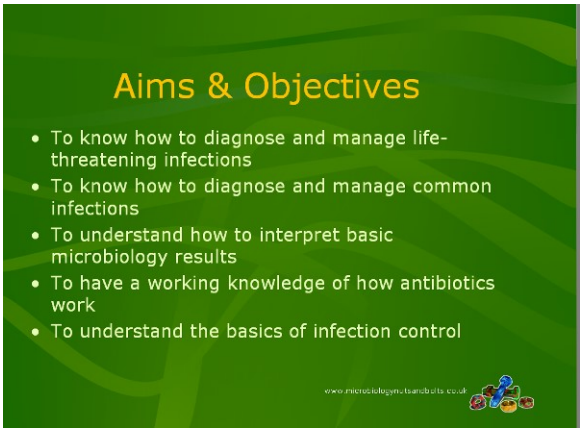
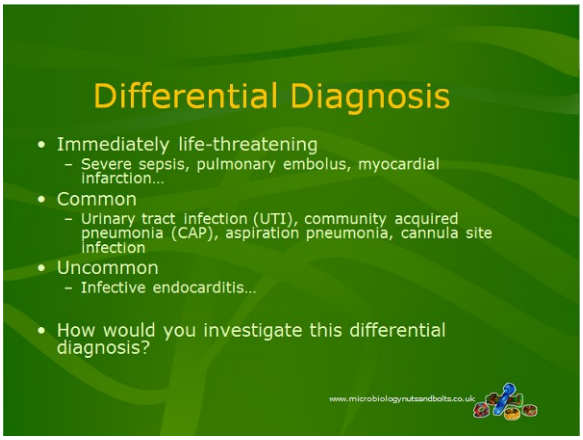
Microbiology Nuts & Bolts: Session 6: Sepsis

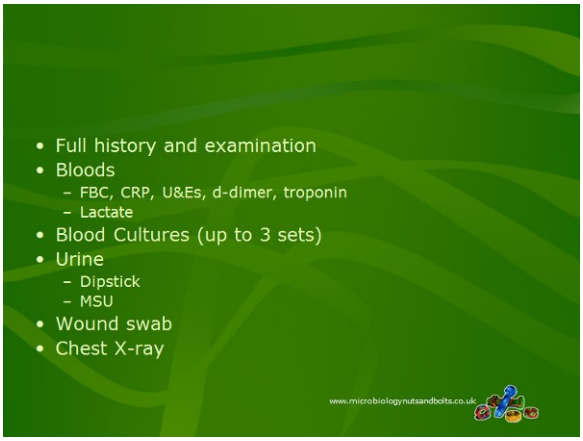


- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common 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

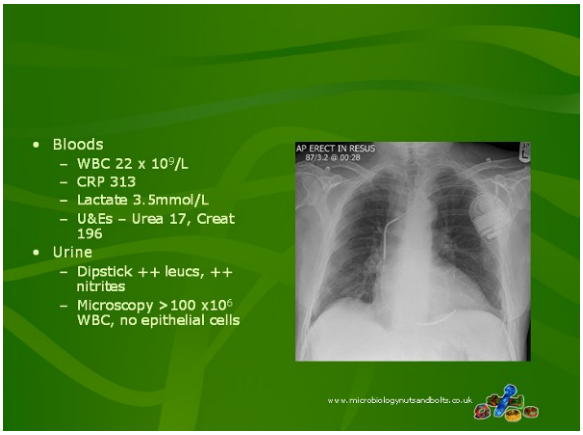
- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for crackles in the chest therefore it is important not to become too fixated on a diagnosis without considering all possibilities
- All doctors should know the limitations of the tests they 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
- Worryingly Geoff is hypothermic and tachycardic, and he has a potential focus of infection in his chest, he is septic and needs urgent treatment



