Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Benzypenicillin (Group 1)	Pencillins β-lactams Group 1 = long acting parenteral Group 2 = oral absorption Group 3 = anti-Staphylococcal Group 4= extended spectrum Group 5 = anti-pseudomonal Group 6 = β-lactamase resistant	• Destruction of antibiotic by β-lactamases • Failure to penetrate outer cell wall of most Gram-negative bacteria • Efflux across outer membrane of Gram-negative bacteria • Low-affinity binding of antibiotic to PBPs	Meningitis: Grp A, Grp B, NM Endocarditis: Streptococcal + Enterococcal Neuro syphilis	• Allergic reactions-skin rashes, serum sickness, delayed hypersensitivity <10% exposed • Anaphylaxis (0.004-0.4%) • GI – diarrhoea, enterocolitis • Haematological – haemolytic anaemia, neutropenia, thrombocytopenia • Elevated transaminases (fluclox), electrolyte abnormalities • Renal – intestinal nephritis. Haemorrhagic cystitis • CNS – encephalopathy/ seizures in renal failure or prolonged high dosing	IV		Concentration dependent bactericidal activity Get persistent survivors, phenomenon known as tolerance Inhibit cell wall synthesis by binding to PBPs and inhibiting transpeptidation of peptidoglycan Synergy with aminoglycosides in order to improve speed of bactericidal effect	
Penicillin V (Group 2)					Oral			
Methicillin (Group 3)								
Flucloxacillin (Group 3)								
Amoxicillin (Group 4)			Use in combination with aminoglycoside for R Gram-ve					
Ampicillin (Group 4)								
Ticarcillin (Group 5)								
Piperacillin (Group 5)								
Timocillin (Group 6)								

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Cefradine (1st gen)	Cephalosporins β-lactams 1st gen = primarily against Gram-pos 2nd gen = enhanced Gram-neg variable Gram-pos Cephamycin grp = better against anaerobes 3rd gen = Gram-neg improved 4th gen = includes Pseudomonas cover	• Destruction of antibiotic by β-lactamases • Failure to penetrate outer cell wall of most Gram-negative bacteria • Efflux across outer membrane of Gram-negative bacteria • Low-affinity binding of antibiotic to PBPs • SHV • TEM • AmpC	UTI Strep and Staph skin and soft tissue infections	• Hypersensitivity – rash, urtcaria, serum sickness • Anaphylaxis (0.01) • GI – diarrhoea, nausea and vomiting, transient hepatitis, biliary sludging (ceftriaxone) • Haematological – eosinophilia, haemolytic anaemia, neutropenia, thrombocytopenia, clotting abnormalities, platelet dysfunction • False laboratory tests – Coombs' test, serum creatinine, glycosuria • Renal – intestinal nephritis. • CNS – seizures • Drug fever • Disulfiram-like reaction • Phlebitis	Oral (PO) IV IM		Concentration dependent bactericidal activity Get persistent survivors, phenomenon known as tolerance Inhibit cell wall synthesis by binding to PBPs and inhibiting transpeptidation of peptidoglycan Synergy with aminoglycosides in order to improve speed of bactericidal effect Post antibiotic effect against Gram-positives	
Cefalaxin (1st gen)					Oral (PO) IV IM			
Cefuroxime (2nd gen)			2nd & 3rd gen are inactivated by β-lactamases. Never use to treat: Enterobacter spp. Serratia spp. *Citrobacter freundii*, Acinetobacter spp, Proteus vulgaris, Providenia spp. *Morganella morganii* (ESCAPPM) 2ng gen – CAP, early Lymes, otitis media Cephamycins-Intra-abdominal Pelvic, gynae, soft tissue 3rd gen – pen R pneumococci, URTI, LRTI, meningitis, Lyme disease, typhoid, severe Shigella, OPAT for endocarditis & osteomylitis		Oral (PO) IV IM			
Cefoxitin (2nd gen) Cephamycin grp					Oral (PO) IV IM			
Cefotaxime (3rd gen)					Oral (PO) IV IM			
Ceftriaxone (3rd gen)					Oral (PO) IV IM			
Ceftazidime (3rd gen)					Oral (PO) IV IM			
Cefixime (3rd gen)					Oral (PO) IV IM			
Cefpodoxime (3rd gen)					Oral (PO) IV IM			
Cefepime (4th gen)			Severe Gram-ve infections		Parenteral			
Cefpirome					Parenteral			

(4th gen)							

