

# Antibiotics

Dr Andrew Smith



# Overview

- Introduction
- Principles of Use
- Bacterial Classification
- Resistance
- Drug Choice Questions

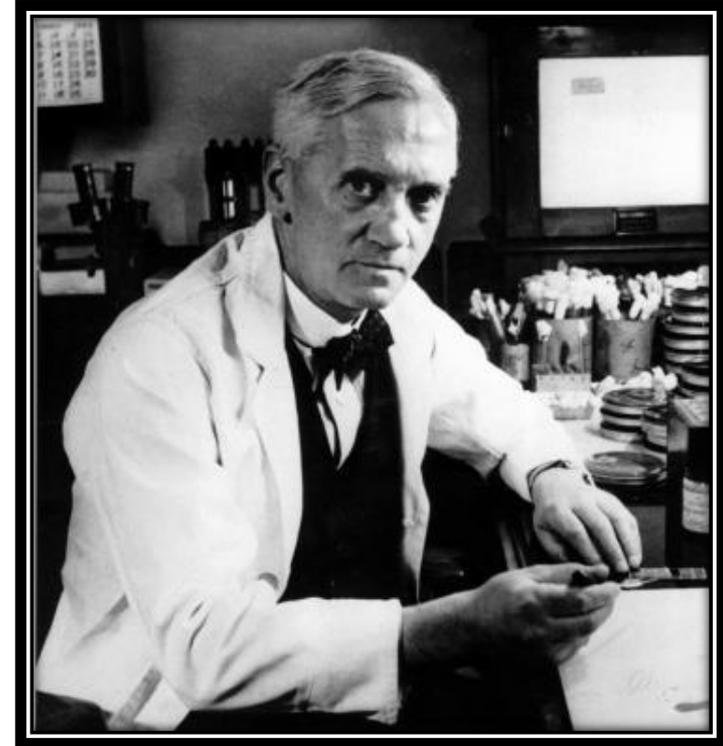
*Extra reading at end:*

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



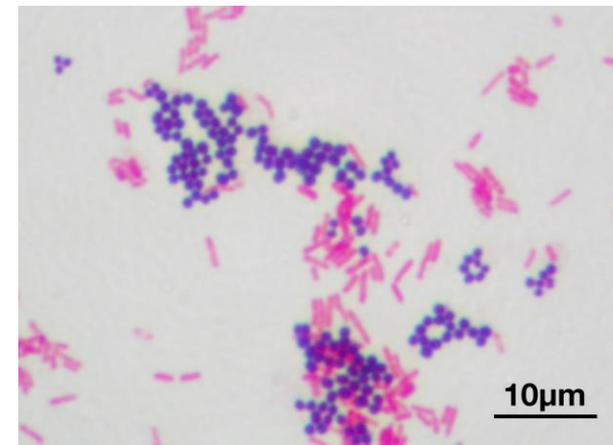
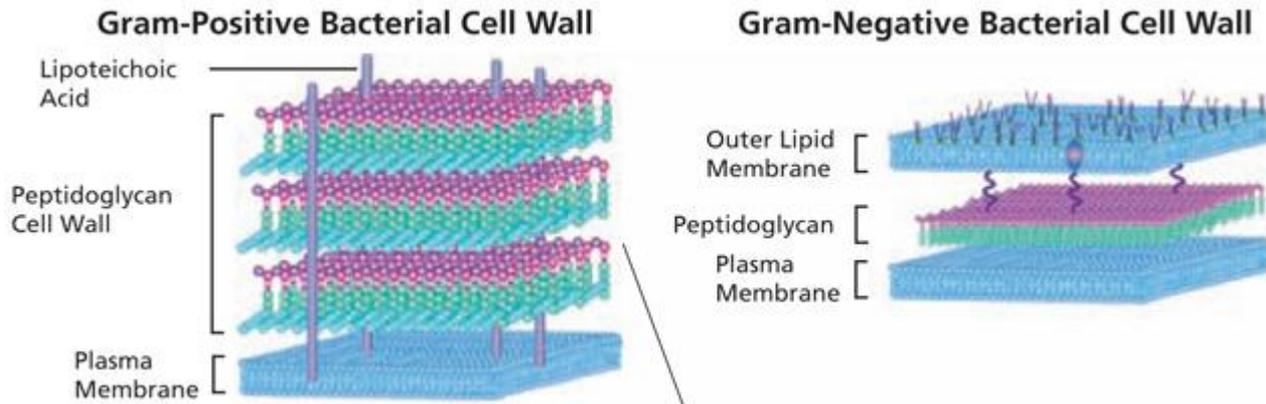
# Introduction