- 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

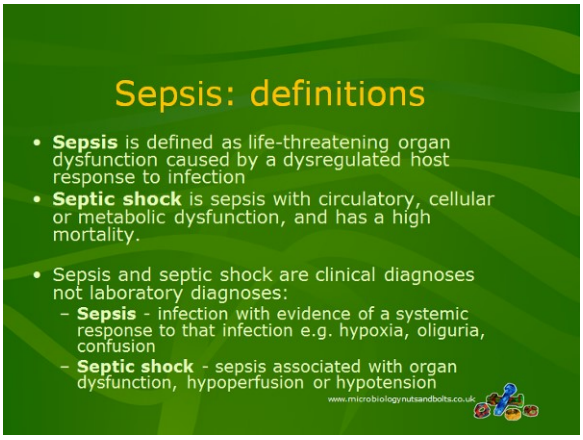


- Patient has raised high white blood cells and CRP indicating a significant inflammatory problem and therefore a likely infection
- U&Es shows a degree of renal failure and may make antibiotic dosing problematic
  - The urine microscopy indicates a possible UTI but requires a culture before being diagnostic as many patients with a systemic inflammatory response will have pyuria
- The chest x-ray shows a device in the upper left chest wall and multiple small shadows throughout the lung fields
  - There are two main types of implantable device seen on chest x-rays, permanent pacemakers (PPM) and implantable cardioverter defibrillators (ICD)
  - PPM usually has 2 wires but can occasionally have

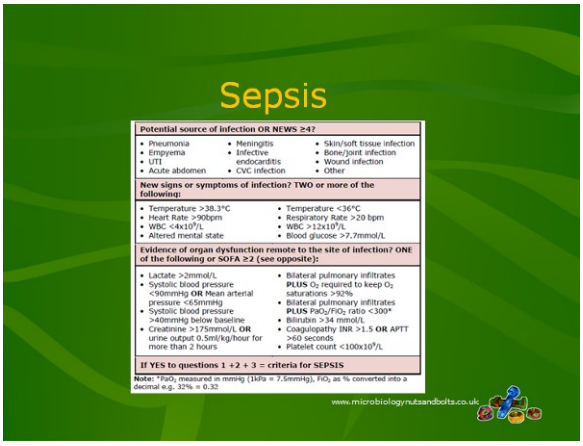
only 1

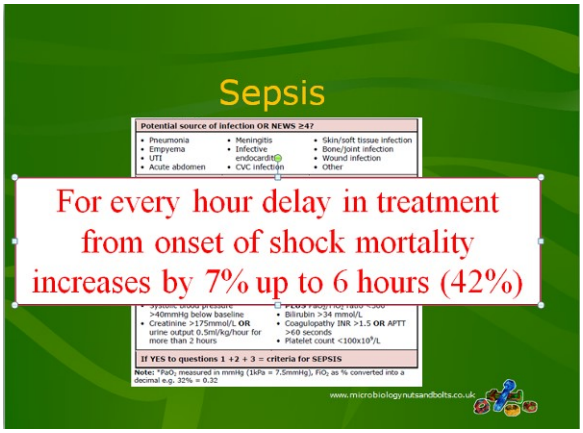
- ICD has 1 wire but it is surrounded by insulation at certain key points to prevent it defibrillating structures it shouldn't when it goes off such as where it enters the atrium and passes through the atrioventricular valve (as in this patients chest x-ray)

