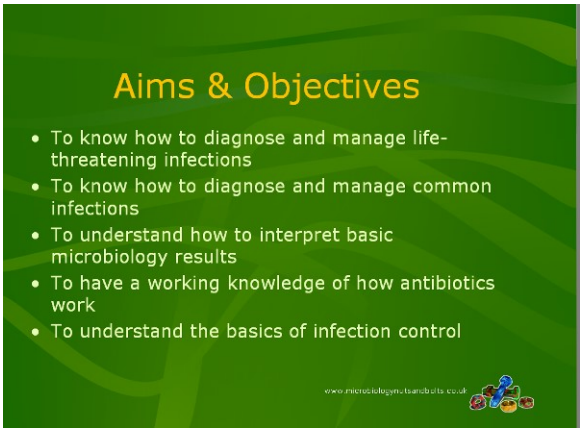
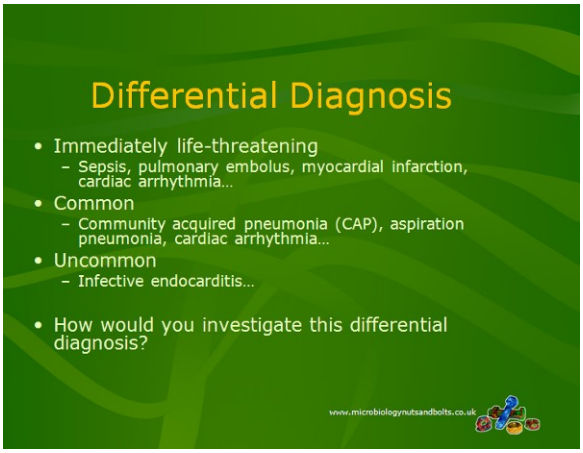
Microbiology Nuts & Bolts: Session 3: Sepsis

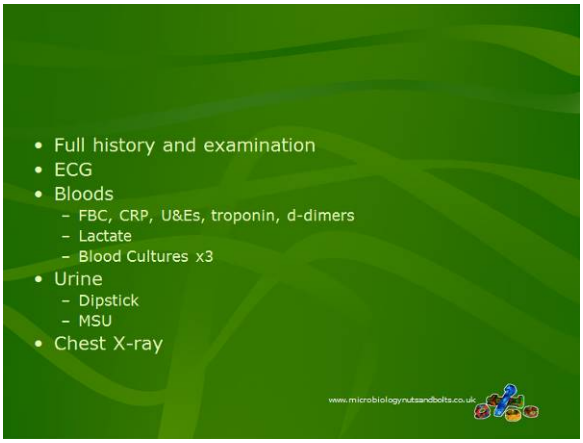


- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common infections so that complications do not occur and patients get better as quickly as possible
- Knowing about antibiotics ensures the correct ones are used for the correct indications, prevents prescribing errors and keeps patients safe
- Everyone working in a healthcare setting has a responsibility to protect patients from harm including cross infection from other patients

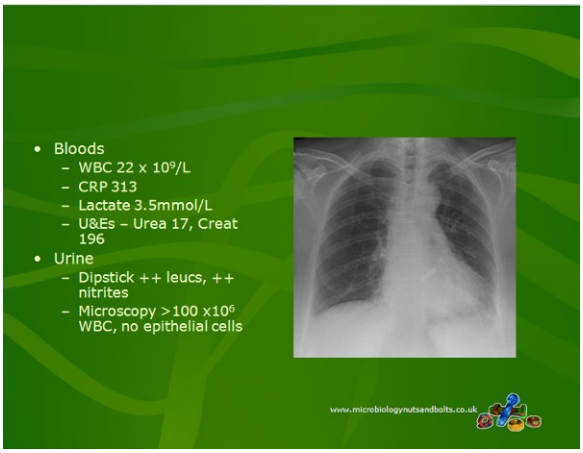
- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for shortness of breath therefore it is important not to become too fixated on a diagnosis without considering all possibilities
- All doctors should know the limitations of the tests they do including basic observations not just laboratory tests
- Normal temperature is 36.5°C to 37.5°C
  - Often a tympanic temperature which is actually a peripheral temperature not a core temperature
  - Can vary from core by up to +/- 1°C
  - Works by infrared looking at the tympanic membrane therefore any obstruction in the ear can lead to a false temperature result