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Co-amoxiclav	β-lactamase inhibitors β-lactams Inhibit β-lactamases due to SHV and TEM	• Destruction of antibiotic by β-lactamases • Failure to penetrate outer cell wall of most Gram-negative bacteria • Efflux across outer membrane of Gram-negative bacteria • Low-affinity binding of antibiotic to PBPs	Otitis media Sinusitis Soft tissue Pneumonia Bite infections Diabetic foot ulcers	Similar to ampicillin	Oral IV		Concentration dependent bactericidal activity Get persistent survivors, phenomenon known as tolerance Inhibit cell wall synthesis by binding to PBPs and inhibiting transpeptidation of peptidoglycan Synergy with aminoglycosides in order to improve speed of bactericidal effect	
Ticarcillin-clavulanate			Use for Pseudomonas and Proteus spp. Pneumonia, intra-abdominal infection, gynae infections skin/soft tissue osteomyelitis	Cholestatic jaundice + other β-lactam side effects	IV only			
Ampicillin-sulbactam			Available in the USA Skin/soft tissue Intra-abdominal Gynae infections *Acinetobacter baumannii* carbapenem resistant	Similar to ampicillin	IV only			
Piperacillin-tazobactam			Pneumonia (especially *Pseudomonas aeruginosa*) Skin/soft tissue Intra-abdominal UTI Polymicrobial Bacteraemia Febrile neutropenia (combined with an amino-glycoside)	Similar to piperacillin	IV only			

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Imipenem	Carbapenems β-lactams Derived from *Streptomyces cattleya* Used for severe infections: Bacteraemia Intra-abdominal infections Obstetric infections Gynae infections Complicated UTI Soft tissue and bone infections	4 mechanisms: • Production of low-affinity PBP target • Reduced membrane permeability due to absence of **OprD** in Gram-neg • Efflux in Gram-negatives • Carbapenemase enzymes ○ Class A (functional grp 2f) SME, IMI, NMC, KPC, GES ○ Class B (functional grp 3): IMP, VIM, GIM, SVM ○ Class D (functional grp 2d): OXA	Slightly more active than others against Gram-pos Serious infections: Polymicrobial Febrile neutropenia Nosocomial infection DON'T USE FOR MENINGITIS! Most appropriate for **ESCAPPM pathogens** **E**nterobacter spp. **S**erratia spp. ***C**itrobacter freudii* **A**cinetobacter ***P**roteus vulgaris* **P**rovidentia spp. ***M**organella morganii*	• Causes seizures so DON'T USE in meningitis cases • Require dose modification in renal failure • Need to co-administer with cilastatin a DHP-1 inhibitor as it's a substrate for renal dehydropeptidase-1 (DHP-1) • Nasusea if infused too quickly	IV		High affinity to most high molecular weight PBPs of Gram-positive and Gram-negative bacteria Traverse Gram-negative outer membrane proteins through different outer membrane proteins than cephalosporins and pencillins – **OprD** rather than OmpC and OmpF, especially Imipenem	
Meropenem			Slightly more active against Gram-neg than Imi Most active against *Pseudomonas aeruginosa* Bacterial meningitis Most appropriate for **ESCAPPM pathogens** Serious infections: Polymicrobial Febrile neutropenia Nosocomial infection	• Require dose modification in renal failure • All carbapenems can cause rash, urticarial, cross-reactivity with penicillin, immediate hypersensitivity	IV			
Ertapenem			Slightly more active against Gram-neg than Imi	Require dose modification in renal	Once daily dosing so			

			Poor activity against *Pseudomonas aeruginosa* and Acinetobacter spp.	failure	good for OPAT IV			
Antimicrobial	**Class**	**Resistance**	**Use**	**Side Effects**	**Delivery**	**Interactions**	**Synergy**	**Action**
Aztreonam	Monobactam β-lactams Produced by *Chromobacterium violaceum*	Susceptible to AmpC but not most other β-lactamases	Only some Gram-negatives Enterobacteriaceae, Neisseria, Haemophilus, Never use as monotherapy UTI Pneumonia Septicaemia Skin/soft tissue Intra-abdominal Gynae Wounds Burns	• Allergic reactions- skin rashes, serum sickness, • GI – diarrhoea, enterocolitis • Haematological – haemolytic anaemia, neutropenia, thrombocytopenia • Electrolyte abnormalities • Renal – intestinal nephritis. Haemorrhagic cystitis	IV IM		Passes through outer membrane protein and binds to PBP3 of Gram-negative bacteria	
Bactitracin			Used to identify Group A Streptococci as they are Bacitracin resistant		Topical only as it is toxic due to similar reactions in eukaryotic cells		Binds to isoprenylphosphate and prevents dephophorylation of the lipid carrier that transports cell wall building blocks across the membrane – means native compound cannot regenerate	
Fosfomycin			UTI Broad spectrum against				Inhibits pyruvyl transferase and therefore the	