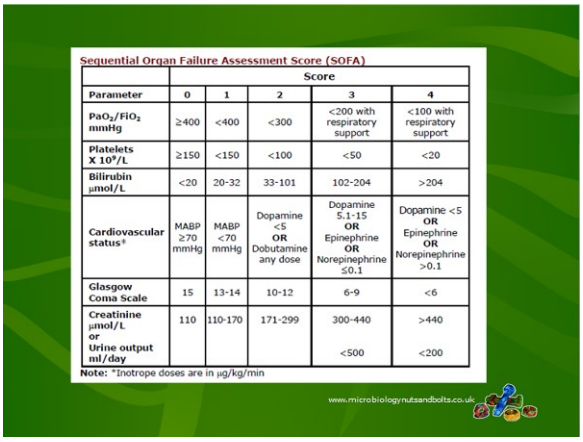
- This chest x-ray appearance would be unusual for a pneumonia but would be consistent with multiple pulmonary emboli
- The ICD leads are implanted in the right side of the heart and therefore if infective and a vegetation forms, micro-emboli would go to the lungs (unless there was a ventriculoseptal defect)
- It is likely that Geoff has an infected ICD, and therefore essentially a right sided endocarditis
- Treatment should be directed at right sided endocarditis and the ICD removed if possible
- The common causes of sepsis are the Gram-negative bacilli and cocci as well as Staphylococcus aureus

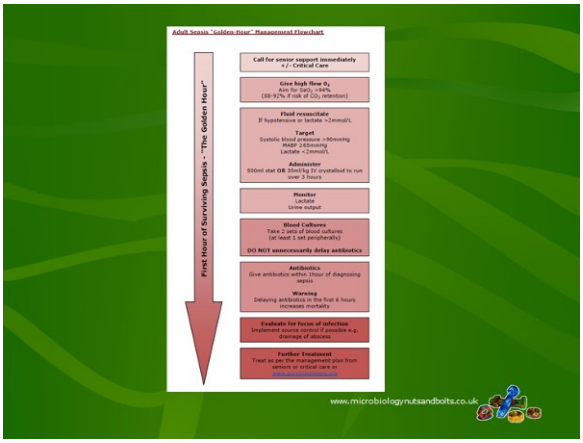


- Sepsis is a clinical diagnosis, not a laboratory one
- Severe sepsis occurs when there is also end organ dysfunction and this can be diagnosed through the use of laboratory tests
- For more information see www.survivingsepsis.org

