

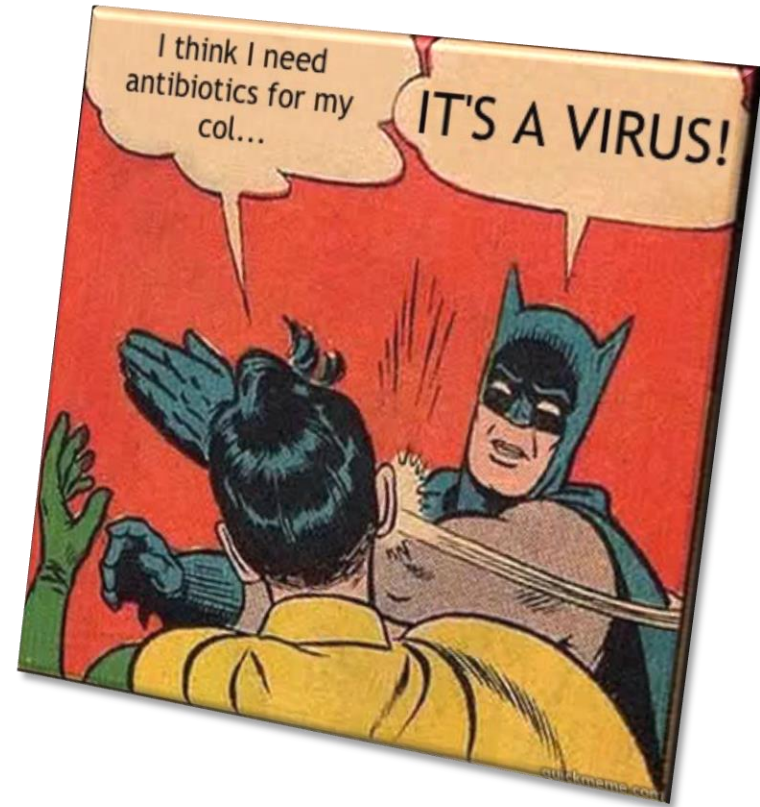
Antibiotics

Dr Andrew Smith



Overview

- Introduction
 - Principles of Use
 - Bacterial Classification
 - Resistance
-
- 20 Questions with explanations and system summaries

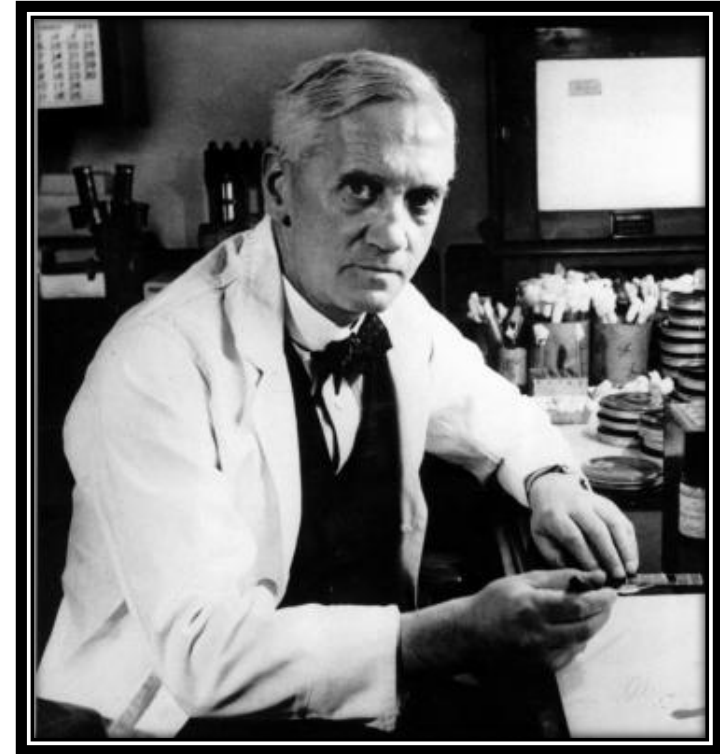


Extra reading at end:

*An overview of antibacterial drugs and classes
(+/- recording from previous years)*

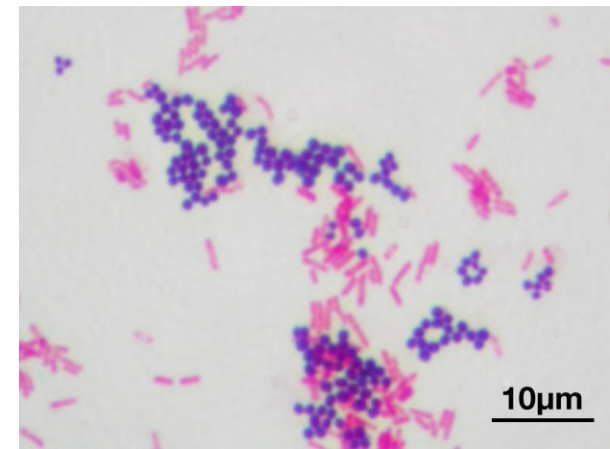
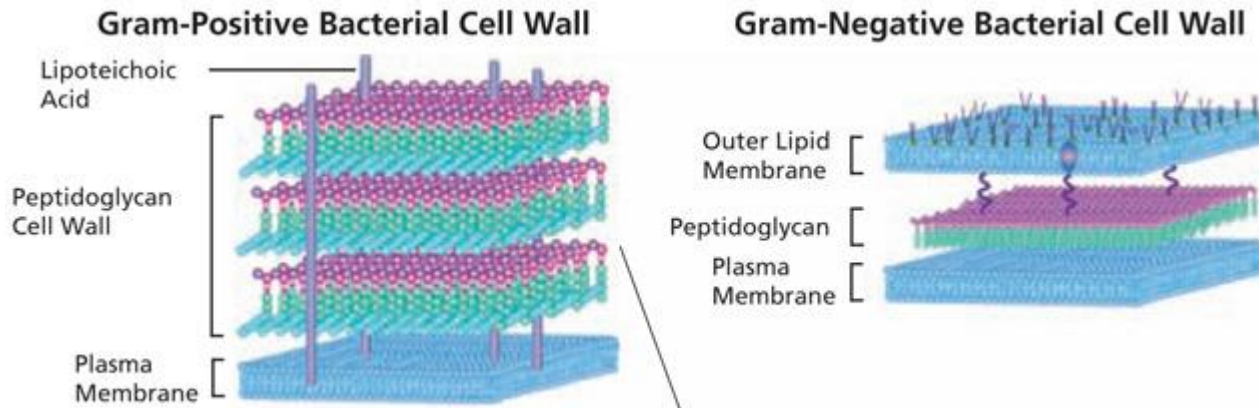
Introduction