			Gram-negative bacilli				formation of N-acetylglucosamine from N-acetylmuramic acid.
Cycloserine			2nd line-regimen for drug resistant tuberculosis				Structural analogue of D-alanine, acts on alanine racemase and synthetase to inhibit the sunthesis of terminal D-alanyl-D-alanine. = prevents the formation of the pentapeptide chain of muramic acid
Isoniazid			1st line treatment for TB				Interfere with mycolic acid synthesis in mycobacterial cell walls
Ethambutol			1st line treatment for TB				Interfere with mycolic acid synthesis in mycobacterial cell walls

Antimicrobial	**Class**	**Resistance**	**Use**	**Side Effects**	**Delivery**	**Interactions**	**Synergy**	**Action**
Vancomycin	Glycopeptides Vancomycin from *Nocadia orientalis* Teicoplanin from *Actinoplanes*	Intrinsic vanc R in : *Leuconooc, Pediococcus, Lactobacillus, Erysipelothric rhusiopathiae* Intrinsic Teic R in *S. haemolyticus*	Broad Gram-positive activity Used for: Severe MRSA infections Meningitis due to pen R Strep pneumoniae Orally for *C. difficile* assoc. diarrhoea	Dose reduction in renal impairment – must monitor trough levels after the 3rd dose, should be 10 – 15mg/l If trough level too high reduce dose	Usually given by IV but can be given orally, intraperitoneally intrathecally, Intraocularly		Inhibit cell synthesis by binding D-alanyl-D-alanine tail of muramylpentapeptide Complex cannot be processed by the enzyme glycosyltransferase. Inhibits the inc of the	

	teichomyceticus – not available in USA	Enterococci: 6 types of glycopeptide R: ○ VanA – *Staph aureus*, *E. faecium*, *E. faecalis* ○ VanB – *E. faecium*, *E. faecalis* ○ VanC – intrinsic in *E.gallinarum*, *E. asselflavius*, acquired in *E. flavescens* ○ VanD – *E. faecium* ○ VanE – *E. faecalis* ○ VanG – *E. faecalis* Named based on lipase genes = result in the formation of a peptidoglycan precursor with decreased affinity for glycopeptides Vancomycin tolerance has been reported in Strep pneumoniae	Febrile neutropenia CAPD peritonitis Endophtalmitis CSF shunt infections (intrathecal) CVL infections Poor CSF penetration in the absence of inflammation	rather than altering dosing frequency (as kill is time dependent) Ototoxicity – rare if no renal toxicity Nephrotoxicity – often associated with concomitant aminoglycoside usage Red-man syndrome associated with rapid infusion Neutropenia, thrombocytopenia, rashes, drug fever			murein monomers (N-acetylmuramic acid & N-acetylglucosamine) into peptidoglycan chain
Teicoplanin			Dose reduction in renal impairment Don't need to monitor for kidney function but monitoring sometimes done in severe infections to monitor therapeutic levels	Usually given by IV but can be given intramuscularly, or intraperitoneally Long half-life so can daily dose Better bone penetration than		

				Neutropenia, thrombocytopenia, rashes, drug fever	vancomycin		

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Streptomycin	Aminoglycosides Streptomycin is from *Streptomyces griseus* 6 membered ring with an amino group (aminocyclitol) 4 Nos No protein synthesis No use in pregnancy No use in Gram-positive N = nephrotoxicity O = ototoxicity	• Intrinsic R can be enzymatic or non-enzymatic: ○ Anaerobes are intrinsically resistant due to the fact that they do not generate a sufficient electrical potential difference across the cell membrane ○ M. tb has a mutation in 16S ribosomal subunit that can result in resistance to Steptomycin (rpsL?) • Acquired R via a variety of mechanisms: ○ Reduced drug uptake ○ Efflux pumps i.e. MexXY in Pseudomonas aeruginosa ○ Enzymatic modification of the drug by aminoglycoside	• No good for anaerobes • No good CSF penetration apart from in neonates **Gentamicin** – empirical therapy for serious infections: • Septicaemia • Febrile neutropenia • Biliary sepsis • Acute pyelonephritis • Endocarditis **Amikacin** – Gent resistant infections, mycobacterial infections, nocardiosis **Tobramycin** – slightly better for *P. aeruginosa* and in CF patients **Neomycin** – SDD **Streptomycin** – TB, if gent R sometimes	Nephrotoxicity – need to do levels if on gentamicin for over 48 hours and dosing modified according to the **Hartford nomogram** Ototoxicity (cochlear and vestibular) may be irreversible Neuromuscular blockade = rare	IV/IM		Bind to the A site of the 30S ribosomal subunit – results in a conformational change that interferes with mRNA translation and translocation and thus protein synthesis Transport of aminoglycosides into the cell in energy dependent (EDP-I and EDP-II). The onset of cell death in coincident with the transition from EDP-I to EDP-II ○ **Concentration dependent bactericidal activity** ○ **Significant post-antibiotic effect (PAE)**	
Neomycin					Topical Oral			
Gentamicin					Drops for eye & ear infections, intrathecal for shunt IV			
Amikacin								
Tobramycin								
Netilmicin								

