jaundice, infectious mononucleosis-like syndrome; dosage should be kept to a minimum; dosage modification not required in renal failure or in dialysis but monitor for myelosuppression; plasma levels increased by amprenavir, probenecid; bioavailability reduced by antacids and didanosine buffered formulations (space doses by 2-3 h); plasma levels reduced by rifabutin and rifampicin (increased risk of methaemoglobinemia from rifampicin metabolite); very weak association with oral contraceptive failure

**Contraindications:** safety in pregnancy not established; avoid breastfeeding glucose-6-phosphate dehydrogenase deficient infants; monitor others for haemolysis and jaundice, especially if premature or < 1 mo

#### **PROTHIONAMIDE**

**Indications:** multibacillary leprosy when clofazimine totally unacceptable

**Contraindications:** careful use in cardiac and pulmonary disease, breast feeding; safety in pregnancy not established

#### **ACETIC ACID**

**Indications:** suppurative otitis media treatment and prophylaxis (topical); otitis externa (topical); toenail and web infections due to *Pseudomonas aeruginosa*

#### **N-ACETYLCYSTEINE**

**Indications:** bronchiectasis; bronchitis; cystic fibrosis

**Side Effects:** stomatitis, nausea, rhinorrhoea, very rare sensitivity, bronchospasm

#### **ACI-JEL**

**Indications:** vaginosis (topical)

**Side-Effects:** occasional local irritation and inflammation

#### **AMMONIUM CHLORIDE**

**Indications:** urine acidification

**Side Effects:** nausea and vomiting in large doses, acidosis and hypokalemia, hepatic encephalopathy with excessive doses

#### **ANTITOXIN**

**Indications:** infections with *Clostridium botulinum*, *Clostridium tetani*, *Corynebacterium diphtheriae*

#### **ASCORBIC ACID**

**Indications:** Chediak-Higashi syndrome; hyper-IgE-recurrent-infection syndrome; radiation-induced injury; repeated infections; surgical prophylaxis (postoperative); urinary acidification

#### **ASPIRATION**

**Indications:** septic arthritis due to *Salmonella*; bursitis; cat scratch disease; endophthalmitis; hepatic abscess

#### **ASPIRIN (ACETYLSALICYLIC ACID)**

**Indications:** reactive arthritis; mucocutaneous lymph node syndrome; rheumatic fever

**Side Effects:** may cause Reye syndrome in interaction with influenza A, influenza B, varicella-zoster and other viruses

#### **BENZOYL PEROXIDE**

**Indications:** mild to moderate acne vulgaris (topical)

**Side Effects:** allergic contact dermatitis and dryness

#### **BETAMETHASONE**

**Indications:** uveitis (topical)

**Side Effects:** hypersensitivity

#### **BISMUTH FORMIC IODIDE**

**Indications:** ischaemic, varicose and decubitus ulcers (topical)

#### **BISMUTH SUBSALICYLATE**

**Indications:** dyspepsia; prevention of travellers' diarrhoea

**Side Effects:** chronic 'encephalopathy'

#### **COLLOIDAL BISMUTH SUBCITRATE**

**Indications:** gastric and duodenal ulcers and non-ulcer-related dyspepsia; simple gastritis; prophylaxis of traveller's diarrhoea

**Side Effects:** acute reversible renal failure with high dose/overuse, chronic 'encephalopathy' with prolonged high dose and renal impairment; impaired absorption of anticoagulants, digoxin, phenytoin, theophylline, hypoglycemics; serum level of theophylline decreased; absorption of oral iron impaired; antacids and H<sub>2</sub> antagonists interfere with action

#### **BORIC ACID**

**Indications:** suppurative otitis media (topical)

#### **BROMHEXINE**

**Indications:** bronchitis

**Side Effects:** occasional mild gastrointestinal, isolated instances of headache, vertigo, perspiration, skin rash

#### **CARBENOXOLONE**

**Indications:** aphthous mouth ulcers (topical)

#### **CETRIMIDE**

**Indications:** impetigo (topical)

**CHLORHEXIDINE:** in WHO Model List of Essential Drugs as antiseptic

**Indications:** burns prophylaxis (topical); pseudomonal folliculitis (topical); impetigo (topical); pericoronitis (topical); wound infections (topical)

**Side Effects:** occasional skin irritation, extremely rare generalised allergic reactions

#### **CLOQUINOL**

**Indications:** 'swimmer's ear' (topical)

**Side Effects:** local irritation, hypersensitivity

#### **COLONY-STIMULATING FACTORS**

**Indications:** necrotising fasciitis due to *Pseudomonas aeruginosa*

#### **CORTICOSTEROIDS**

**Indications:** meningoencephalitis due to *Brucella*, *Streptococcus pneumoniae* infections

**Contraindications:** purulent conjunctivitis due to *Mycobacterium tuberculosis*

#### **CORYNEBACTERIUM PARVUM**

**Indications:** systemic infections prophylaxis in hyposplenism/splenectomy

#### **DEXAMETHASONE**

**Indications:** croup; endophthalmitis; enteric fever (critically ill patient in shock); epiglottitis; postneonatal pyogenic meningitis; otitis externa (topical)