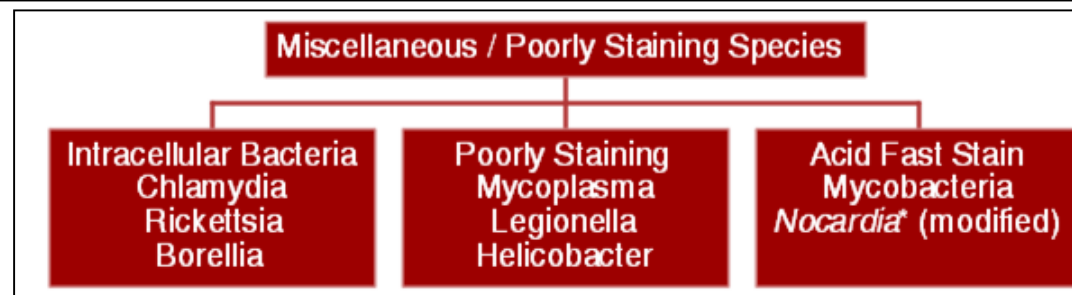
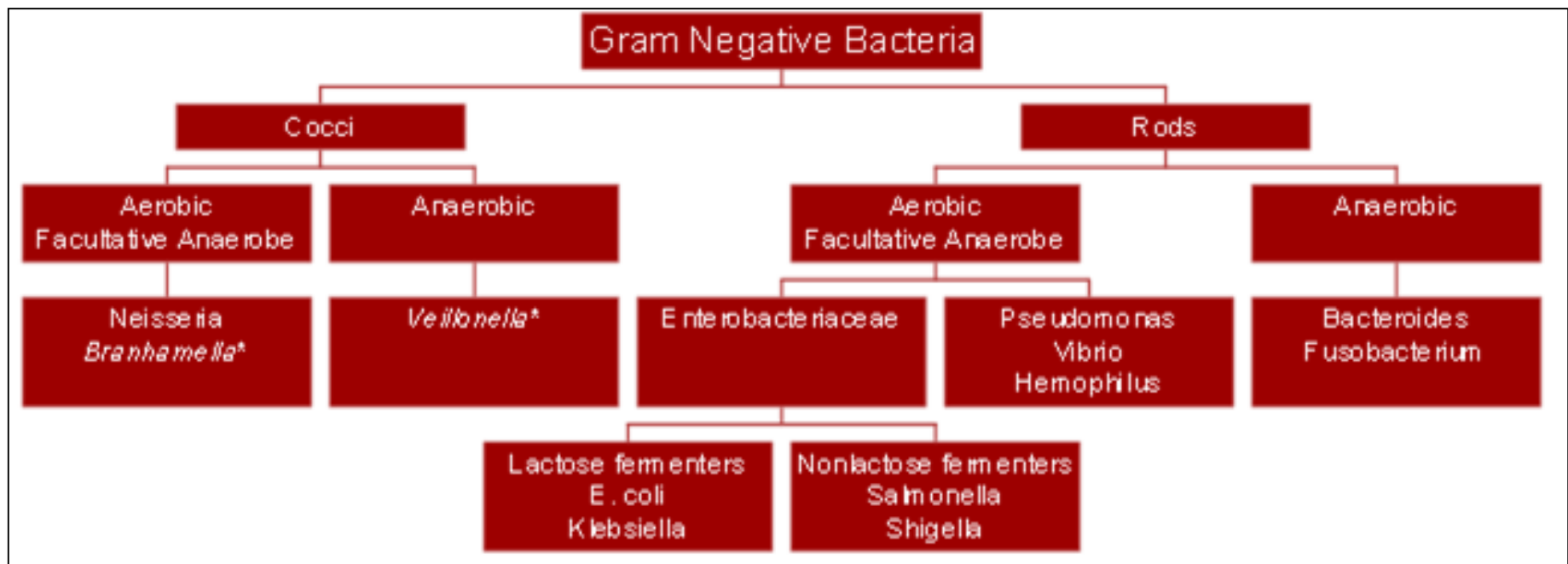
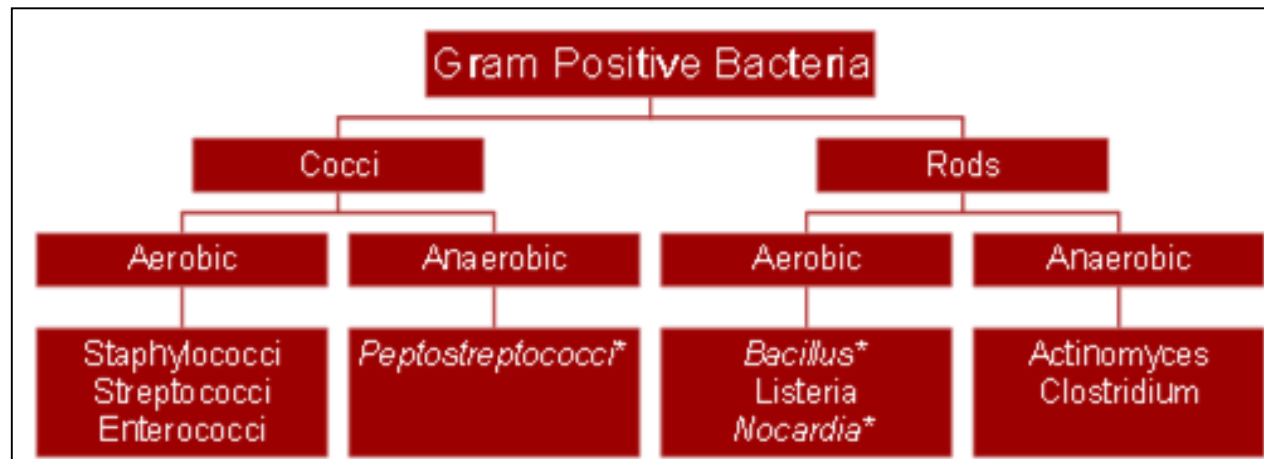
- Natural products with antimicrobial properties were used millennia ago.
- Late 19th century - Pasteur and Koch described effects of compounds towards microbes
- 1928 - Alexander Fleming (*a colleague of Grandad Dooley!*) discovered the antimicrobial effect of the mold *Penicillium*.