		modifying enzymes (AMEs) that: ○ Phosphorylate ○ Acetylate ○ Adenylate Exposed amino or hydroxyl groups	use synergistically in endocarditis **Netilmicin** – infections R to Gent **Spectinomycin** – Gonorrhea **Paromycin** - Cryptosporidiosis				○ **Synergism with cell wall agents**

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Erythromycin	Macrolides Erythromycin – derived from *Saccharopolyspora erythraea*	4 resistance mechanisms: • Decreased outer membrane permeability – Enterobacteriaceae, Pseudomonas, Acinetobacter = intrinsically resistant • Efflux pumps – *msr(A)* gene in SA *mef(A)* in S. pn and GAS • Alterations of 23S rRNA by methylation of adenine. = confers resistance to macrolides, lincosomides and Streptogrammins type B. Referred to as the MLS_8 phenotype & encoded for by the *erm*	CAP + atypical pneumonia, *B. pertussis*, Campylobacter gastroenteritis	GI symptoms – nausea, vomiting, abdominal cramps Skin rash Fever Eosinophilia Cholestatic jaundice Transient hearing loss Candidiasis Transient hearing loss Pseudomembranous colitis OT prolongation Infantile pyloric stenosis	Oral – stimulates GI motility IV		Erythromycin – Erythromycin A = active component – 14 membered macrocylic lactone ring with 2 sugars Macrolides: Inhibit RNA-dependent protein synthesis at the chain elongation stage by interacting with the peptidyl transferase site. Also inhibits the formations of the 50S ribosomal sub-unit	
Clarithromycin			M. avian complex & other non-tuberculous mycobacteria H. pylori eradication Lyme disease		Oral IV			
Azithromycin			Similar to Ery + trachoma, *B. microti*, *B. burgdorferi*, cryptosporidosis					
Spiramycin			Cryptosporidia Prevention of congenital toxoplasmosis					

Clindamycin	Lincosamides Lincomycin was isolated from Streptomyces lincolnensis. Clindamycin was produced by chemical modification	(erythromycin ribosomal methylase) gene • Enzymatic inactivation by phosphotransferases, mediated by *mph* genes. Hydrolysis of macrocyclic lactone is encoded by esterase genes *ere(A)* and *ere(B)* on plasmids	• Highly active against anaerobes • Alternative to β-lactams in allergic patients for bone & joint infections • Severe GAS infections (necrotizing fasciitis, toxic shock syndrome • PCP (used with primaquine) • *P. falciparum* malaria when used with qunine	C. difficile colitis = discontinue Clindamycin Allergic reactions – rashes, fever, erythema multiforme, analphylaxis Transient hepatitis, neutropenia, thrombocytopenia	Oral, IV IM		Inactivation of 3-lincomycin,4-clindamycin 0-nucleotide transferases by *linA* & *linA'* genes endocded on plasmids
Telithromycin	Ketolides Derived from Erythromycin A		CAP, acute exacerbation of COPD, tonsillitis, pharyngitis, sinusitis	Similar to Macrolides - Reports of exacerbation of myasthenia gravis	Oral		14 membered ring with a ketone prevents induction of MLS_8 SA with constitutive *erm* genes are R, S. pn with constitutive *erm* genes are S
Quinopristin-Dalfopristin	Streptogramins Derived from *Streptomyces* spp.	***E. faecalis* is intrinsically resistant** Three mechanisms of resistance: • Modification of the ribosomal target (quinopristin) – MLS8 phenotype encoded for by *erm* gene • Enzymatic inactivation of acetyltransferases encoded for by *vat(A), vat(B), vat(C)* in Staphylococci and *vat(D)* in *E faecalis* –	Resistant Gram-pos infections Vancomycin resistant *E. faecium* infections (not *E. faecalis* as intrinsically resistant) MSSA & GAS skin and soft tissue infections Serious Gram-pos infections where there is no alternative antibiotic available	Injection site reactions in 30% so drug should go into a central line Arthralgia & myalgia common Nausea, vomiting, diarrhoea, skin rash, pruritis Hepatitis, hyper-bilirubinaemia	Pref into a CVL		Consist of 2 macrolytic lactone peptolide components = streptogramin A and streptogramin B Act on elongation stage of protein synthesis. 2 components acts synergistically: • Streptogramin A (dalfopristin) binds to the 50S ribosomal sub unit and prevents aminoacyl—tRNA

		quinopristin & dalphopristin • Active transport out of cells by efflux pumps encoded for by *vga(A)* and *vga(B)* genes in Staphylococci – quinopristin & dalphopristin	Poor CSF penetration Significant PAE	Inhibition of hepatic CYP3A4 resulting in increased levels of drug metabolised by this enzyme			attaching to the catalytic site of the peptidyl transferase = inhibits transfer of the growing peptide chain • Streptogramin B molecules (Quinopristin) prevents the peptide bond forming leading to premature release of incomplete polypeptides