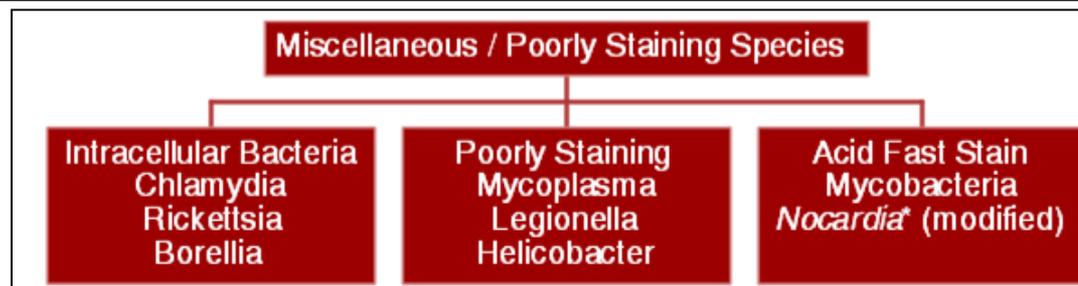
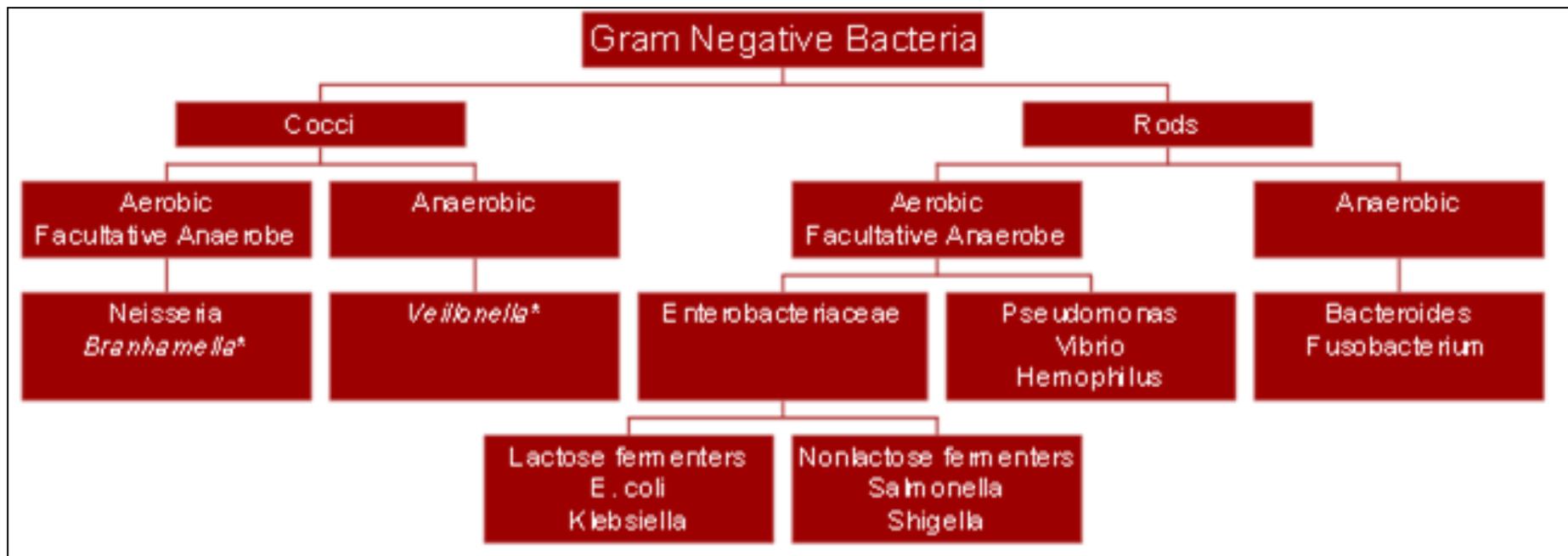
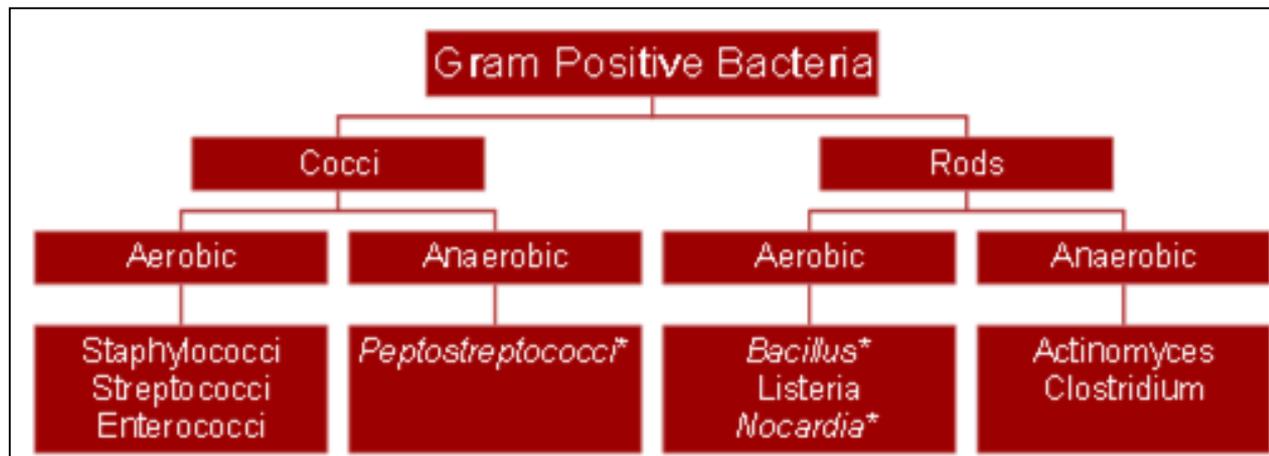
- Natural products with antimicrobial properties were used millennia ago.
- Late 19<sup>th</sup> century - Pasteur and Koch described effects of compounds towards microbes
- 1928 - Alexander Fleming (*a colleague of Grandad Dooley!*) discovered the antimicrobial effect of the mold *Penicillium*.



