Cephalosporins

Cephalosporins are **bactericidal** beta-lactam antibiotics derived from the fungus ***Acremonium*** — they disrupt peptidoglycan formation in the cell wall.

They have no activity against **LAME**: Listeria, Atypicals (Mycoplasma/Chlamydia), MRSA and Enterococci. (Only MRSA exception being 5th Generation drugs: Ceftobiprole etc.)

1st Gen	2nd Gen	3rd Gen	4th Gen	5th Gen
Cefadroxil Cefalexin Cefazolin Cefazedone	Cefaclor Cefuroxime Cefotetan Cefprozil	Cefixime Ceftriaxone Cefdinir Cefodizine Cefotaxime Ceftazidime	Cefepime Cefquinome	Ceftobiprole Ceftaroline Ceftolozane

General Rule

1st Gen are predominantly active against gram-positives, with succeeding generations progressively more active against gram-negative strains (often with reduced gram-positive activity, except 4th, which are extended spectrum agents).

Adverse Effects

Nausea, diarrhoea, rash, pain and inflammation at injection site.

Those allergic to penicillins may show cross-sensitivity with some cephalosporins, but the figure is thought to be considerably less than the 10% commonly cited.

Aminoglycosides

Protein Synthesis Inhibitors (Bactericidal)
Inhibit protein synthesis by irreversibly binding to 30S subunit of the ribosome.

Gentamicin
Netilmicin
Streptomycin
Tobramycin

Poorly absorbed from the gut and, as a result, are administered **parenterally**. They have short half-lives (1-4 hours) and rapidly eliminated via the kidney. They do not cross the blood-brain barrier, but they do cross the placenta.

Side effects include **ototoxicity**, which may lead to vestibular and auditory dysfunction.

Renal damage through concentration of the drug in the proximal tubular cells of the kidney — usually reversible.

Spectrum of Activity

Particularly useful in treating **aerobic gram-negative** infections: *Pseudomonas*, *Acinetobacter* and *Enterobacter etc.*

Inactive against **anaerobic** organisms.

Sulfonamides

Sulfonamides is a term encompassing many groups of drugs, each of which is based on the sulfa-functional group. Antibacterial sulfonamides act as competitive inhibitors of the enzyme **dihydroopteroate synthetase** (DHPS); an enzyme involved in **folate synthesis.**

Sulfonamides are therefore **bacteriostatic** — inhibiting growth and multiplication — but do not cause cell death. Resistance today is common.

Clinically Approved Sulfonamides

Sulfacetamide	Sulfadiazine	Silver Sulfadiazine
Sulfasalazine	Sulfamethoxazole	Mafenide

Acne/Seborrheic Dermatitis

IBS/Rheumatoid Arthritis

Burns

Urinary Tract Infections

General Points

Sulfamethoxazole is often used as part of a 5:1 ratio with **trimethoprim.**

Evidence regarding use of silver sulfadiazine in the effective treatment of burns is **poor.**

Sulfasalazine can cause **hemolytic anemia** in those with G6PD deficiency.

Adverse Effects

Nausea, Vomiting, Diarrhoea
Skin Rash/Allergy
Neutropenia
Sunlight Sensitivity
Crystals in Urine

Carbapenems

Carbapenems are a class of **beta-lactam antibiotics** with a broad spectrum of bactericidal activity - their structure renders them **highly resistant** to beta-lactamases.

Imipenem can be hydrolysed in the kidney by the enzyme **dehydropeptidase 1**, hence why it is given with an inhibitor of dehydropeptidase — **cilastatin.**

Clinically Approved Carbapenems

Imipenem	Meropenem	Ertapenem	Doripenem

General Points

All are given by **IV and IM** routes, except meropenem, which is only IV. At high doses, imipenem is **seizuregenic.**

Doripenem is particularly active against *Pseudomonas aeruginosa*, compared to ertapenem which is not.

Meropenem is bactericidal, **except** against *Listeria monocytogenes*, where it is bacteriostatic.

Marketing slogan of ertapenem is **The Power of One**, as the dose is 1g once daily.

Pharmacokinetics

Carbapenems have **short half-lives** — between 1-5hrs.

Primarily undergo **renal** metabolism.

Lincosamides

Lincosamides are a class of antibiotics that work by interfering with protein synthesis, specifically by binding to the **23s portion of the 50s subunit** of bacterial ribosomes.

The first discovered lincosamide — **lincomycin** — was isolated from the *Streptomyces lincolnensis* strain, its name deriving from the soil sample taken from Lincoln, Nebraska.

Clinically Approved Lincosamides

Lincomycin | Clindamycin

General Points

Lincomycin is **narrow spectrum** in effect, mostly used for gram-positive infections. It is available **IM** and **IV**.