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Daptomycin	Lipopeptides Fermentation product of *Streptomyces roseoporus*	Resistance is rare	Complicated skin and soft tissue infection due to Gram-positive bacteria	Nausea Vomiting Diarrhoea Headache Rash Injection site reactions Muscle toxicity – myalgia, muscle weakness. Check serum creatinine kinase (CK) before starting and weekly during treatment – stop if symptoms develop Take a clotting sample before starting as interfers with prothrombin time	IV infusion		13-membered cyclic amino acid lipo-peptide antibiotic with a lipophilic tail Exact mechanism is unknown, appears to bind to cell membrane of Gram-pos in a calcium dependent manner, disrupting the cell membrane potential	
Linezolid	Oxazolidinones (purely synthetic)	Mutation in the 23SRNA domain V region – usually	Gram-positive infections: Pneumonia and	• GI symptoms – nausea, vomiting, diarrhoea • Myelosuppression-	Oral IV		Bacteriostatic protein synthesis inhibitors that bind	

		associated with long durations of therapy or prior exposure	complicated skin/soft tissue infections Serious infections due to MRSA, VRE, pen R pneumococci Good tissue & CF penetration	thrombocytopenia Neutropenia Pancytopaenia More common with prolonged therapy & usually reversible – FBC weekly • Monoamine oxidase inhibition – avoid tyramine-rich food • Serotonin syndrome in patients taking serotonin reuptake inhibitors • Optic neuropathy in patients >28 days, patients should report visual symptoms			to the 50S ribosomal subunit at its interface with the 30S ribosomal subunit preventing the formation of the 70S initial complex

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Chloramphenicol	Isolated from *Streptomyces venezuelae* CSF and ocular penetration is good	3 mechanisms: • Reduced permeability/uptake • Ribosomal mutation • Production of acetyl transferase, enzyme that acetylates the antibiotic into inactive form – mechanism also confers resistance to tetracyclines = responsible for widespread epidemics of R *S. typhi* & *S. dysenteriae*	Rarely used in the developed world: • Enteric fever due to S. typhi & S. paratyphi • Severe infections due H. influenza – meningitis, septicaemia, epiglottitis • Exacerbations of COPD • Alternative agent in pregnancy, patients with pen allergy • Eye drops for	• Bone marrow suppression is common, dose related and reversible. Manifestations include: ○ Anaemia ○ Reticulocytosis ○ Leucopaenia ○ Thrombocytopaenia ○ Monitor FBC 2x weekly during treatment • Aplastic anaemia is a rare idiosyncratic and often fatal complications which can occur during or after completion of therapy – discontinue if FBC falls below $2.5x10^9$/L • Haemolytic anaemia in	Oral Topical IM IV		Inhibits protein synthesis by binding to the 50S subunit of the 70S ribosome at a site that prevents the attachment of tRNA – prevents the association of the aminoacid with peptidyltransferase and peptide band formation = bacteriostatic effect in most pathogens Bactericidal in some meningeal pathogens – *H. influenza, S.*	

			superficial eye infections • Ear drops for otitis externa	patients with G6PD deficiency and childhood leukaemia • Grey baby syndrome due to high doses in neonates • Jarisch-Herxheimer reactions • Bleeding disorder • Acute intermittent porphyria			*pneumoniae, N. meningitis*

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Tetracycline 1st gen	Tetracyclines	Acquisition of genes on mobile genetic elements – most belong to *tet* family, some belong to *otr* family Three mechanisms: • Efflux pumps – membrane assoc. proteins pumps tetracyclines out of the cell = resistance to 1st gen • Ribosomal protection proteins = cytoplasmic proteins that release tetracyclines from their binding site by guanosine diphosphate	• Chlamydial infections – trachoma, psittacosis, salpingitis, urethritis, LGV • Rickettsial infections • Q-fever • Brucellosis (doxycycline + streptomycin/ rifamipicin) • Lyme disease (Borrelia burgdorferi) • Infective exacerbations of	• Nausea, vomiting, diarrhoea, dysphagia, oesophageal irritation • Photosensitivity reactions – toxic rather than allergic • Prolonged minocycline use – skin, nail & scleral pigmentation • Deposition in bones & teeth, not to be given	Oral		Inhibit bacterial protein synthesis by reversible binding to the 30S ribosomal subunit. Block binding of aminoacyl-tRNA to ribosomal A site site, prevents adding of new amino acids. = bacteriostatic Also inhibit mitochondrial protein synthesis by 70S ribosomal subunits in mitochondria of eukaryotic parasites	
Doxycycline 2nd gen					Oral			
Minocycline 2nd gen					Oral			
Tigecycline 3rd gen **(glycyclines)**					Oral Absorption of tetracycline is reduced by milk antacids and some salts			