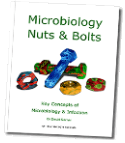
- Formulating a differential diagnosis appears to be going out of fashion but it is essential if diagnoses are not to be missed
- A systems approach (e.g. respiratory, cardiac, Gastrointestinal, genitourinary, neurological, skin, bone, joint, etc) can be fitted to a template of life-threatening, common, uncommon in order to complete the differential but considering the life-threatening first ensures these are dealt with as early as possible
- It is not a static process but can change throughout a patients management as new information becomes available and their clinical condition changes

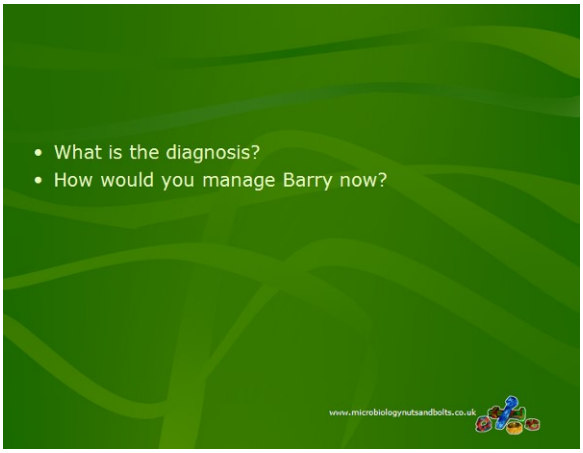


- It is essential to know the normal values of all tests within your hospital
- Full blood count (FBC)
  - The total white blood cell count can go up or down in infection
  - The differential white blood cell count can help to point to the type of organism but nothing is 100% (neutrophils = bacteria/fungi, lymphocytes = viruses, eosinophils = parasites)
  - Platelets are an acute phase reactant and go up in infection (they can go down in severe infections when disseminated intravascular coagulation DIC develops)
- CRP (C reactive protein)
  - Produced in liver in response to inflammation, often goes up in bacterial infection
  - >200 usually significant, otherwise need to know what the trend is i.e. increasing, decreasing
  - Beware, patients in liver failure do not produce much CRP – use other markers of liver synthetic function to guide you e.g. INR, Albumin
- Urea & Electrolytes (U&Es)
  - Antibiotics can only be prescribed safely if the patients kidney function is known
- Lactate
  - High lactate indicates inadequate tissue perfusion and anaerobic metabolism, and can be a sign of severe sepsis
- Urine point of care includes a dipstick test
  - Leucocytes indicate the presence of white blood cells and hence inflammation in the urinary tract
  - Bacterial nitrites are breakdown products from the action of bacteria on Urea and indicate the presence of bacteria
  - Urine samples are prone to contamination so it is important to advise patients how to take a proper MSU
    - Part the labia or retract the foreskin, void the first part of the urine stream and discard, then catch the middle part of the stream.
    - The first part of the urine is prone to bacterial contamination from the urethra giving false positive results
- Chest X-ray is required by the British Thoracic Society in order to diagnose pneumonia in hospital