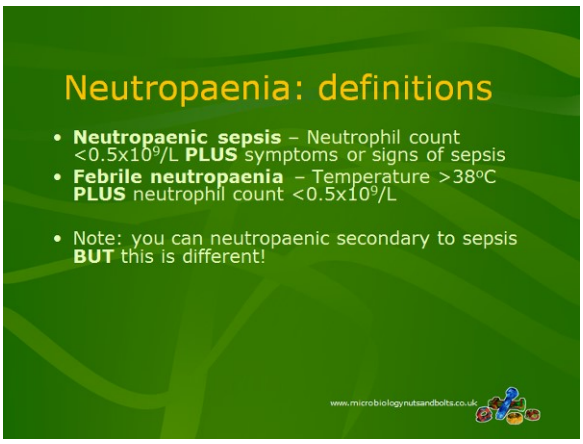






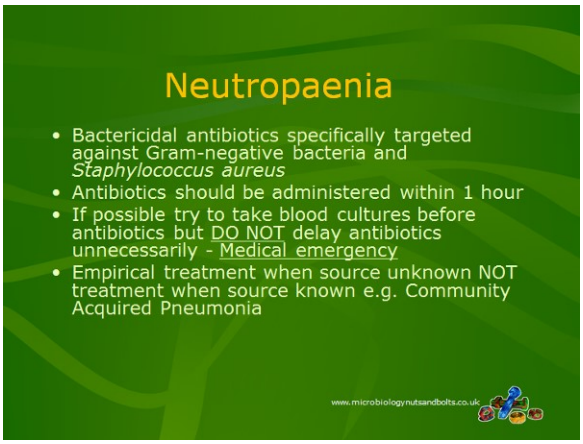


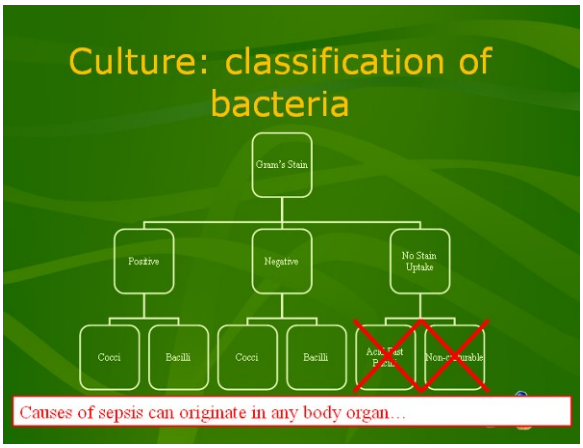
- Every hour counts when treating septic patients and early intervention really does save lives
- Resuscitation and antibiotics should be given as fast as possible, ideally within an hour of arrival in the hospital



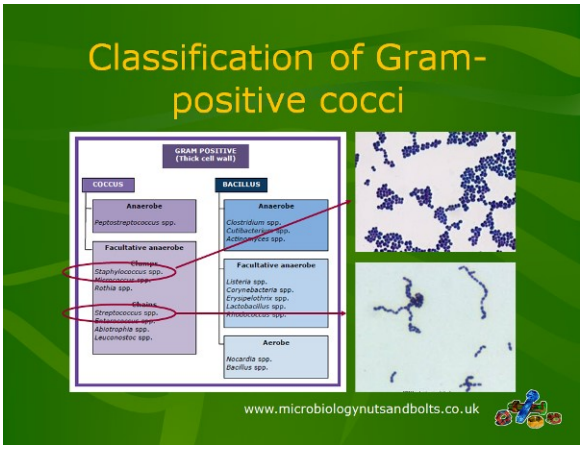
- Sepsis in a patient who is already neutropaenic is a different clinical entity to sepsis causing neutropaenia and yet many doctors make the mistake of assuming that if you are septic and neutropaenic then you should always be treated as neutropaenic sepsis
- The distinction is important because the causes can be different
- Sepsis in a patient who is already neutropaenic can be due to opportunistic micro-organisms as well as those which can cause sepsis in immunocompetent patients
- Sepsis which is overwhelming and induces neutropaenia itself is usually caused by the Enterobacteriaceae, Neisseria meningitidis or Staphylococcus aureus and the neutropaenic aspect is a sinister sign and shows that the patient is unable to cope with the infection

- Both are emergencies requiring urgent management

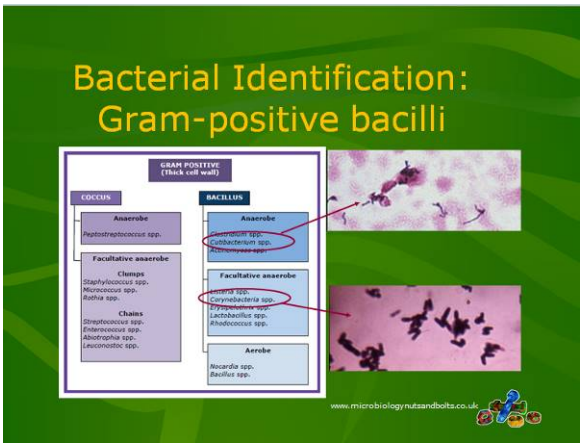




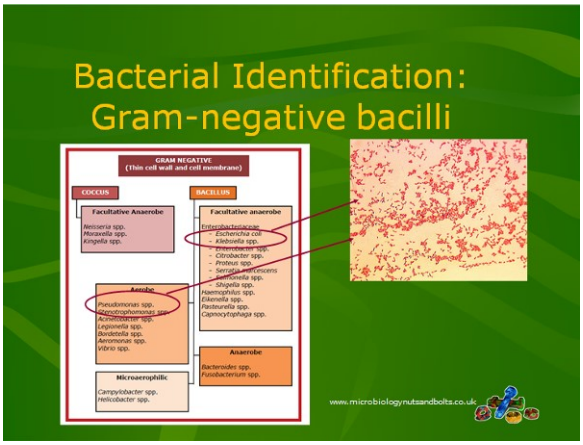
- Any bacteria can cause sepsis but the most common are the Enterobacteriaceae, Neisseria sp and Staphylococcus aureus