		(GDP)-dependent mechanisms – protect from 1st & 2nd gene • Enzymatic inactivation – seen in *B. fragilis* where *tet(X)* gene codes for a protein that modifies tetracyclines in the presence of nicotinamide adenine dinucleotide phosphate oxidase (NADPH) & oxygen	COPD – due to HI activity • Acne • Refractory periodontal disease • Chronic prostatitis • Pelvic inflammatory disease • Melioidosis Tigecycline – complicated skin & soft tissue infections, abdominal infections due MDR organisms	<12, pregnant or breast feeding women • Exacerbate renal impairment, avoid all but doxycycline/ minocycline in renal failure • Vertigo in minocycline • Superinfections mucocutaneous candidiasis, ? C. difficile			= mechanism of antiprotozoal activity is unknown

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Sulfamethoxazole Short/ medium acting	Sulfonamides	Chromosomal resistance due to mutation in: • Overproduction of PABA e.g. SA and *N. gonorrheae* • Alterations in dihydropteroate synthetase that results in reduced affinity for sulfonamides e.g. *E. coli* Plasmids that carry genes encoding for: • Production of drug-resistant enzymes	Combined with Trimethoprim to treat infections	• Dose modification is required in renal impairment • Nausea • Vomiting • Diarrhoea • Drug-induced lupus • Serum sickness-like syndrome • Acute haemolytic anaemia • Agranulocytosis • Leucopaenia • Thrombocytopaenia • Drug eruption	IV Sub-cut		Bacteriostatic Inhibit bacterial growth by interfering with folic acid synthesis = analogues of PABA and competitively inhibit the incorporation of PABA into tetrahydropteroic acid by the enzyme tetrahydropteroic acid synthetase	
Sulfadiazine Short/ medium acting			Used to prevent rheumatic fever Used in combination with pyrimethamine for toxoplasmosis		IV Sub-cut			
Sulfadoxine Long acting			Used in combination with pyrimethamine to treat falciparum malaria					
Sulfasalazine Limited to GI tract			Used topically to treat burn infection		Topical			

Mafenide acetate		• Decreased bacterial permeability	Used topically to treat burn infection	• Vascultitis • Erythema nodosum • Erythema multiforme • Stevens-johnson syndrome • Anaphylaxis • Neonatal kernicterus (if given during the last month of pregnanacy	Topical		
Sulfacetamide sodium					Topical – eye drops		

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Trimethoprim	Diaminopyrimidine	• Common in Enterobacteriaceae • Chromosomal mutations in the gene for DHFR, or its promoter = leads to overproduction or modification of target enzyme • Plasmid encoded resistance (*dfr* gene in Enterobacteriaceae) leads to synthesis of an additional trimethoprim resistant DHFR enzyme • Change in cell permeability/efflux pumps	• UTIs (3 days for cystitis) • Prophylaxis for recurrent UTIs • Prostatitis • Epididymo-orchitis • Oral treatment for MRSA + rifampicin/ fusidic acid distributed in tissues & fluids inc. CSF	Avoid in pregnancy (as it's an anti-folate) Contraindicated in blood dyscrasias GI disturbance Pruritis Rashes hyperklemia	Oral		Inhibits the bacterial enzyme dihydrofolate reductase (DHFR) – prevents the conversion of dihyrofolate to tetrahydrofolate in the folate synthesis pathway. Same pathway but different point to sulphonamides. Bactericidal/ bacteriostatic depending on organism &	

		• Alterations in metabolic pathway • More than 1 mechanism can occur leading to high level resistance					concentration Synergisy with Sulfamethoxazole, polymixins & aminoglycosides	
Pyrimethamine								
Flucytosine								
Cycloguanil								
Co-trimoxaole		See Trimethoprim and Sulfamethoxazole Inc. rates in S. aureus, PCP and many Enterobacteriaceae	• PCP – treatment & prophylaxis • Toxoplasmosis – prophylaxis & 2nd line treatment • Nocardiosis (2nd line treatment) • MDR orgs • UTI • Acute otitis media • COPD	Avoid in: • blood disorders • infants <6 wks • hepatic impairment • pregnancy & breast feeding • see indiv drugs	IV Oral		Synergistic combination of trimethoprim & sulfamethoxazole, inhibition of 2 enzymes (tetrahydroteroic acid synthtase & dihydrofolate reductase) in the bacterial folate synthesis pathway	