# Simple Bacterial Classification

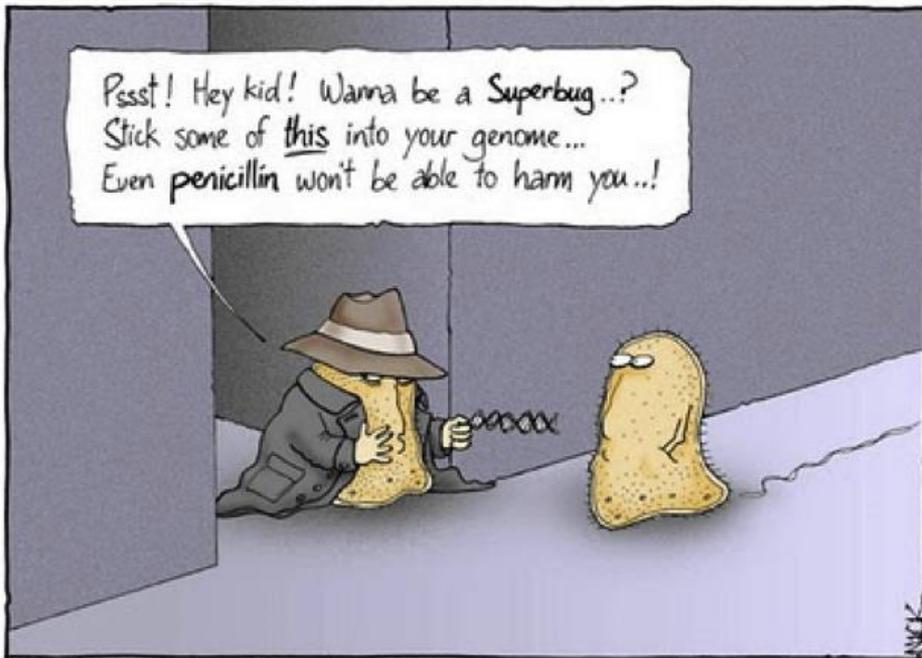
- **Shape:**
  - Cocci – spheres
  - Bacilli – rods
  - Spirochaetes
  - Diplo – two bacteria
  - Strep – line of bacteria
  - Staph – cluster
- **Aerobic, facultative or strict anaerobic**
- Also by virtue of staining characteristics:
  - **Gram-Positive** – Have a large peptidoglycan rich cell wall – 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
- 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