Simple Bacterial Classification

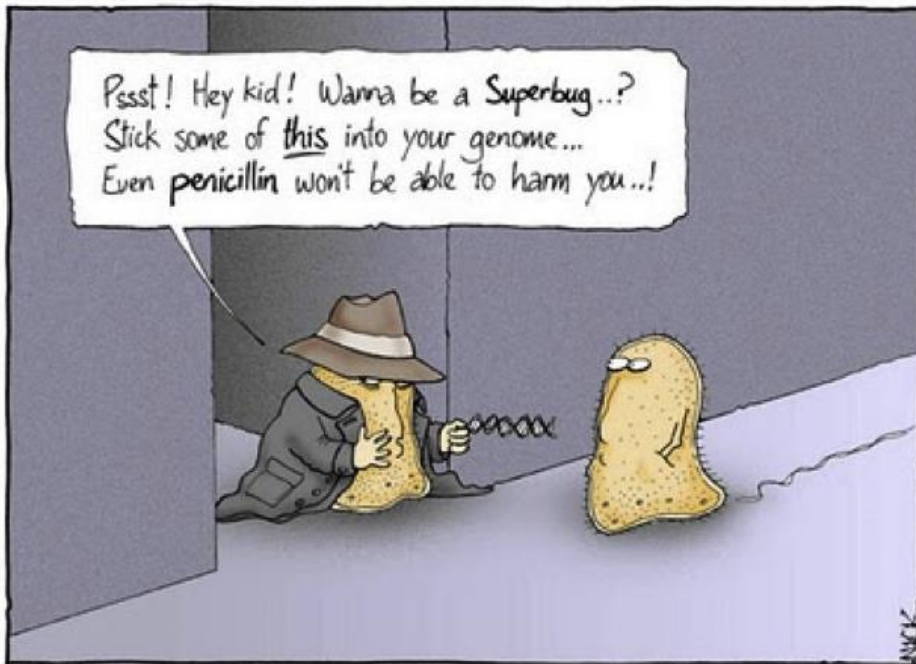
- **Some common descriptors:**
 - Cocci – spheres
 - Bacilli – rods
 - Spirochaetes
 - Diplo – two bacteria
 - Strep – line of bacteria
 - Staph – cluster
- **Aerobic, facultative or strict anaerobic**
- Also by virtue of staining characteristics:
 - **Gram-Positive** – Have a large peptidoglycan rich cell wall – stain purple on the gram stain.
 - **Gram-Negative** – have a thinner cell wall so do not absorb as much stain – appear pink.
 - **Special Stains** e.g. Acid-fast
- Other methods: Genetic profiling, biochemical tests, serology etc.





Resistance

- Not all microbes are sensitive to all agents.
- Previously sensitive microbes may develop resistance due to the acquisition of resistance genes, via:
 - Random mutation
 - Genetic transfer (e.g. Plasmids)



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

- Resistance may be due to:
 - Impermeable membranes
 - Metabolism/destruction of the drug
 - No active sites
- Resistance is increased by poor prescribing and compliance.

Principles of Use

- Antimicrobials should usually only be prescribed with clinical evidence of infection.
 - Exceptions include prophylaxis e.g. Pre-surgery, post-splenectomy, post-exposure, post-chemotherapy
- Cultures (e.g. blood, urine, swabs etc.) should ideally be taken before initiating therapy. Exceptions may include presumed meningitis (i.e. in the community)
- Consideration must be given to:
 - **Dose** - will depend on age, renal/hepatic function, weight, site/severity of infection
 - **Route** – Oral, IV, IM etc., (de-)escalating as appropriate. Consider bioavailability.
 - **Duration** – Often depends on clinical judgement but good evidence exists for certain infections.
- **Where possible, hospital guidelines should be used.**



"The patient in the next bed is highly infectious. Thank God for these curtains."

Questions 1-5: What is the most appropriate antibiotic choice?

- 1) A 55 year old man attends his GP with a cough productive of yellow sputum. O/E there are some creps in the left lower zone. He is otherwise well.
- 2) A 7 year old attends the E.D. with a 3 day history of cough and fever. The observations in the department are normal, however, an X-ray shows bilateral patchy changes.
- 3) A 28 year old attends the E.D. with a 2 day history of cough, sore-throat, fevers and muscle aches. O/E they're coryzal with a red throat but clear chest.
- 4) A 65 year old is an inpatient following a #NOF repair. Three days into the admission they develop a cough and fevers with crackles at the right base. They are haemodynamically stable.
- 5) A 73 year old with known COPD presents with a 5 day history of a worsening productive cough and the sputum has changed from clear to yellow. They are penicillin allergic.

- a) **Amoxicillin**
- b) **Coamoxiclav**
- c) **Clarithromycin**
- d) **Ciprofloxacin**

- e) **Doxycycline**
- f) **Cefalexin**
- g) **Tazocin + Gentamicin**
- h) **None of the above**



Answers 1-5

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- 3) **H** A 28 year old attends the E.D. with a 2 day history of cough, sore-throat, fevers and muscle aches. O/E they're coryzal with a red throat but clear chest.
- 4) **B** A 65 year old is an inpatient following a #NOF repair. Three days into the admission they develop a cough and fevers with crackles at the right base. They are haemodynamically stable.
- 5) **E** A 73 year old with known COPD presents with a 5 day history of a worsening productive cough and the sputum has changed from clear to yellow. They are penicillin allergic.

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Community Acquired Pneumonia

- Commonly caused by *Strep. pneumoniae*, *Haemophilus influenzae*. More rarely *Mycoplasma pneumoniae*, *Legionella spp.*, *Chlamydia spp.*, *Coxiella burnetii*. Also consider *Staph. aureus* if recent influenza infection; TB if no response to treatment or in at risk group.
- CURB-65 can be used (but use clinical judgement)
- Treatment is typically 5-10 days. Longer in *Staph* infections.