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Nalidixic acid (Group 1)	Quinolones Group 1 – active against Enterobacteriaceae Group 2 – active against Enterobacteriaceae, Pseudomonas spp. & some GPC Group 3 – not available in UK active against GPC Group 4 –	• mainly due to spontaneous chromosomal mutation • alter the target enzymes – stepwise inc. resistance by sequential mutations of *gyrA/gyrB* and *parC/parE* • alter cell membrane permeability – due to mutations that reduce	UTIs	• Dose adjustments need to be made on renal function • GI side effects • CNS – headache, dizziness, insomnia • May induce	Oral	Reduced bioavailability by co-administration of antacids	Prevent bacterial nucleic acid synthesis by inhibiting DNA gyrase & topoisomerase IV DNA gyrase consists of α & β subunits which are encoded for by *gyrA* & *gyrB* Quinolones inhibit DNA supercoiling mainly through action on the α-subunit of	
Ciprofloxacin (Group 2)			• UTIs, prostatitis, gonorrhoea, pseudomonal infections in CF patients, anthrax, prophylaxis in *N. meningitidis* • Give high dose Cipro where penetration sub-optimal VAP, septic arthritis, CF, osteomyelitis,		Oral IV			

	enhanced activity against GPC & anaerobes	porin channel entry or inc. efflux – In *P. aeruginosa*
		• due to over expression of MexAB-OprM efflux pump
		  ○ MexA – membrane fusion protein
		  ○ MexB – inner membrane efflux pumps
		  ○ OprM – outer membrane protein
		• Plasmid-mediated resistance encoded by the qnr gene on *K. pneumoniae, E. coli* etc
			meningitis, intra-ocular infections + serious Pseudomonal infections	seizures so MUST NOT be used in epileptics
				• Not used in young children or adults with a history of tendon disorders (Beagles)
				• Moxi – leucopenia, eosinophilia hepatitis
				• Allergic reactions – rash etc
							DNA gyrase.
							
							Topoisomerase IV consists of 2 units encoded fro by *parC* and *parE* genes. Topoisomerase is involved in DNA relaxation and chromosomal segregation.
							
							DNA gyrase = main target in Gram-ves
							
							Topoisomerase = main target in Gram-pos
							
							=bactericidal

Levofloxacin (Group 2)			Sinusitis, COPD exacerbation, CAP, UTI, Chronis prostatitis, skin & soft tissue, M. tb		Oral IV		
Norfloxacin (Group 2)			UTI Chronic prostatitis		Oral		
Ofloxacin (Group 2)			UTIs, chronic prostatitis, LRTI, skin & soft tissue, gonorrhoea, genital chlamydia, non-gonococcal urethritis, pelvic inflammatory disease				
Moxifloxacin (Group 4)			COPD exacerbations, CAP (2nd line) M. tb		Oral		

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Metronidazole	Nitroimidazoles	• Rare and a combination of mechanisms is required – both chromosomal & plasmid mediated • Bacteroides spp. have transferable genes *nimA* & *nimD* • *H. pylori* resistance associated with mutational	• Parasitic infections • Anaerobic infections • C. difficile enterocolitis • H. pylori eradication therapy • Small bowel overgrowth • Pouchitis	• Abnormal metallic taste • GI • Peripheral neuropathy with prolonged treatment • Disulfiram-like reaction with alcohol • CNS symptoms • Mucocutaneous	• Oral • IV • Per vagina • Per rectum • Topical	BEWARE of using if patient is on: Co-amoxiclav Imipenem Meropenem Clindamycin Piperacillin-tazobactam As these drugs already have	Pro-drug that needs to be activated. Has a low molecular weight and enters the organism by passive diffusion. Activated by reduction in its nito group by a nitroreductase	

		inactivation of *rdxA, frxA, fdxB* • Resistance in T. vaginalis & Giardia is probably multifactorial with reduced activation of metronidazole and/or reduced transcription of the ferrodoxin gene	• Infected leg ulcers • Pressure sores • Pelvic inflammatory disease • Surgical prophylaxis • Acute ulcerative gingivitis	candidiasis • Transient darkened urine		anaerobic cover	results in formation of metronidazole radicals. Leads to highly reactive compounds that interact with nucleic acids & proteins leading to cell death = bactericidal