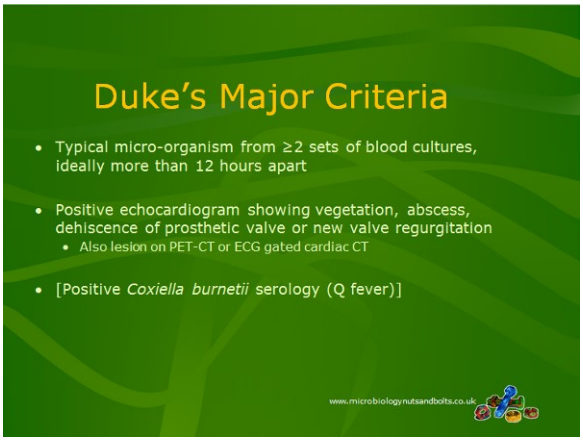


- Patient has raised high white blood cells and CRP indicating a significant inflammatory problem and therefore a likely infection
- U&Es shows a degree of renal failure and may make antibiotic dosing problematic
  - The urine microscopy indicates a possible UTI but requires a culture before being diagnostic as many patients with a systemic inflammatory response will have pyuria
- The chest x-ray shows a large heart with a device within the heart shadow
  - This is a prosthetic heart valve, although they are often difficult to see on chest X-rays

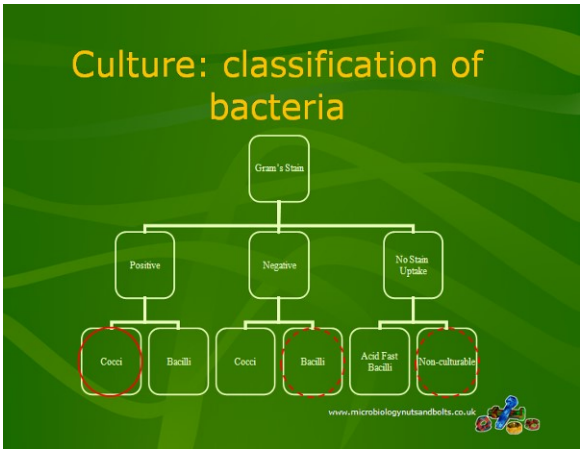




- The heart valve raises the possibility of an infected heart valve and hence a diagnosis of infective endocarditis
- Management should be directed at making a definite diagnosis of infective endocarditis
- It is not usually necessary to rush in with antibiotics at this stage as doing so makes it very hard to prove the diagnosis



- Infective endocarditis is diagnosed based upon Duke's Criteria
- The reason for taking 3 sets of blood cultures spaced out in time is to demonstrate an ongoing bacteraemia. Most patients with infections are intermittently bacteraemic and so only a small proportion of their blood cultures are positive. Patients with Infective endocarditis are continuously bacteraemic because the infection is inside the heart and therefore in the blood stream itself
- These are divided into Major and Minor criteria and the diagnosis is made with a combination of:
  - 2 Major
  - 1 Major PLUS 3 Minor
  - 5 Minor



- The most common causes of infective endocarditis are the Gram-positive cocci:
  - Alpha-haemolytic (Viridans) Streptococcus
  - Enterococcus spp.
  - Staphylococcus aureus
  - Coagulase-negative Staphylococcus
  - HACEK (Gram-negative bacilli part of oral flora)
  - Culture negative bacteria (Q fever, Bartonella, Brucella)

Causes of endocarditis

- Common:
  - *Staphylococcus aureus*
  - Viridans *streptococcus* spp.
  - *Enterococcus* spp.
- Uncommon:
  - Coagulase negative *Staphylococcus* spp.
  - HACEK bacteria
  - *Candida* spp. (Nosocomial or IVDUs)
- Rare:
  - *Coxiella burnetii*, *Brucella* spp., *Bartonella* spp., *Mycoplasma* spp., *Chlamydia* spp., *Legionella* spp., *Tropheryma whipplei*

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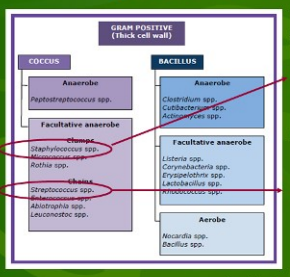
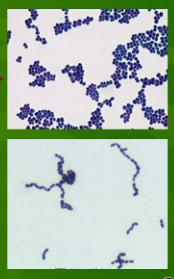
- The most common causes of infective endocarditis are Gram-positive cocci with the ability to bind to the heart valves and coagulate platelets
- Most of the causes are also upper and lower gastrointestinal flora, which frequently translocate into the blood stream from where they can adhere to abnormal or damaged heart valves if not cleared quickly enough by the immune system