Mild/Moderate

- Amoxicillin +/- a Macrolide (e.g. Clarithromycin) or Doxycycline

Severe

- Coamoxiclav and Clarithromycin;
- Cephalosporins can also be used.
- Levofloxacin can be used in penicillin allergy



Hospital Acquired Pneumonia

- Can be similar organisms to CAP, but also gram-negatives and multi-resistant organisms.
 - Simple HAP if admitted >48 hours but <5 days,
 - Late-onset HAP >5 days after admission
- Treatment:
 - Simple: Coamoxiclav
 - Late-Onset: Tazocin (or a cephalosporin) +/- Aminoglycoside
 - If MRSA, add Vancomycin/Teicoplanin.

Aspiration Pneumonia

- Those at risk include those with decreased GCS, neuro-muscular disorders etc.
- May be chemical rather than infective.
- If infective, anaerobes are common (e.g. *Klebsiella*).
- Generally treated as for CAP/HAP (depending on situation) with Metronidazole added if required for extra anaerobic cover.



Infective Exacerbation of COPD

- Antibiotics have been shown to be effective **only** if there is a history of at least 2 of the following:
 - increased dyspnoea
 - increased sputum purulence
 - Increased sputum volume



Treatment

- Typically mono-therapy
- A penicillin (Amoxicillin), Tetracycline (Doxycycline) or a macrolide (Clarithromycin)
- If recent course of first line therapy, consider alternative combinations.

Other Chest Infections

Pneumocystis jireveci (PCP*)

- Opportunistic pathogen
- Causes bilateral patchy changes on X-ray
- Prophylaxis and treatment with co-trimoxazole (Septrin)

based on the old name *Pneumocystis carinii



Tuberculosis

- Complex topic (as in real life!)
- NICE Pathway: <https://pathways.nice.org.uk/pathways/tuberculosis>
- Standard treatment for pulmonary TB consists of:
 - Isoniazid (with pyridoxine), Rifampicin, Pyrazinamide and Ethambutol for 2 months, then;
 - Isoniazid (with pyridoxine) and Rifampicin for a further 4 months.

Questions 6-10: What is the most appropriate antibiotic choice?

- 6) A 27 year old patient who is 8 weeks pregnant presents with a 2 day history of urinary frequency. Urine testing is positive for leucocytes and nitrites. She has a known type 1 allergy to Penicillin.
 - 7) An 18 year old female visits her GP with a short history of dysuria and frequency. A urine sample is positive for nitrites. β hCG negative.
 - 8) A 76 year old, male, catheterised patient has a urine dip performed on a catheter-bag urine sample. It is positive for nitrites, leucocytes, blood and protein. The patient is clinically well, with no abdominal pain or fevers.
 - 9) A 5 year old girl is brought to E.D. with high-temperatures, vomiting and loin pain. She is tachycardic. The urine is foul smelling and a clean catch sample is sent to the lab for urgent microscopy and gram-negative rods are identified.
 - 10) An 84 year old lady is due for a change in her long-term catheter. On previous occasions she has suffered UTIs following catheter insertion.
- | | |
|---------------------------------|------------------------------|
| a) Trimethoprim 5 days | e) Amoxicillin 7 days |
| b) Nitrofurantoin 3 days | f) Gentamicin STAT |
| c) Nitrofurantoin 7 days | g) Cefuroxime 10 days |
| d) Cefadroxil 7 days | h) None of the above |



Answers 6-10

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Urinary Tract Infections

- Commonly caused by *E.coli*, other coliforms, *Enterococci*, *Staph. saprophyticus* (generally in young women). *Proteus mirabilis* classically causes triple phosphate ('struvite') stones.

Classic Symptoms

- In adults
 - Dysuria, frequency, urgency, suprapubic tenderness
- In children
 - Less specific: fevers, abdo pain, vomiting

Brief Summary of Urine Dip Results:

- Leucocyte and Nitrite positive – treat as UTI
- Nitrite positive – treat as UTI if symptomatic
- Leucocyte positive – possible UTI, send for MCS and consider delaying antibiotics. Start antibiotics if severe symptoms.
- Leucocyte and Nitrite negative – unlikely UTI



UTI Treatment

- Trimethoprim or Nitrofurantoin
 - 3 days for females
 - 5-7 days for men (often indicative of underlying urinary tract pathology).
- Amoxicillin or an oral cephalosporin are alternatives.
- Add an Aminoglycoside (Gentamicin/Amikacin) if a catheter is in-situ
- *NB: All catheter bags become infected so a positive urine dip alone is not indication for treatment.*

Pregnancy

- Trimethoprim is usually avoided in first trimester (?safe if used with folic acid)
- Nitrofurantoin can be given, but should be avoided in third trimester
- Oral Cephalosporin or Amoxicillin are options.
- Treatment for 7 days. Asymptomatic bacteruria should be treated.

In Pyelonephritis

- IV Cephalosporin e.g. Cefuroxime, or
- Gentamicin +/- penicillin
- 10-14 days treatment (can switch to oral if clinically well)



Questions 11-15: What is the most appropriate antibiotic choice?

- 11) A 13 year old boy is brought to your GP surgery with a short history of increasing lethargy and fevers. The parents have noticed a purpuric rash developing since booking the appointment this morning.
- 12) A 20 year old university student is brought to E.D. by her friends due to a severe headache and fevers. She reports that light is hurting her eyes.
- 13) A 73 year old inpatient is on IV Co-amoxiclav for a hospital acquired pneumonia following an admission for a fall. They have had ongoing fevers and a recent blood culture has identified an ESBL organism.
- 14) A 37 year old patient who received chemotherapy for Hodgkin's Lymphoma 7 days ago, attends E.D. with a fever of 38.9.
- 15) A 14 day old term infant is blue-lighted to E.D. with a seizure. They had been more sleepy during the day, with reduced feeding and had had a temperature of 37.9. The seizure self-terminated after 10 minutes.

- | | |
|--------------------------------|--------------------------|
| a) Ceftriaxone | e) Coamoxiclav |
| b) Flucloxacillin | f) Meropenem |
| c) Benzylopenicillin | g) Cefotaxime and |
| d) Tazocin + Gentamicin | Amoxicillin |



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Acute Meningitis/Encephalitis

- Causative agent depends on age and risk factors for each individual patient.
- In adults, commonly *Strep. pneumoniae*, *Neisseria meningitides*, *Haemophilus influenzae*, enteroviruses.
- Less commonly *Listeria monocytogenes* (typically in elderly or neonates), Herpes viruses, TB.
- With underlying immune compromise: *Cryptococcus neoformans*.
- Length of treatment varies from 7-21 days.