**Side Effects:** usually not significant at dosages and duration of therapy used for these indications

#### **DEXTRANASE**

**Indications:** streptococcal endocarditis

#### **DIENOESTROL**

**Indications:** recurrent dysuria-frequency syndrome related to menopause

**Side Effects:** theoretical risk of adverse effects associated with estrogens

#### **DIETARY RESTRICTION**

**Indications:** acute diarrhoea and/or vomiting; diverticulitis

#### **DRAINAGE**

**Indications:** septic arthritis; cervical fascial space infections; acute empyema; hordeolum; nocardiosis; parotitis and submandibular sialadenitis due to *Burkholderia pseudomallei*; perinephric abscess; peritonsillar abscess; streptococcal and meningococcal pneumonia; prostatic abscess; pulmonary abscess; local and generalised sepsis due to *Mycobacterium*, *Salmonella*, *Aeromonas*; mastitis and breast abscess (unresponsive acute and advanced chronic); nasal septal abscess; postseptal cellulitis; acute sinusitis due to *Pseudomonas aeruginosa*; thyroiditis; tooth abscess; *Vibrio* wound and soft tissue infection

#### **ELECTROLYTE REPLACEMENT**

**Indications:** cholera

#### **EXCISION**

**Indications:** infections with *Corynebacterium pseudotuberculosis*, *Mycobacterium*, *Nocardia*

**FLUMETHASONE**

**Indications:** 'swimmer's ear' (topical)

**Side Effects:** occasional local irritation, hypersensitivity

**GENTIAN VIOLET (METHYLOSANILINE CHLORIDE):** antiinfective dermatological drug; in WHO Model List of Essential Drugs

**GRAMICIDIN:** polypeptide; increases permeability of plasma membrane; used topically, often in combination with other antimicrobials

**Indications:** 'swimmer's ear'

**Side Effects:** rare hypersensitivity; pregnancy

**GRANULOCYTE TRANSFUSIONS**

**Indications:** systemic infection prophylaxis in granulocytopenia

**HEPARIN**

**Indications:** cervical fascial space infections; meningococcal postneonatal pyogenic meningitis

**Side Effects:** occasional allergy, thrombocytopenia

**HEXACHLOROPHENE**

**Indications:** methicillin resistant *Staphylococcus aureus* control (topical); prophylaxis of recurrent *Staphylococcus aureus* skin infections (topical)

**HUMIDIFICATION**

**Indications:** acute chest infections; acute tracheitis

**HYDROCORTISONE**

**Indications:** eczema and allergic dermatitis; haemorrhoids and proctitis (topical); meningococcal post-neonatal pyogenic meningitis with evidence of Waterhouse-Friderichsen syndrome

**Side Effects:** usually not significant at dosages and duration of therapy used in these indications

**HYDROGEN PEROXIDE**

**Indications:** impetigo (topical); necrotising ulcerative gingivostomatitis (topical)

**HYPERBARIC OXYGEN**

**Indications:** clostridial cellulitis

**IMMUNOGLOBULIN**

**Indications:** mucocutaneous lymph node syndrome; systemic infection prophylaxis in agammaglobulinemia, granulocytopenia

**INDOMETHACIN**

**Indications:** ankylosing spondylitis; reactive arthritis

**Side Effects:** causes neutropenia by myelosuppression

**INTERFERON**

**Indications:** systemic infection prophylaxis in cell-mediated immunity disorders

**Side Effects:** flu-like symptoms, fatigue, headache, myalgia, rigour/chills, malaise in nearly all patients; haematological, hepatic, cardiovascular and neurological toxicities with higher doses; single case report of tinnitus and hearing loss; safety in pregnancy not established; caution in breastfeeding (insufficient data but low transfer anticipated)

**INTERLEUKIN 2**

**Indications:** systemic infection prophylaxis in cell-mediated immunity disorders

**INTRAVENOUS FLUID**

**Indications:** dehydration in acute diarrhoea and/or vomiting, diverticulitis, emphysematous gastritis

**ISOTRETINOIN**

**Indications:** severe acne vulgaris

**Side Effects:** severe local intolerance in 5%

**LEUCOCYTE TRANSFUSIONS**

**Indications:** infection and debilitation in cases involving malignancy, chemotherapy or organ transplantation with a documented chemotactic defect; necrotising fasciitis due to *Pseudomonas aeruginosa*