Classification of Gram-positive cocci





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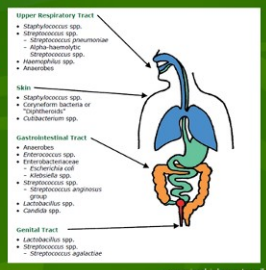
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Staphylococci from Streptococci but these are of no use to ward doctors
- In practical terms Gram-positive cocci can be distinguished by:
  - Staphylococci form clumps
  - Streptococci (and Enterococci) form chains

Community Normal Flora

HACEK bacteria also part of upper GI flora



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- If a septic patient grows a bacteria from their blood culture then knowing normal flora allows you to focus attention on the likely originating part of the body and hence a potentially reversible cause e.g. Enterococcus sp. is likely to originate in an intra-abdominal organ such as the bowel and hence a patient with infective endocarditis due to Enterococcus spp. should be investigated for an underlying bowel problem

Duke's Minor Criteria

- Predisposing heart condition OR IVDU
- Fever >38°C
- Vascular phenomena – emboli, mycotic aneurysm, haemorrhages, Janeway lesions
- Immunological phenomena – glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
- Microbiological evidence – positive blood culture but falls short of major criteria (e.g. 1 set with typical micro-organism, 2 or more sets with uncommon micro-organism)

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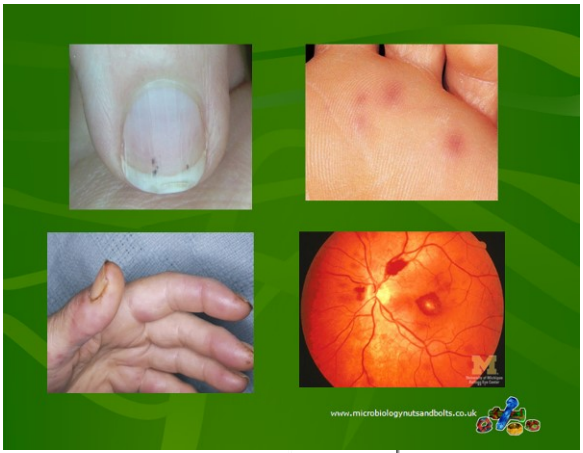

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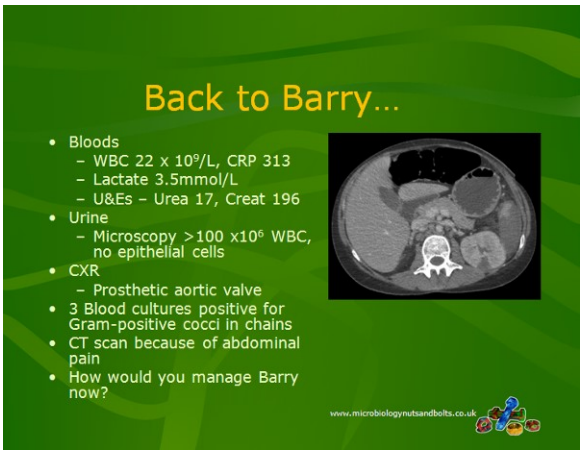
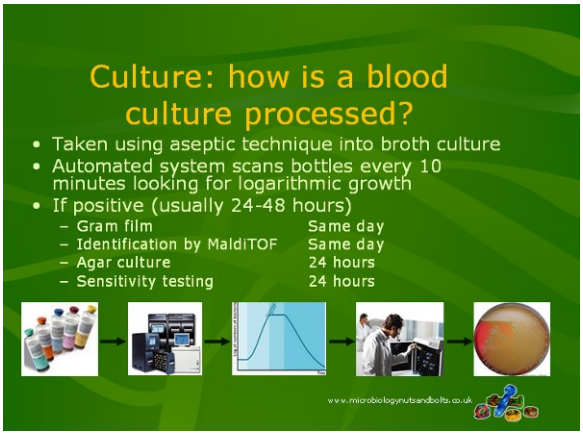
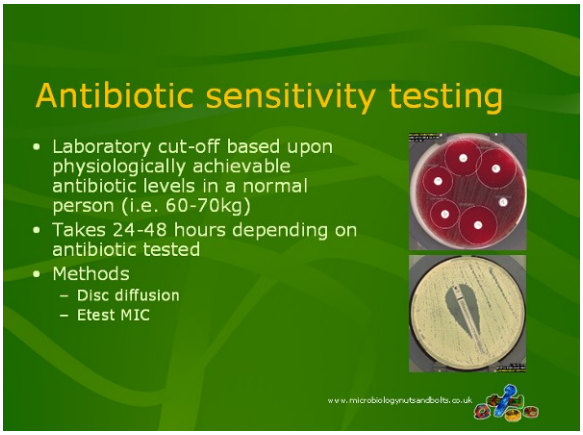