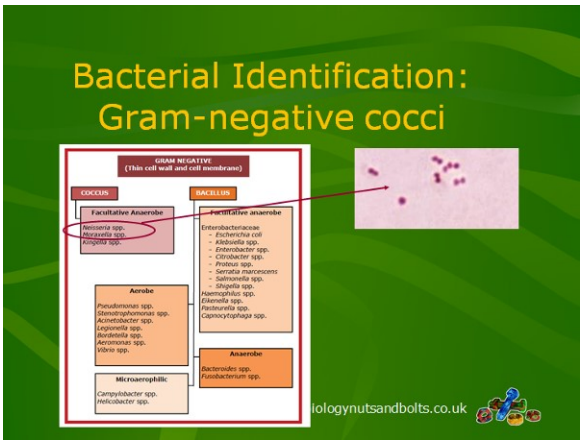
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Staphylococci from Streptococci but these are of no use to ward doctors
- In practical terms Gram-positive cocci can be distinguished by:
  - Staphylococci form clumps
  - Streptococci form chains



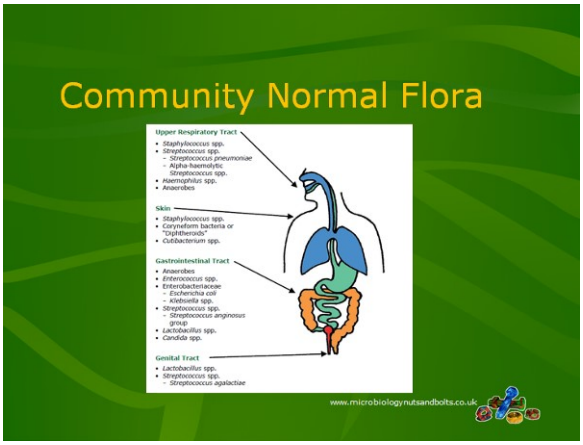
- The most clinically significant Gram-positive bacillus is Listeria monocytogenes
- The more common isolates are the skin bacteria such as the Diptheroids and Propionibacteria which are common blood culture contaminants



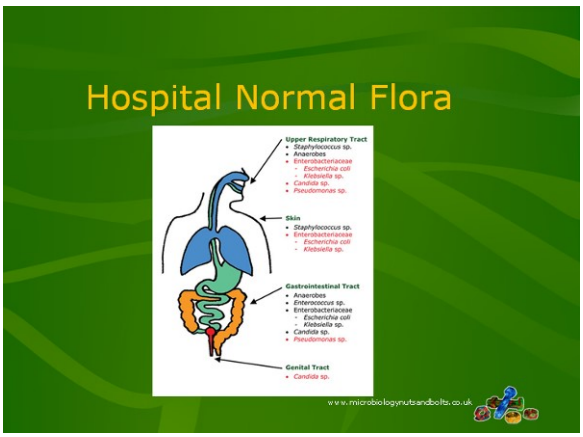
- The Enterobacteriaceae and Pseudomonas sp. are the most common clinical isolates from the Gram-negative bacilli
- The main distinguishing features for these two groups are that the Enterobacteriaceae are Facultatively anaerobic (i.e. will grow both aerobically and anaerobically) whereas Pseudomonas sp. are aerobic only
- In clinical terms if a blood culture has a Gram-negative bacillus in both the aerobic and anaerobic bottle it will be an Enterobacteriaceae, whereas if it's only in the aerobic bottle it may well be a Pseudomonas sp.