**LITHIUM**

**Indications:** selected patients with increased cyclic adenosine monophosphate

**LOCAL HEAT**

**Indications:** mild dacryocystitis, adenitis and canaliculitis; hordeolum; chronic ulcers due to *Mycobacterium ulcerans*

**MAGENTA**

**Indications:** paronychia (topical)

**MERCUROCHROME**

**Indications:** wound infections (topical)

**NONSTEROIDAL ANTI-INFLAMMATORY DRUGS**

**Indications:** burn infections; prostatitis and seminal vesiculitis due to *Mycobacterium avium-intracellulare*

**Side Effects:** may cause necrotising fasciitis if used in treating inflammatory cutaneous lesions

**OMEPRAZOLE**

**Indications:** simple gastritis, duodenal ulcer and peptic ulcer

**Side Effects:** possible blindness or reduced vision

**OXINDANAC**

**Indications:** neonatal and postneonatal pyogenic meningitis

**OXYGEN**

**Indications:** acute chest infections

**PENTOVIS**

**Indications:** recurrent dysuria-frequency syndrome related to menopause

**PHENYLBUTAZONE**

**Indications:** ankylosing spondylitis; reactive arthritis

**Side Effects:** causes neutropenia by myelosuppression

**PHENYLEPHRINE**

**Indications:** mild dacryocystitis, adenitis and canaliculitis (topical)

**Side Effects:** may precipitate latent glaucoma

**Contraindications:** thyrotoxicosis, hypertension, tachycardia, patients on  $\beta$ -blockers

**PIROXICAM:** nonsteroidal anti-inflammatory drug

**Indications:** possible benefit in *Pseudomonas aeruginosa* chronic pulmonary infection in cystic fibrosis

**Side Effects:** gastrointestinal effects in 20%, dizziness in 4%, headache in 4%, oedema in 3%, skin rash in 2%, sedation/drowsiness in 2%, pruritis in 1%, stomatitis in 1%

**PLASMA**

**Indications:** systemic infection prophylaxis in complement deficiency, granulocytopenia

**PLASMA EXCHANGE**

**Indications:** haemolytic uraemic syndrome

**POVIDONE IODINE:** topical; in WHO Model List of Essential Drugs, replacing iodine as topical antiseptic agent of choice

**Side Effects:** hypersensitivity

**Indications:** burns; catheter lubrication; conjunctivitis; pseudomonal folliculitis; gingivitis; impetigo; keratitis and iritis due to Gram positive bacteria; methicillin resistant *Staphylococcus aureus* control; otitis externa; suppurative otitis media; paronychia; pericoronitis; stomatitis; surgical prophylaxis (skin antiseptics, postoperative wound spraying, intestinal instillation and lavage); ischaemic, varicose and decubitus ulcers

**PREDNISONE ACETATE + PHENYLEPHRINE**

**Indications:** uveitis

**Contraindications:** bacterial, fungal or viral infections

**PREDNISOLONE**

**Indications:** bacterial keratitis and iritis; tuberculous meningitis; nonspecific proctitis; cardiovascular syphilis and neurosyphilis; ulcerative colitis; ? tetanus

**Side Effects:** usually not significant in dosages and duration of therapy used in these indications

**PREDNISONE**

**Indications:** Epstein-Barr virus infection (impending airway obstruction, patients exhausted by generalised infection); Lyme disease (meningoencephalitis, heart block); myocarditis and pericarditis due to *Mycobacterium tuberculosis*

**Side Effects:** usually not significant in dosages and duration of therapy used in these indications

**PROBENECID:** potentiates penicillins and some cephalosporins

**Indications:** streptococcal endocarditis; *Neisseria gonorrhoeae* infections; chronic pulmonary infection due to *Haemophilus influenzae* or *Staphylococcus aureus* in cystic fibrosis; *Salmonella* carriers; syphilis in human immunodeficiency virus infected patients

**Side Effects:** headache, gastrointestinal symptoms, urinary frequency, hypersensitivity, sore gums, flushing, alopecia, dizziness, anaemia (including haemolytic and aplastic), nephrotic syndrome, leucopenia, hepatic necrosis, exacerbation of gout and uric acid stones

**PROCAINE HYDROCHLORIDE**

**Indications:** acute epididymitis and epididymo-orchitis

**PROPAMIDINE ISETHIONATE**

**Indications:** mild purulent conjunctivitis (topical)

**PROSTAGLANDIN E<sub>1</sub>**

**Indications:** mucocutaneous lymph node syndrome

**Side Effects:** fever in 14%, flushing in 10%, bradycardia in 7%, hypotension in 4%, seizures in 4%, tachycardia in 3%, diarrhoea in 3%, sepsis in 2%, cardiac arrest in 1%, oedema in 1%, disseminated intravascular coagulation in 1%, hypokalaemia in 1%; apnoea in 12% of neonates