Treatment

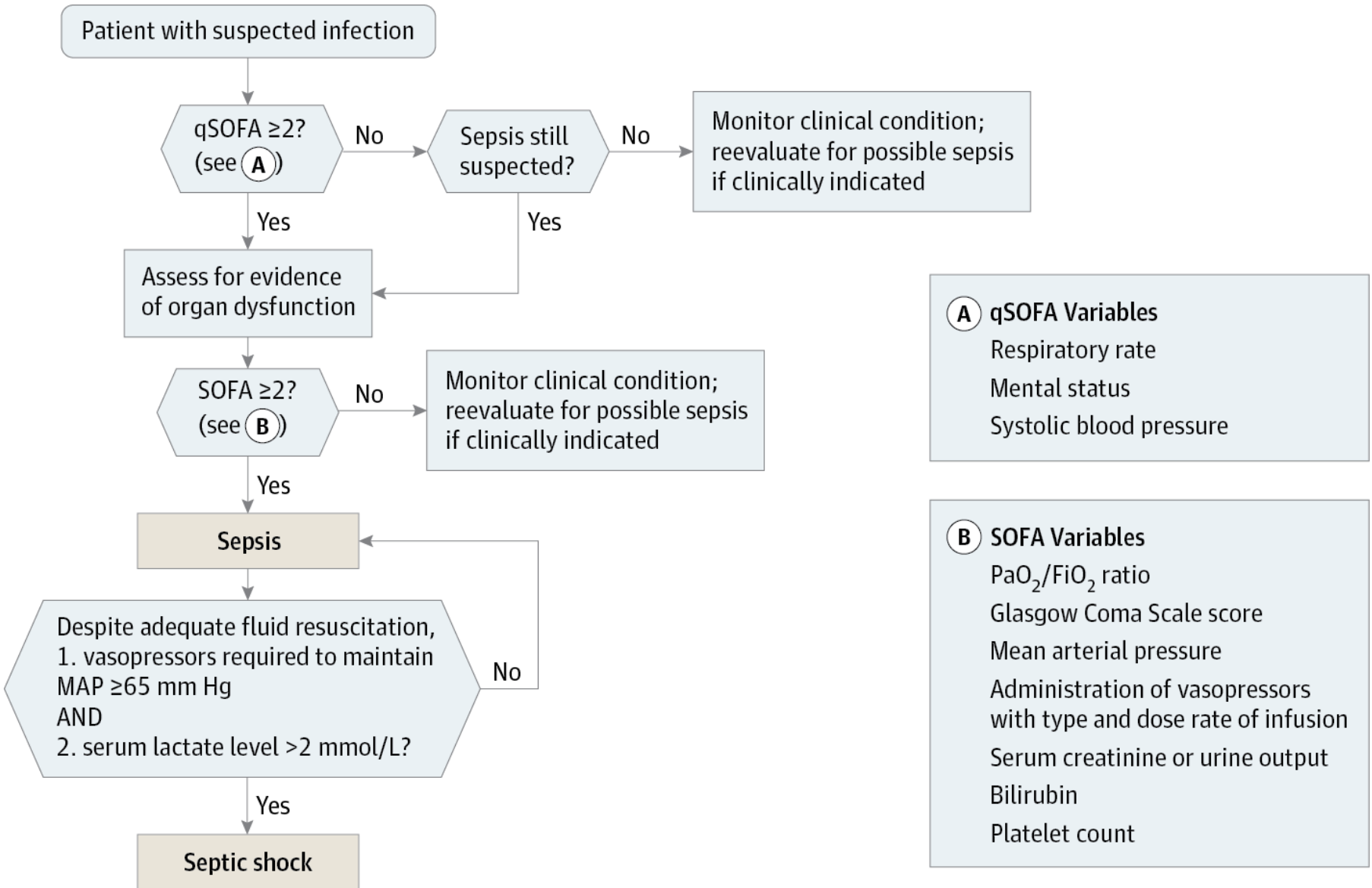
- Benzylpenicillin (if in community)
- IV Cephalosporin (e.g. Ceftriaxone/Cefotaxime) is 1st line in hospital
- +/- Amoxicillin (to cover *Listeria* in high-risk groups)
- Type 1 Pen-allergy: Chloramphenicol +/- Vancomycin

Also consider:

- Adding Dexamethasone
- Adding Aciclovir if concerned about Herpes Encephalitis



Sepsis (NB: there will be a whole lecture on sepsis)



Sepsis – Antibiotic Treatment

If a source is known, treatment should be targeted to that, e.g. urosepsis, cellulitis.

Sepsis of Unknown Origin

- Broad-spectrum penicillin (e.g. Co-amoxiclav/Tazocin) or Cephalosporin (e.g. Ceftriaxone) +/- Aminoglycoside (e.g. Gentamicin).
- If MRSA is presumed/known, add Vancomycin
- If anaerobic organism presumed, add Metronidazole
- If hospital acquired or previous resistant organisms, consider a Carbopenem (e.g. Meropenem)

Febrile Neutropaenia – is a medical emergency

- Temp ≥ 38 and neutrophil count < 0.5 , or;
- Reason to suspect sepsis with temp < 38 or neutrophil count > 0.5

Generally, treatment consists of broad-spectrum antibiotics, e.g. Tazocin and Gentamicin

NB: there may be restrictions to certain antibiotics in certain chemotherapy protocols

- *e.g. penicillins restricted with high-dose methotrexate, Aminoglycosides restricted with nephrotoxic regimes.*
- *Alternatives in these situations might include Cephalosporins and Quinolones (e.g. Ciprofloxacin).*



Questions 16-20: What is the most appropriate antibiotic choice?

- 16) A 5 year old is brought to your GP practice with for the third time with a painful ear and ongoing temperatures (38.6 in the practice today). On otoscopy, the ear drum is erythematous and appears tense.
- 17) A 13 year old attends your GP practice with a sore throat. They have inflamed exudative tonsils, tender lymphadenopathy and fevers. They deny a cough.
- 18) A previously well 56 year old is admitted via E.D. with a cellulitis affecting the lower leg. They have an Early Warning Score of 5. They are penicillin allergic.
- 19) A septic patient whose MRSA swab has come back positive has just been given an IV medication. They have developed a widespread erythematous rash.
- 20) A 62 year old patient has recently completed a course of Ciprofloxacin which was given to them for a presumed Salmonella diarrhoea. The diarrhoea has become more profuse and they have abdo pain. A *C. diff.* antigen test is positive.