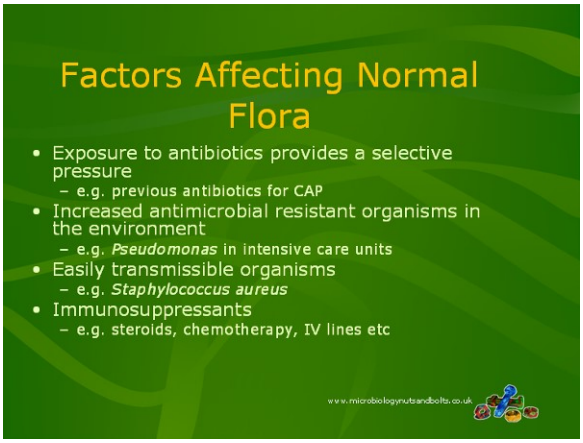
- There are 2 main Neisseria sp. which can cause disseminated infection and sepsis though in the UK it is really only Neisseria meningitidis that we see
- Some countries (such as the USA) appear to have a strains of Neisseria gonorrhoea which is more likely to disseminate and cause sepsis than the UK strains



- 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. E. coli is likely to originate in an intra-abdominal organ such as the urinary tract, biliary tree or bowel

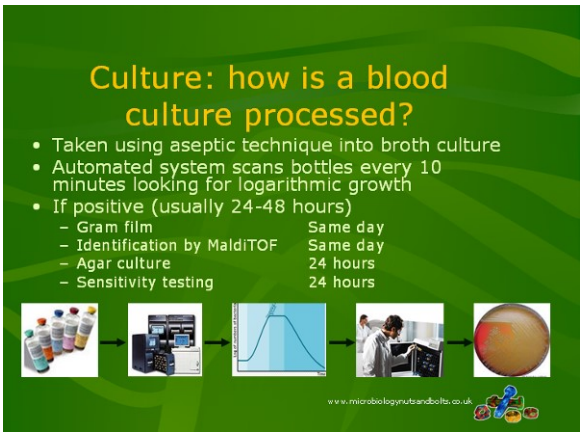


- It is important to remember that normal flora starts to change in hospitalised patients and so the causes of sepsis from specific body sites also changes

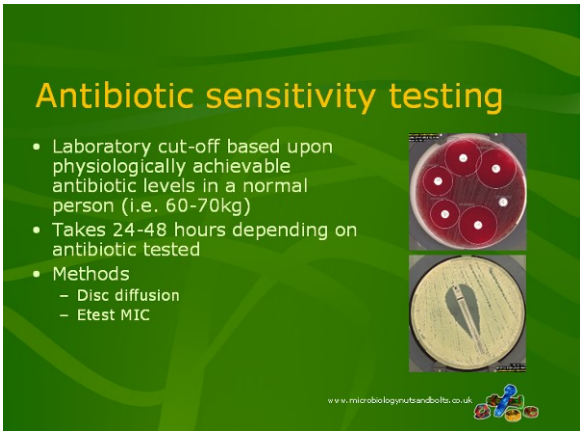


- There are many circumstances that can affect a patients normal flora
- Understanding how this happens can allow predictions to be made as to how the flora will change and therefore how this will influence the types of bacteria causing infections
- Antibiotics will tend to remove sensitive bacteria from the flora leaving the resistant ones behind, for this reason if antibiotics have been used as prophylaxis for a procedure any infection occurring immediately after the procedure is likely to be resistant to those antibiotics

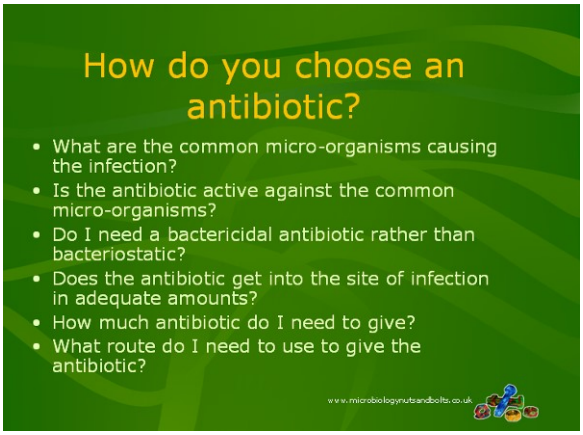
- The CT scan suggests multiple pulmonary metastases but this is unlikely to have occurred out of the blue
- Remember, most support services like pathology laboratories and radiology are only as good as the information they receive, in this case the radiology lab were given no information about the patient 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