- Antibiotics should only be prescribed with clinical evidence of infection.
  - Exceptions include prophylaxis (e.g. Pre-surgery, post-splenectomy)
- Cultures (e.g. blood, urine, swabs) 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.
  - **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.”

# Cases 1-5

- 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**



# Cases 1-5

- 1) **A** 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.
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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 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.

# Cases 6-10

- 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 leucocytes.  $\beta$ 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) <b>Trimethoprim 7 days</b>   | e) <b>Amoxicillin 7 days</b> |
| b) <b>Nitrofurantoin 3 days</b> | f) <b>Gentamicin STAT</b>    |
| c) <b>Nitrofurantoin 7 days</b> | g) <b>Cefuroxime 10 days</b> |
| d) <b>Cefadroxil 7 days</b>     | h) <b>None of the above</b>  |



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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 catheters become infected so a positive urine dip is not indication for treatment without clinical infection. A clean catch urine sample from freshly inserted catheter is ideal sample to prove infection.*

## Pregnancy

- Trimethoprim should be avoided in pregnancy – especially in first trimester
- Nitrofurantoin can be given, but should be avoided in third trimester, however;
- Oral Cephalosporin or Amoxicillin is preferred. Treatment should be for 7 days.

## In Pyelonephritis

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



# Cases 11-15

- 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 Coamoxiclav 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 a 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.

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| b) <b>Flucloxacillin</b>       | f) <b>Meropenem</b>                  |
| c) <b>Benzylopenicillin</b>    | g) <b>Cefotaxime and Amoxicillin</b> |
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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

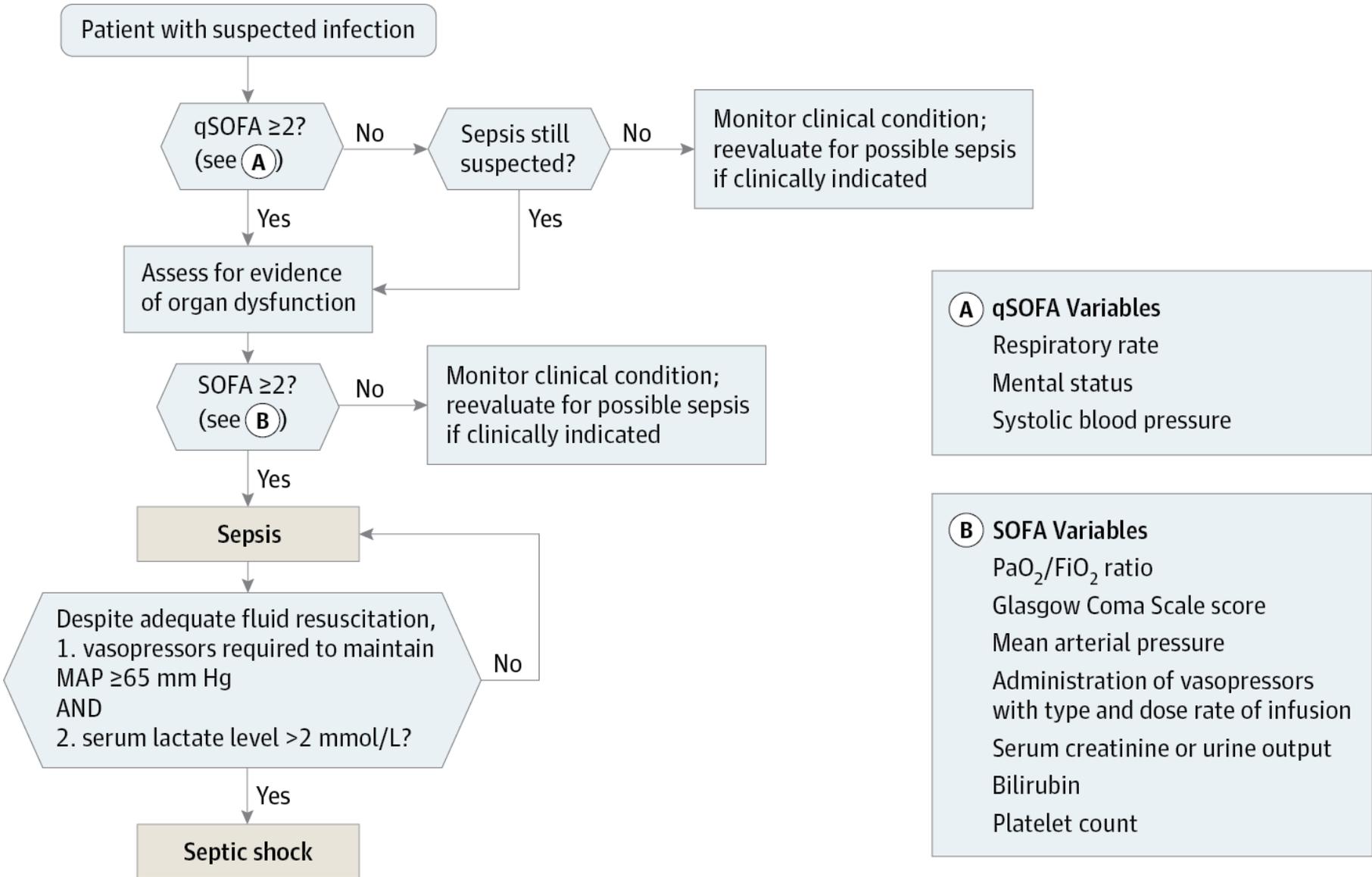
- Benzylpenicillin (if in community)
- IV Cephalosporin (e.g. Ceftriaxone/Cefotaxime) is 1<sup>st</sup> line in hospital
- +/- Amoxicillin (to cover *Listeria* in high-risk groups)
  