- | | |
|------------------------------|----------------------|
| a) Amoxicillin PO | f) Clindamycin IV |
| b) Clarithromycin PO | g) Metronidazole IV |
| c) Phenoxyethylpenicillin PO | h) Metronidazole PO |
| d) Flucloxacillin PO | i) Vancomycin IV |
| e) Flucloxacillin IV | j) None of the above |



Answers 16-20

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Tonsillitis/Pharyngitis

- Assessed by the modified CENTOR criteria

Fever (>38)	+1
Tonsillar exudates	+1
Tender cervical lymphadenopathy	+1
Absence of cough	+1
Age <15	+1
Age >44	-1

Score	Action
≤ 1	Low risk of Strep. Avoid Abx
2-3	15-30% risk. Send swab and delay Abx
≥ 4	~50-60% risk. Send swab and consider treating with Abx

- Mx:** Pen V (or a macrolide). *Avoid Amoxicillin due to risk of rash if actually EBV.*

Otitis Media

- Over 60% are viral and self-limiting
- Consider delaying antibiotics
- First line:
 - Amoxicillin
- Second Line/Pen-allergic
 - Macrolide, e.g. Clarithromycin or Azithromycin



Cellulitis (and friends)

- Commonly *Staph aureus* (including MRSA) or Group A *Strep*. Less commonly coliforms or anaerobes.
- Treatment is typically for 7-14 days.

Mild/Moderate

- Flucloxacillin (PO/IV)

Severe

- Flucloxacillin +/- Clindamycin
- If penicillin allergy: Clarithromycin (or Clindamycin if severe).
- If MRSA colonised and Vancomycin/Teicoplanin
- If human/animal bites: Co-amoxiclav (and consider Tetanus booster)
- If periorbital cellulitis, assess for eye involvement
- The above antibiotics form general antibiotic management of osteomyelitis and septic arthritis also.



Gastro (and friends)

Gastroenteritis

- Typically due to viruses so antibiotics not indicated. Even bacterial infections are often self-limiting. If indication to treat, however:
- *Salmonella*, *Campylobacter* and *Shigella* can be treated with Ciprofloxacin or a Cephalosporin

***Clostridium difficile* infection** – oral Metronidazole +/- Vancomycin

Helicobacter pylori eradication regimens, Omeprazole with:

- Clarithromycin and Amoxicillin, *or*;
- Metronidazole and Clarithromycin.
- These should be given for 7 or 14 days.

Intra-abdominal infection (e.g. Post-surgery) is typically treated with Tazocin/Coamoxiclav +/- Gentamicin +/- Metronidazole



Infective Endocarditis

- Depends on risk factors for each individual patient. Commonly for native valve endocarditis, oral *Streptococci*, *Staph. aureus* (including MRSA), *Enterococci*, less commonly *Coxiella burnetii* (*Q fever*), HACEK organisms
- Diagnosis by Modified Dukes Criteria
- Treatment 4-6 weeks – involve microbiology!

Simple Endocarditis

- Amoxicillin +/- Gentamicin

Acute presentation

- Benzylpenicillin, Flucloxacillin and Gentamicin

Pen-Allergy (or prosthetic valve):

- Vancomycin, Rifampicin and Gentamicin



Summary

- There are many factors that influence the choice of antimicrobial.
- Always try to send cultures/swabs prior to commencing antibiotics.
- Always re-assess the antibiotic choice, route and duration.
- Hospital guidelines should be used, but there are general principles/common uses.

Overview of Bacterial infections

Bacterial meningitis

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Streptococcus agalactiae*
- *Listeria monocytogenes*

Otitis media

- *Streptococcus pneumoniae*

Pneumonia

Community-acquired:

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Staphylococcus aureus*

Atypical:

- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Legionella pneumophila*

Tuberculosis

- *Mycobacterium tuberculosis*

Skin infections

- *Staphylococcus aureus*
- *Streptococcus pyogenes*
- *Pseudomonas aeruginosa*

Eye infections

- *Staphylococcus aureus*
- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*

Sinusitis

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

Upper respiratory tract infection

- *Streptococcus pyogenes*
- *Haemophilus influenzae*

Gastritis

- *Helicobacter pylori*

Food poisoning

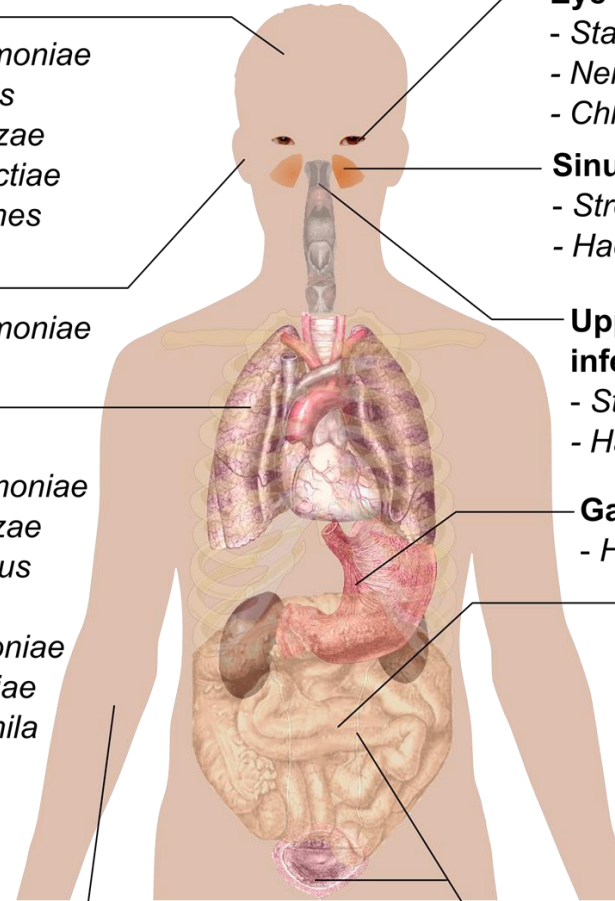
- *Campylobacter jejuni*
- *Salmonella*
- *Shigella*
- *Clostridium*
- *Staphylococcus aureus*
- *Escherichia coli*

Sexually transmitted diseases

- *Chlamydia trachomatis*
- *Neisseria gonorrhoeae*
- *Treponema pallidum*
- *Ureaplasma urealyticum*
- *Haemophilus ducreyi*

Urinary tract infections

- *Escherichia coli*
- Other Enterobacteriaceae
- *Staphylococcus saprophyticus*
- *Pseudomonas aeruginosa*



Thank-you
Any Questions?