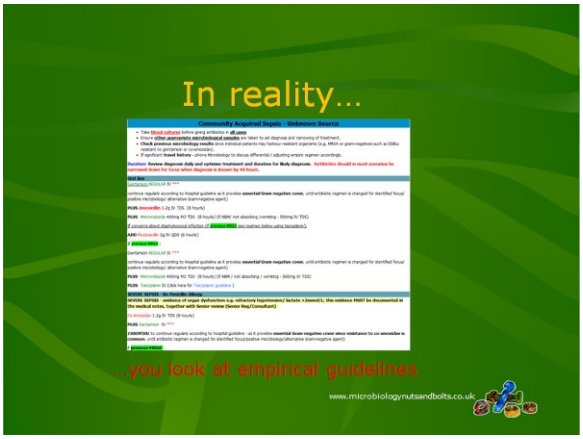
- Most healthcare staff are under the mistaken belief that microbiology laboratories do something special with blood cultures when they arrive in the lab and that they will be ready in 48 hours
- In fact the system is completely automated
- The blood culture bottles are loaded on to an automated incubator 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



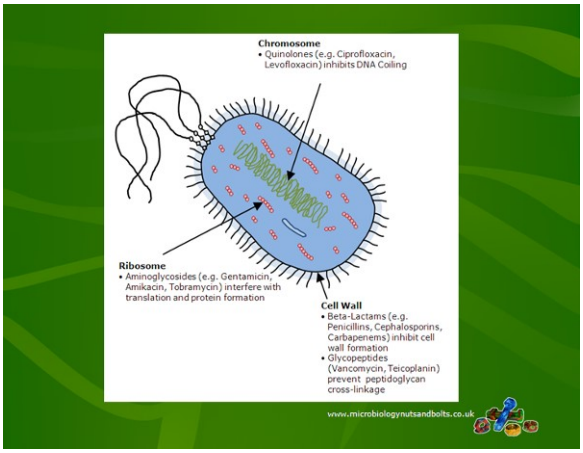
- Antibiotic sensitivity in UK laboratories is usually tested for using the BSAC method where antibiotic impregnated filter paper discs are put on agar inoculated with bacteria and then incubated overnight
- The size of the zone where the bacteria have been unable to grow is then measured and compared 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



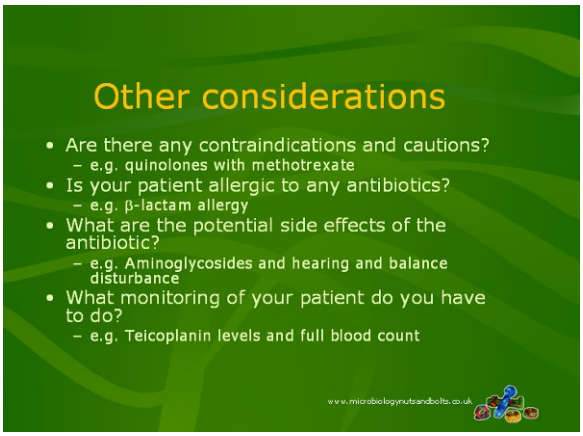
- In this case the patient clearly needs antibiotics
- Because he is so unwell he needs antibiotics that will kill the bacteria as quickly as possible
- The antibiotics should be bactericidal and should be given intravenously in the high doses