**PYRIDOXINE**

**Indications:** prevention of peripheral neuritis in treatment with isoniazid; tetanus

**Side Effects:** interacts with L-dopa

**PSYLLIUM HYDROPHILIC MUCILLOID**

**Indications:** diverticulitis prophylaxis

**REHYDRATION**

**Indications:** cholera; acute diarrhoea and/or vomiting; parotitis and submandibular sialadenitis; toxic shock syndrome

**SACCHAROMYCES BOULARDII**

**Indications:** prophylaxis of antibiotic-associated diarrhoea and pseudomembranous colitis

**Side Effects:** fungemia in critically ill patients

**SELENIUM SULPHIDE**

**Indications:** seborrhoeic blepharitis (topical)

**SILVER NITRATE:** in WHO Model List of Essential Drugs as antiinfective ophthalmological agent

**Indications:** prophylaxis of gonococcal ophthalmia neonatorum (topical); rash due to *Pseudomonas aeruginosa*, *Yersinia* (topical)

**SODIUM BICARBONATE**

**Indications:** alkalinisation in treatment with sulphadiazine; seborrhoeic blepharitis (topical); geographic tongue, hairy tongue and black hairy tongue (mouthwash); mouth ulcers (mouthwash)

**SODIUM CHLORIDE**

**Indications:** geographic tongue, hairy tongue and black hairy tongue (mouthwash); mouth ulcers (mouthwash); pericoronitis (mouthwash); acute viral throat infections (gargle)

**SODIUM CROMOGLYCAT**

**Indications:** allergy

**SODIUM DEOXYCHOLATE**

**Indications:** prophylaxis of necrotising enterocolitis

**SODIUM HYPOCHLORITE:** in WHO Model List of Essential Drugs

**Indications:** wound infections (topical)

**SURGERY**

**Indications:** appendicitis; septic arthritis; brain and epidural abscess; bursitis; carpal tunnel syndrome; cholangitis and cholecystitis; diverticulitis; chronic empyema; endocarditis (patient with prosthetic valve; due to *Brucella*, where appropriate therapy fails to control infection; refractory congestive cardiac failure); endophthalmitis; false aneurism; mastoiditis; mesenteric lymphadenitis; mycotic aneurism; myonecrosis; necrotising enterocolitis; necrotising fasciitis; osteomyelitis and osteochondritis; pancreatic abscess; perianal and perinatal abscess and cellulitis in patients with malignant disease (unresponsive); pneumonitis due to *Rhodococcus equi*; psoas abscess; pulmonary abscess; rhinoscleroma; chronic sinusitis; splenic abscess; granulomatous synovitis; tenosynovitis; tooth abscess; mycobacterial chronic ulcers

**TRIAMCINOLONE**

**Indications:** 'swimmer's ear' (topical)

**Side Effects:** infrequent local adverse reactions, may damage collagen of tympanic membrane, may delay healing, systemic absorption may occur

**TRICLOSAN:** topical

**Indications:** mild acne vulgaris; methicillin resistant *Staphylococcus aureus* control; prophylaxis of recurrent *Staphylococcus aureus* skin infections

**Side Effects:** occasional redness/drying

**TRANSFER FACTOR**

**Indications:** hyper-IgE-recurrent infection syndrome; systemic infection prophylaxis in cell-mediated immunity disorders

**VITAMIN E**

**Indications:** deficiency of glutathione synthetase

**ZINC**

**Indications:** acrodermatitis enteropathica; Downs syndrome; leprosy

**ZINC SULPHATE**

**Indications:** mild dacrocystitis, adenitis and canaliculitis (topical)

**DIPHENOXYLATE HYDROCHLORIDE:** antimotility drug used in diarrhoea but no evidence that it alters the course of acute diarrhoea or that it diminishes the losses of fluids; CNS toxicity may occur in therapeutic dosages and bacillary dysentery may be aggravated

**LOPERAMIDE:** antimotility drug used in diarrhoea but no evidence that it diminishes losses of fluids or electrolytes when administered in conventional dosages; adverse effects on CNS have been observed in therapeutic dosages; paralytic ileus has been associated with its use in infants and children

**KAOLIN AND PECTIN:** absorbents used in diarrhoea but induce only a slight change in stool consistency; no evidence that they reduce the duration or severity of the diarrhoeal episode or that they reduce the losses of fluids or electrolytes; may interfere with antibiotic treatment when indicated

**ACTIVATED CHARCOAL:** absorbent used in diarrhoea but no evidence that it shortens the duration of diarrhoea or that it reduces the number or volume of stools; as an absorbent, it can bind antibiotics or enzymes

**ATTAPULGITE AND SMECTITE:** absorbents used in diarrhoea but no evidence that they have any effect on the losses of fluids and electrolytes; may bind or inactivate other drugs