Bibliography

Medical Management and Therapeutics – Kumar, Clark
Oxford Handbook Clinical Medicine – Longmore et.al.
The BNF
Barts Health/BHRUT/UCLH Antimicrobial Guidelines



Information Slides

- The following slides contain summaries of the different antibiotic classes and common drugs within them.
- The slides are fairly self-explanatory, but you may like to watch them along with the recording from 2016, where time was spent discussing them.
- Video recording available at:

www.tinyurl.com/antibiotics2016



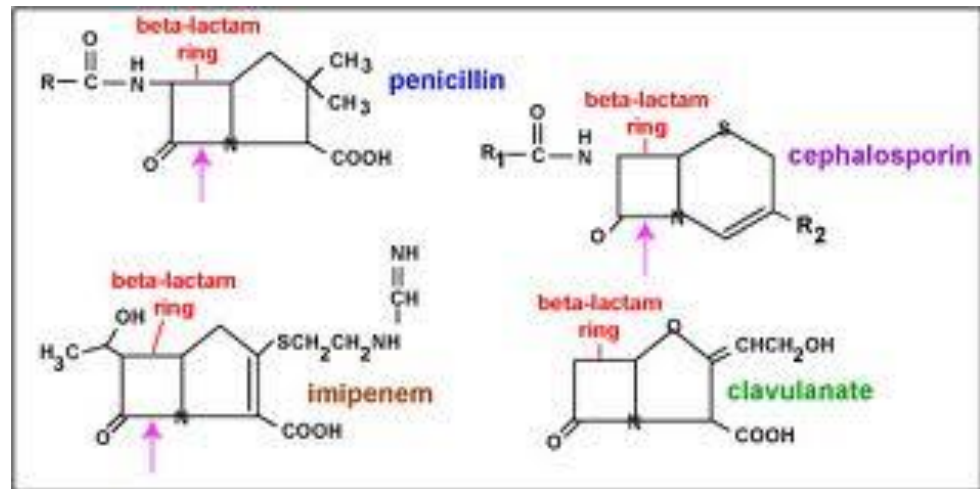
Classification of Antibiotics

- Although of dubious clinical significance, they can be broadly classified as:
 - Bacteriocidal – actively kill bacteria
 - Bacteriostatic – inhibit bacterial growth
- They are better thought of in terms of their class and their spectrum of activity.



β -lactams

- Named because they contain a β -lactam ring.
- They interfere with bacterial cell wall synthesis, inhibiting the peptidoglycan link formation
- They are bacteriocidal agents.
- The class includes the:
 - Penicillins
 - Cephalosporins
 - Carbapenems
 - Monobactams



β -lactams - Penicillins

- Effective against a wide variety of bacteria including the *Streptococci*, *Meningococci* and *Pneumococci* species.
- **Benzylopenicillin** (Pen G) – the natural penicillin, used in a number of situations (e.g. meningitis, neonatology) but given parenterally (IM, IV).
- **Phenoxymethylpenicillin (Pen V)**– another old penicillin, mainly used for *Strep.* throat and prevention of rheumatic fever. Used in post-splenectomy patients as prophylaxis against encapsulated organisms.
- **Amoxicillin** – Broad spectrum penicillin, semi-synthetic, which gives it some action against Gram-Negs due to hydrophilic side chain. Not effective against β -lactamase producing organisms.
- **Flucloxacillin** – a penicillinase resistant drug which is active against *S. aureus* (not MRSA). Useful in skin infections.
- **Piperacillin/Ticarcillin** – semi-synthetic which have an extended spectrum including activity against *Pseudomonas*. Good anaerobic cover also.
- **β -lactamase inhibitors** – These protect against enzymes of resistant bacteria and increase the spectrum to cover gram-negatives and anaerobic organisms. They're combined with standard antibiotics;
 - Clavulanic acid and Amoxicillin – **Coamoxiclav**
 - Tazobactam and Piperacillin - **Tazocin**



β -lactams - Cephalosporins

- Are more resistant to β -lactamases than the penicillins.
- In penicillin allergic individuals, there is a 10-15% cross-over with Cephalosporins – use is based on clinical need/judgement
- They have poor oral availability, but good CSF penetration if given parenterally.
- They increase the risk of *C. difficile* infection.
- They are generally classed in ‘generations’ with new generations having wider gram-negative cover.
 - **First Generation**
 - e.g. Cefalexin, good against *Staph. and Strep.*,
 - **Second Generation**
 - e.g. Cefuroxime, better against gram-negs (e.g. *E. coli*, *Klebsiella*, *Proteus spp.*), slightly less cover against gram-positives.
 - **Third Generation**
 - Cefotaxime, Ceftriaxone (long-half life), Ceftazodime – penetrate the CSF well. More potent against anaerobic gram-negs. Useful in severe sepsis.
 - **Fourth** – Cefepime
 - **Fifth** - Ceftobiprole



β -lactams - Carbapenems

- Stable against Extended-Spectrum β -lactamases (ESBLs) although not active against MRSA. Normally require microbiology approval.
- CREs (Carbopenem-resistant enterococci) are a growing concern.
- **Meropenem** – used in sepsis or ESBL infection. Good CNS penetration.
- **Imipenem** – broad spectrum. Good against *Enterococci*. It is neurotoxic and is metabolised by the kidney.



Macrolides

- Bind to the 50S subunit of bacterial ribosomes and inhibit protein synthesis. They are bacteriostatic.
- Have action against atypical organisms (e.g. *Mycoplasma*, *Legionella*), so often an add on in pneumonias.
- **Erythromycin** – similar range to penicillin so are often used in pen-allergy. Has pro-kinetic effect in the bowel.
- **Clarithromycin** – has higher tissue concentration than erythromycin. More widely used.
- **Azithromycin** has good intracellular penetration so useful *Salmonella typhi* and *Chlamydia* infections. Can be given once daily so useful in paediatrics!