Clindamycin is available orally, topically, IV and intravaginally. Mostly used to treat **anaerobic gram-negative** infections, but may be used against some gram-positive cocci.

Clindamycin **may prolong effects** of neuromuscular blocking drugs such as vecuronium.

Adverse Effects

Nausea, Vomiting
Abdominal Pain, Cramps
Rash, Metallic Taste

Clindamycin is also associated with *Clostridium difficile*-associated diarrhoea.

Glycopeptides

Glycopeptide antibiotics are a class of drugs of microbial origin, which work by inhibiting peptidoglycan synthesis — the antecedent of cell walls.

These drugs are principally effective against **gram-positive cocci**, exhibit a **narrow spectrum** of action, **bactericidal** only against enterococci and tend to be used in those who are either critically ill, hypersensitive to β-lactams, or infected with β-lactam-resistant species.

Clinically Approved Glycopeptides

Vancomycin	Teicoplanin	Telavancin

General Points

All three are given by **IV** due to poor absorption, though vancomycin may be given orally to treat pseudomembranous colitis. Teicoplanin may be given IM.

Vancomycin should be administered both dilute and slowly, to avoid **red man syndrome.**

Telavancin is associated with a higher rate of kidney failure than vancomycin.

Adverse Effects

Ototoxicity
Nephrotoxicity (enhanced with aminoglycosides)
Thrombophlebitis at injection site
Rash
Neutropenia/Thrombocytopenia
Nausea

Thionamides

Carbimazole **Propylthiouracil**

Thionamides
- Used to treat hyperthyroidism and Graves disease.
- Inhibit thyroxine peroxidase which, in turn, inhibits thyroid hormone.

Given that T_4 has a long half-life, it may take up to **6 weeks** for circulating T_4 and T_3 concentrations to return to normal. Both drugs accumulate in the thyroid gland over time, meaning their duration of action is longer than half-life expectations.

Carbimazole is converted by first-pass metabolism into the active ingredient **methimazole**. Methimazole has a short half-life of around 3-5 hours.

Propylthiouracil has 1/10 the activity of methimazole — usually reserved for those intolerant to carbimazole. **Cross-sensitivity** occurs between carbimazole and propylthiouracil.

Unwanted effects include GI upset, headache, arthralgia and pruritic rash common in first 8 weeks. **Bone marrow suppression** may also occur.

Quinolones

Quinolones are broad-spectrum antibacterial drugs. The first quinolone — nalidixic acid — was discovered in1962 by George Lesher and subsequentlyused in the treatment of urinary tract infections.

Quinolones work by selectively inhibiting topoisomerase II, thereby disrupting cell division. Later generation drugs — such as gemifloxacin and moxifloxacin — have enhanced activity at topoisomerase IV.

Clinically Approved Quinolones

Nalidixic Acid	Ciprofloxacin	Norfloxacin	Levofloxacin	Gemifloxacin	Moxifloxacin

General Points

Nalidixic acid is primarily active against gram-negatives, and was historically used for urinary tract infections – a condition that norfloxacin treats today.

Ciprofloxacin should not be taken with magnesium, aluminium, calcium, iron or zinc products. The drug is also contraindicated for use with the muscle relaxant tizanidine.

Levofloxacin exhibits greater activity against gram-positives than gram-negatives; exhibits enhanced activity against *Streptococcus pneumoniae*.

Gemifloxacin and moxifloxacin are effective in the treatment of bacterial exacerbations of chronic bronchitis/pneumonia.

Adverse Effects

Tendonitis/tendon rupture, particularly in those with myasthenia gravis

QT prolongation, particularly with moxifloxacin

Clostridium difficile-associated diarrhoea

CNS effects: dizziness, headache, tremor, risk of seizures

Nausea, vomiting, abdominal pain

Tetracyclines

Protein Synthesis Inhibitors (Bacteriostatic)
Inhibit protein synthesis by reversibly binding to 30S subunit of the ribosome.

Doxycycline
Minocycline
Oxytetracycline

Tetracyclines **stain** developing teeth and **discolour** permanent teeth.

Tetracyclines are **inactivated** by ions of calcium, aluminium, iron and zinc. Avoid associated foods and remedies.

Tetracyclines may render patients **photosensitive.**

Tetracyclines have average half-lives between **8 and 22 hours.**

They have **poor penetration** into the CSF.

Concentrated in the liver, may cause microvesicular **fatty liver.**

Broad Spectrum Antibiotics

Particularly useful in *Chlamydia*, *Mycoplasma*, *Rickettsia*, Lyme Disease, *Coxiella*, Leptospirosis, Syphilis, *Legionella* and *Brucella* species.
Also used in treatment of acne.