Antimicrobial	Class	Resistance	Use	Side Effects	Delivery	Interactions	Synergy	Action
Nitrofurantoin	Nitrofurans	Most ESCAPPM pathogens are resistant + pseudomonas In *E. coli* resistance is chromosomal or plasmid mediated and assoc. with inhibition of nitrofuran reductase action	Acute non-complicated cystitis (NOT pyelonephritis) – 3 days Recurrent UTIs – 7 days Prophylaxis of recurrent UTIs	Dose modification required in renal patients GI – nausea & vomiting Pulmonary – acute hypersensitivity (fever, cough, dyspnoea, pulmonary infiltrates, myalgia, eosinophilia)	Oral enhanced by food		Mechanism poorly understood Like Metronidazole required enzymatic reductions within the bacterial cell Appear to damage bacterial DNA like the quinolones and inhibit DNA repair Bactericidal against	

				Chronic (pulmonary fibrosis, bronchiolitis obliterans organizing pneumonia)			urinary pathogens
Rifampicin	Rifamycins Smeisynthetic derivatives of rifamycin B, naturally isolated from Streptomyces mediterranei, converted rifamycin B into rifamycin S which is more active (also Rifapentine, Rifamide, Rifamycin SV, Rifaximin – not available UK)	• Rapid emergence of resistance due to mutation in *rpoB* gene(encodes a β-subunit of DNA-dependent polymerase) • Use in combination with unrelated antibiotics to suppress emergence of resistance • Rifabutin resistance less than Rifampicin	• TB • Leprosy • Serious or device related Staphylococcal infection • Pneumococcal • Legionella • Elimination of nasal carriage – *N. meninigitidis* & *H. influenzae*	Orange fluids Skin rashes **STOP DRUG if thrombo-Cytopaenia** 'Rifampicin Flu' – in intermittent therapy		• All stimulate hepatic metabolism by CYP450 enzyme system • Rifabutin interacts with Clarithryomycin and ritonavir • Rifampicin enhances own activity & that of other drugs: ○ Warfarin ○ Cortico-Steroids ○ Protease inbitors ○ Oral contraceptives	A number of shared features: • Inhibit bacterial DNA-dependent RNA polymerase • Bactericidal
Rifabutin			• Atypical mycobacteria • Treatment of M. tb in those who can't have Rifampicin • MAC prophylaxis in AIDS patients	Skin rashes GI upset Hepatitis Neutropenia Uveitis Arthralgia – with high doses	Oral		

Antimicrobial	**Class**	**Resistance**	**Use**	**Side Effects**	**Delivery**	**Interactions**	**Synergy**	**Action**
Polymixin B	Polymixins		Severe infections due to MDR Gram-ve organisms	Dose related nephrotoxicity Dose related neurotoxicity: Paraesthesia Peripheral neuropathy Neuromuscular blockade	Topical IV IM		Cyclic cationic polypeptide detergents = penetrate cell membranes & interact with phospholipids to disrupt membranes = rapidly bactericidal	
Polymixin E/Colistin			SDD Aerosolized for CF patients IV for severe MDR Gram-ve i.e. VAP		Colistin sulfate = topical nebulized Colistimethate = IV IM			

Fusidic acid	Fusidane Derived from *Fusidium coccineum*	• Chromosomal mutations in the *fusA* gene which encodes for the elongation factor • Plasmid mediated mutations result in reduced permeability to the drug • Use fusidic acid combined with another agent	Staphylococcal infections: • Skin & soft tissue • Bacteraemia • Septic arthritis • Osteomyelitis • LRTI in CF Erythrasma due to *Corynebacterium minutissium* Lepromatous leprosy	Nausea Vomiting Reversible jaundice IV form assoc. with thrombophlebitis & jaundice Opthalmic preparations may itch/sting Drug induced, immune mediated thrombocytopaenia	Oral Topical IV	Metabolized by CYP	Bacteriostatic Inhibits protein synthesis by blocking elongation factor G
Mupirocin	Pseudomonal acid produced by *Pseudomonas fluorescens*	• Low level resistance is due to spontaneous mutation resulting in altered access to binding sites in isoleucyl tRNA synthetase • High level resistance is via transferable plasmids by the *mupA* gene which codes for a modified enzyme	• Prolonged use of >7 days discouraged • Skin infections i.e. impetigo, folliculitis • Nasal decolonisation of SA or MRSA • Used for secondarily infected eczema, burns, ulcers	Local reactions such as pruritis, burning sensation, rash, urticarial = particularly on broken skin	Topically as a cream = bactroban or nasal ointment Bactroban nasal		Bacteriostatic Inhibits bacterial RNA & protein synthesis by binding to bacterial isoleucyl tRNA synthetase = prevents incorporation of isoleucine into protein chains in the bacterial cell wall