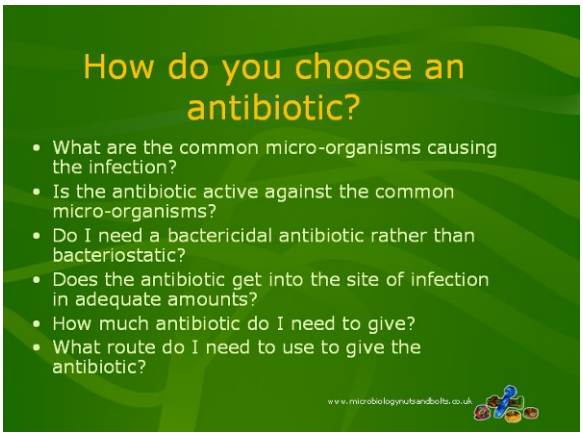
- The CT scan suggests shows splenic and renal infarcts due to emboli which have become detached from an aortic valve vegetation
- Remember, most support services like pathology laboratories and radiology are only as good as the information they receive, in this case the radiology lab were given no information about the patient being septic and were only asked to look for a lung pathology
- Always provide as much clinical information as you can when liaising with support specialties, it is in the interest of both you and your patients
- Barry is now getting complications from his infective endocarditis and so he should be started on empirical treatment whist waiting for his blood cultures to grow a bacteria



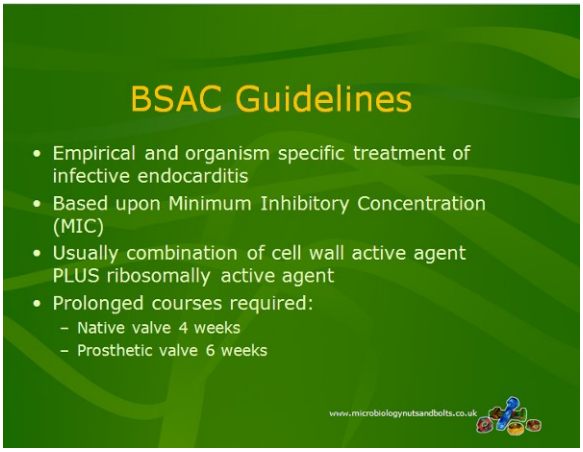
- Most healthcare staff are under the mistaken belief that microbiology laboratories do something special with blood cultures when they arrive in the lab and that they will be ready in 48 hours
- In fact the system is completely automated
- The blood culture bottles are loaded on to an automated incubator and left
- The incubator scans the bottle every 10 minutes looking for logarithmic growth (the incubator is actually looking for logarithmic CO_2 production from replicating bacteria causing a pH change in the bottle)
- Once this growth phase occurs the bottle is taken off the incubator and further work including Gram's stain and culture on agar begins, as well as identification by mass spectrometry (MaldiTOF – Matrix-assisted laser desorption/ionisation time of flight))
- Most significant blood cultures will signal within 48 hours but it is entirely dependent on the amount of organism that went in to the bottle, whether the patient was on antibiotics and the species of bacteria in question
- Most laboratories will telephone out all positive blood cultures when a result is available