Tetracyclines

- Bind to the 30S subunit of the ribosome and are bacteriostatic.
 - Have a wide spectrum of action against both gram positives and negatives including some rarer, tropical organisms such as *Borrellia*, *Coxiella* and *Rickettsia spp.*
 - Are all typically given orally and have similar profiles. They can cause photosensitivity and are deposited in growing bone and teeth (avoid in pregnancy and children).
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- **Tetracycline**
 - **Doxycycline**
 - **Minocycline**



Aminoglycosides

- Bind to the 30S subunit of the bacterial ribosome, therefore interfere with protein synthesis
 - They are bacteriocidal.
 - Poor oral availability so most are given parenterally. Eye-drops exist.
 - Mainly active against gram-negatives, but *S. aureus* is often sensitive as well. Poor action against the *Strep.* and *Enterococci*.
 - Resistance to Aminoglycosides does occur, but it is drug specific.
 - Rarely used as monotherapy.
 - Drug level monitoring is required due to nephro and oto-toxicity.
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- **Gentamicin and Amikacin** are the most widely used.
 - **Streptomycin** is a second line anti-TB drug.
 - **Tobramycin** – similar to Gentamicin but also used as inhaled therapy against *P. aeruginosa* in Cystic Fibrosis.



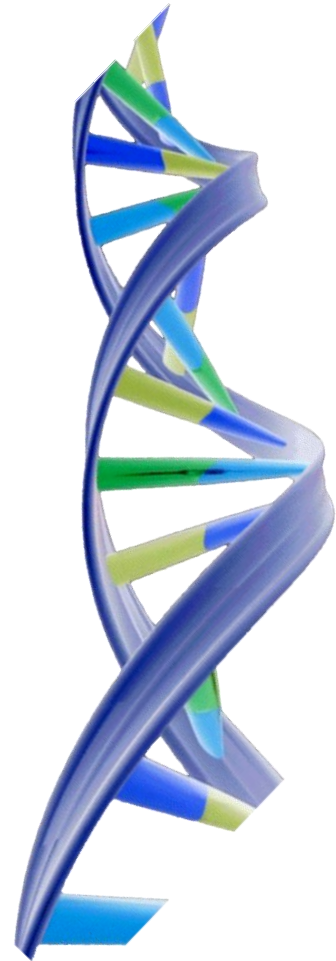
Glycopeptides

- These interfere with bacterial cell wall synthesis and are bacteriocidal.
- Some enterococci are now resistant (GRE).
- Therapeutic drug monitoring is required due to nephrotoxicity. Vancomycin can also cause profound histamine release causing 'red-man syndrome'.
- **Vancomycin** – active only against gram-positive organisms. Usually given IV, but given PO to treat *C. diff* infection. It is reserved for when other antibiotics cannot be used and is effective against MRSA.
- **Teicoplanin** – given IV



Quinolones

- These affect bacterial DNA synthesis by inhibiting topoisomerases – they are bacteriocidal.
- Given orally or IV.
- There is growing resistance.
- There is an increased risk of *C. difficile* infection and other more serious effects include toxic epidermal necrolysis and prolongation of the QT interval.
- **Ciprofloxacin** – mostly active against gram-negatives. Typically used in UTIs, GI infections and gonorrhoea.
- **Moxifloxacin** – growing role in the treatment of TB.
- **Levofloxacin** – often used in severe pneumonia where penicillin allergy exists.



Other antibiotics - Trimethoprim

- **Trimethoprim** is a synthetic diaminopyrimidine which inhibits dihydrofolate reductase (involved in folate synthesis). It has good bacteriocidal action against aerobic organisms. Typically used to treat UTIs.
- Generally not for use in first trimester of pregnancy.
- It can be combined with a sulphonamide drug (sulfamethoxazole) to create **Co-trimoxazole** which is used to treat/prevent rarer infections such as *Pneumocystis jirovecii* pneumonia (PCP) in the immunocompromised.



Other antibiotics

- **Metronidazole** destabilises DNA and is active against anaerobic and protozoal infections. It is often used in the treatment of *C. difficile*, bacterial vaginosis and tetanus; as well as part of *H. pylori* eradication.
- It has a disulfiram-like reaction if used with alcohol.
- **Clindamycin** is a liconsamide antibiotic inhibiting ribosome translocation and is given IV in severe infections.
- It has good action against gram-positives, especially *staph* and *strep*, as well as anaerobes. Topical treatment is also used for bacterial vaginosis.
- Can increase the risk of *C. diff*.



Other antibiotics

- The **Polymyxins** (e.g. **Colistin**), are only active against Gram negative bacteria.
- They have poor oral absorption, but can be used topically, i.e. to treat ear infections, nebulised in cystic fibrosis, or as bowel decontamination in neutropaenic patients.
- **Chloramphenicol** inhibits protein synthesis by binding to the 50S subunit of the ribosome.
- Most often used for topical treatment of eye infections.
- Can be given IV in cases of allergies/multi-resistance. Has good tissue penetration.



Other antibiotics

- **Nitrofurantoin** is a nitrofuran drug which is used in UTIs. It can cause brown urine and more severe effects such as pneumonitis, lung fibrosis and peripheral neuropathy.
- **Fusidic Acid** is most active towards gram-positives, especially *S. aureus*. It shouldn't be used as monotherapy, but can be added in serious infections such as osteomyelitis.
- **Linezolid** is a newer antibacterial agent which is only effective against gram-positives. Only used for MRSA or GRE infections.



Other antibiotics – Anti-TB drugs

- **Rifampicin** is a rifamycin that inhibits RNA synthesis and is typically used as an anti-TB drug. However, it has wide spectrum against bacteria as well as some protozoa (and even some viruses). Hepatotoxicity can occur. It stains bodily excretions red.
- **Isoniazid** is an anti-TB drug which inhibits mycobacterial cell wall synthesis. Can be used as a single drug for prophylaxis of TB contacts. Hepatotoxicity and peripheral neuropathy are risks.
- **Ethambutol** acts against typical and atypical mycobacteria, inhibiting cell wall synthesis. Can cause optic neuritis so visual acuity should be tested. Colour recognition can decrease.
- **Pyrazinamide** is only active against TB and its mechanism of action is not fully understood, but likely due to interfering with fatty acid synthesis. Hepatotoxicity can occur.