- Type 1 Pen-allergy: Chloramphenicol +/- Vancomycin

## 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  $\geq 38$  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).



# Cases 16-20

- 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 56 year old is admitted via E.D. with a cellulitis affecting the foot and lower leg. They have an Early Warning Score of 7 and appear confused.
- 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) Flucloxacillin and Clindamycin IV |
| b) Clarithromycin PO       | g) Metronidazole IV                  |
| c) Phenoxymethylpenicillin | h) Metronidazole PO                  |
| d) Flucloxacillin PO       | i) Vancomycin IV                     |
| e) Flucloxacillin IV       | j) None of the above                 |



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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
$\leq 1$	Low risk of Strep. Avoid Abx
2-3	15-30% risk. Send swab and delay Abx
$\geq 4$	~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: 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 and Clindamycin
- If penicillin allergy: Clarithromycin (+/- Clindamycin).
- If MRSA colonised Vancomycin/Teicoplanin
- If evidence of shock, add Gentamicin
- If human/animal bites: Co-amoxiclav (and consider Tetanus)
- 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.

## 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

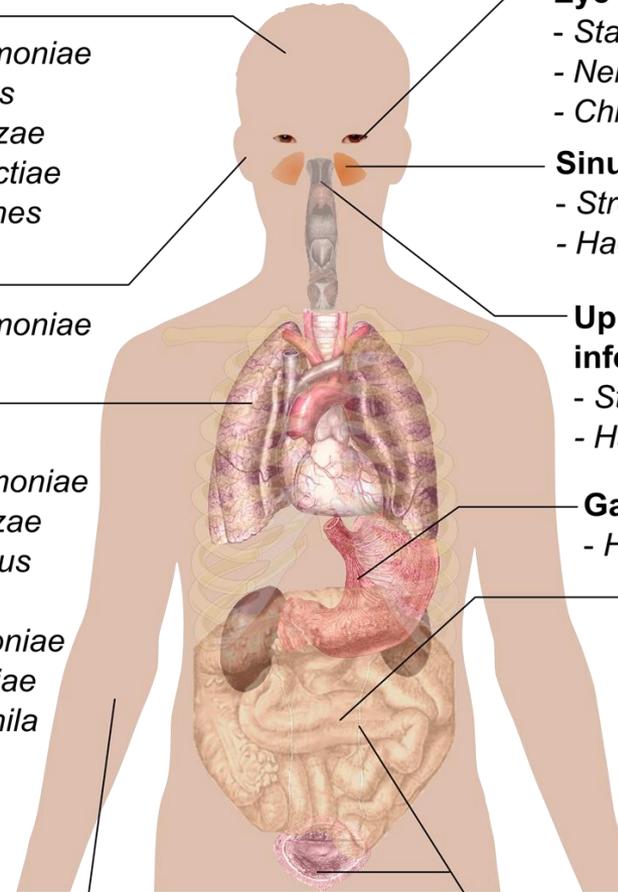
- *Campylobacter jejuni*
- *Salmonella*
- *Shigella*
- *Clostridium*
- *Staphylococcus aureus*
- *Escherichia coli*