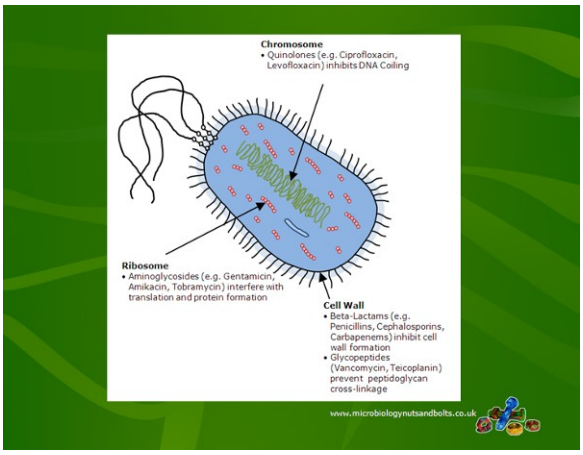
- Antibiotic sensitivity in UK laboratories is usually tested for using the BSAC method where antibiotic impregnated filter paper discs are put on agar inoculated with bacteria and then incubated overnight
- The size of the zone where the bacteria have been unable to grow is then measured and compared to a known standard value
- The value is related to the combination of antibiotic, bacterial species and body site
- Most antibiotic resistance is relative, i.e. it is not possible to get enough antibiotic into the body site to treat the organism however some is absolute e.g. MRSA is completely resistant to the Beta-lactam antibiotics
- For more serious infections such as infective endocarditis antibiotic advice is based upon the minimum inhibitory concentration (MIC) which is the lowest concentration required to prevent the bacteria from growing, usually test for with the Etest method where an antibiotic graduated impregnated strip is place on the agar and the MIC corresponds to where the bacteria intercept the strip



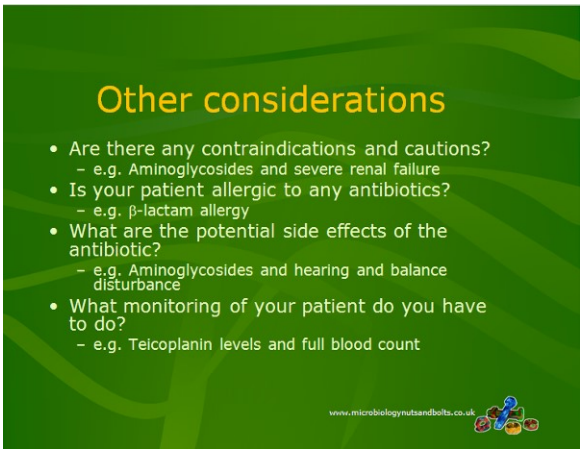
- In this case the patient clearly needs antibiotics
- Because he is so unwell he needs antibiotics that will kill the bacteria as quickly as possible
- The antibiotics should be bactericidal and should be given intravenously in the high doses



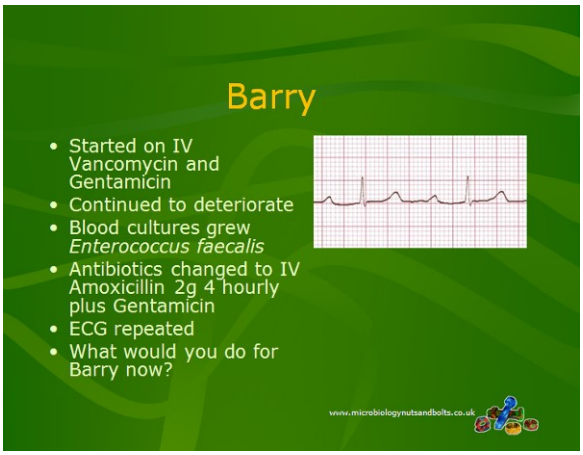
- There is a nationally accepted guideline for the treatment of infective endocarditis produced by the British Society for Antimicrobial Chemotherapy (BSAC) which all Microbiologists will follow
- They include empirical (when the cause is unknown), and definitive treatments (when the cause is known)
- Once the cause of an infection is known the antibiotics should be changed to specifically target that infection
- Infective endocarditis is treated with prolonged courses of intravenous antibiotics and usually include two antibiotics in combination



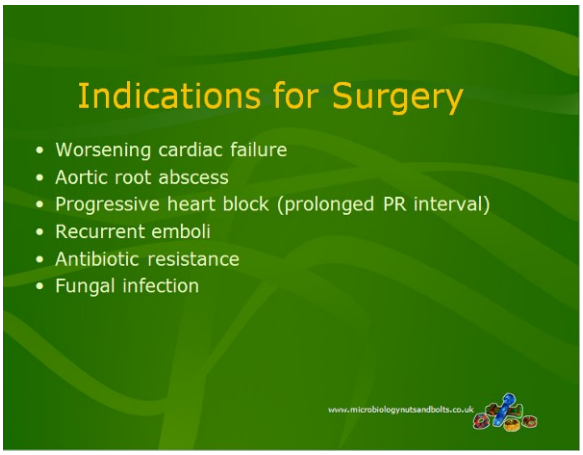
- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list to a more manageable size:
  - Mainly act on the cell wall
    - If no cell wall or unable to penetrate Gram-negative cell membrane to cell wall then no activity i.e. glycopeptides have no Gram-negative activity
  - Mainly act on the ribosome
    - Gentamicin acts on the ribosome but actually also displays concentration dependent killing of bacteria so is very useful in sepsis
  - Mainly act on the chromosome
    - Quinolones interfere with DNA coiling and are broad spectrum and cidal, however there is some evidence that they promote mutation and therefore resistance in bacteria



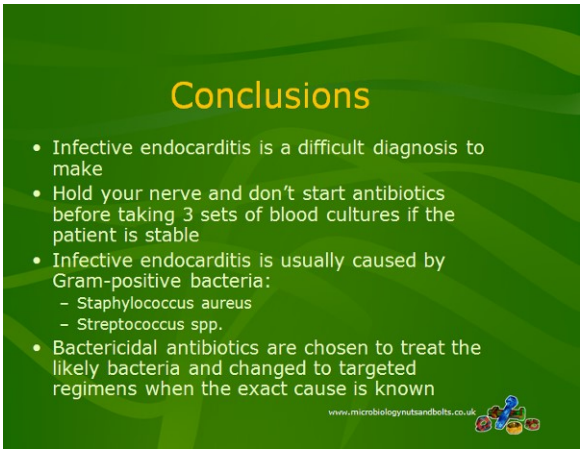
- It always worth checking if a patient is allergic to whatever drug you are going to give them although be sure they are describing an allergy not just a recognised side-effect
- Some antibiotics have common or severe side effects and doctors should be familiar with these and warn patients about them, as part of the informed consent to treatment process
- Many antibiotics also require monitoring for these side effects and this should be checked in the BNF at the time of prescribing
- Patients given aminoglycosides such as gentamicin should be assessed for hearing and balance disturbance as well as renal failure



- Because Barry is getting complications empirical treatment is started targeting Staphylococci and Streptococci (including Enterococci)
- Once the blood cultures have grown an organism the antibiotics are changed to the definitive treatment for this organism
- The ECG shows a prolonged PR interval which indicates the onset of heart block, which can be a marker for the development of an aortic root abscess
- Barry should be referred for assessment for cardiothoracic surgery



- Barry has evidence of progressive heart block, possibly aortic root abscess and recurrent emboli



- Infective endocarditis is a difficult diagnosis to make and it relies on the fulfilment of Duke's criteria
- In order to fulfil Duke's criteria it is important to take blood cultures off antibiotics, if possible 3 sets spaced out in time, once antibiotics are started the blood cultures are likely to be negative and it will be almost impossible to fulfil Duke's criteria
- Most infective endocarditis is caused by Gram-positive bacteria such as Staphylococci and Streptococci (including Enterococci)
- Infective endocarditis is treated with bactericidal antibiotics wherever possible as most patients treating with bacteriostatic agents relapse when those antibiotics are stopped