### 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 last year, where time was spent discussing them.
- Video recording available at:
  - [www.tinyurl.com/antibiotics2016](http://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.

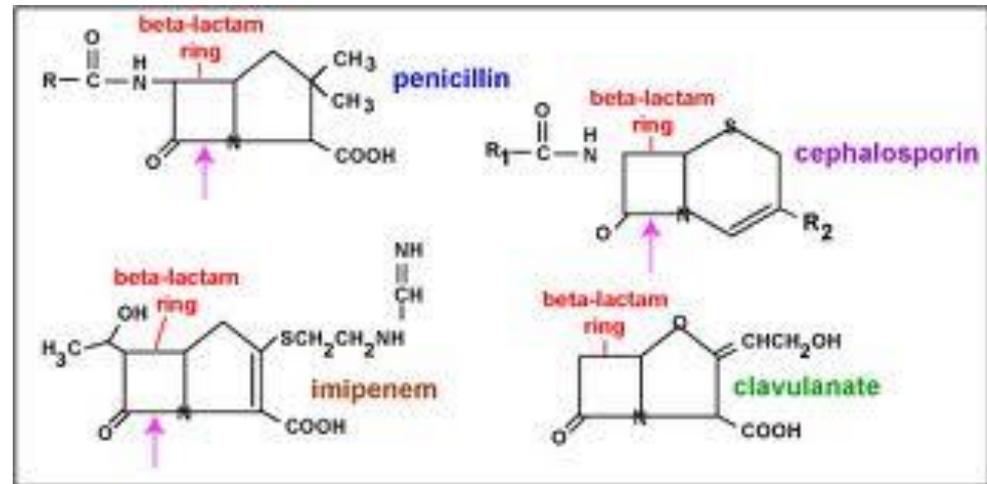


# $\beta$ -lactams

- Named because they contain a  $\beta$ -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)



# $\beta$ -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  $\beta$ -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.
- **$\beta$ -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*



# $\beta$ -lactams - Cephalosporins

- Are more resistant to  $\beta$ -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



# $\beta$ -lactams - Carbapenems

- Stable against Extended-Spectrum  $\beta$ -lactamases (ESBLs) although not active against MRSA. Normally require microbiology approval.
- **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.
- **Clarithromycin** – has higher tissue concentration than erythromycin. More widely used.
- **Azithromycin** has good intracellular penetration so useful *Salmonella typhi* and *Chlamydia* infections.



# 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).
- 
- **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 be given parenterally.
- 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.
  
- **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



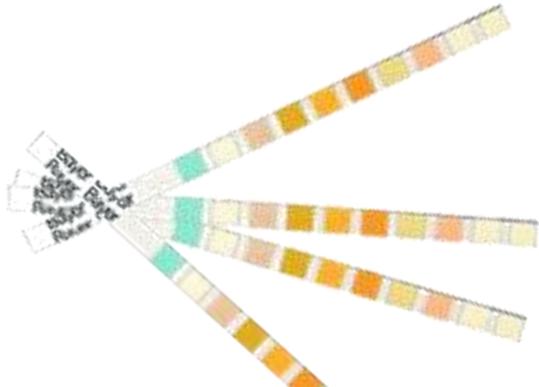
# Quinolones

- 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.
- **Norfloxacin**
- **Levofloxacin**



# 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.
- 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.