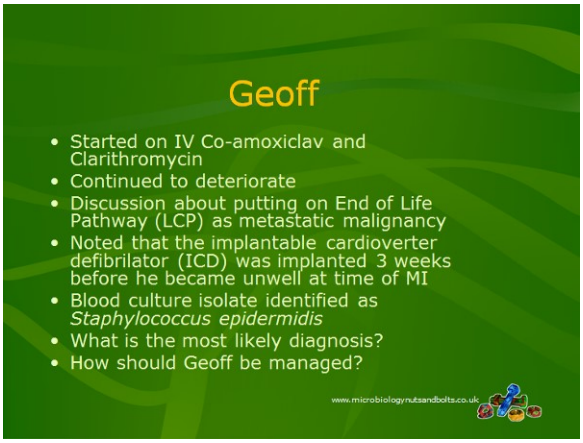
- Empirical antibiotic guidelines vary a little between hospitals based upon local epidemiology, therefore it is important to know your own guidelines
- They are empirical, that is they are designed to initiate treatment when the cause is unknown, they are not definitive for a specific cause
- Once the cause of an infection is known the antibiotics should be changed to specifically target that infection, the guidelines have done their job by that time and are no longer required



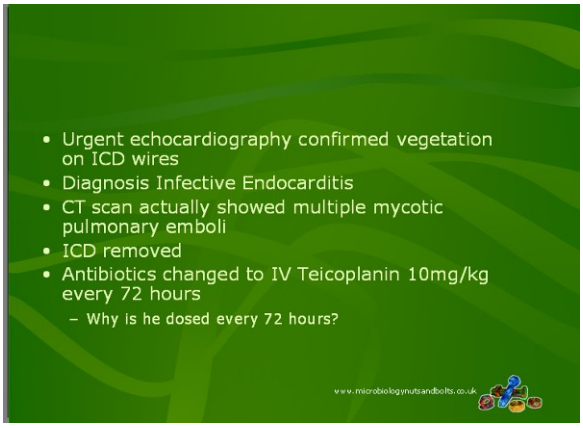
- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list 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



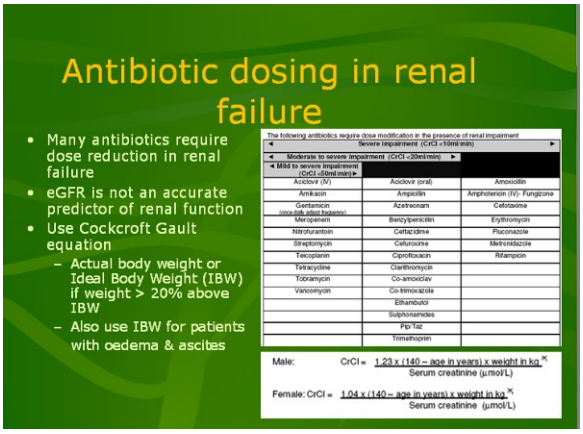
- It always worth checking if a patient is allergic to whatever drug you are going to give them although be sure they are describing an allergy not just a recognised side-effect
- Some antibiotics have common or severe side effects and doctors should be familiar with these and warn patients about them, 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



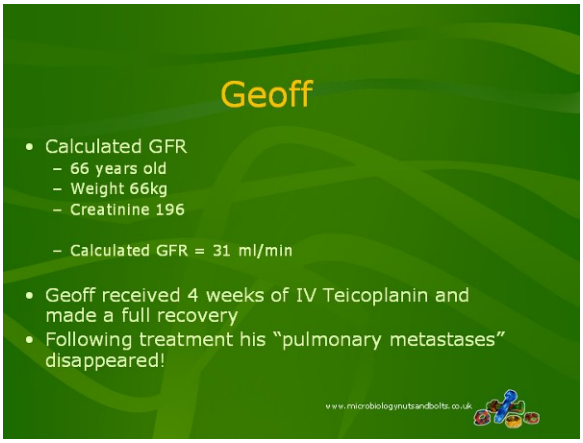
- The ICD is still the most likely source of this patients infection, and the "metastases" are almost certainly septic emboli
- He should be started on a high dose of a glycopeptide such as Teicoplanin or Vancomycin
- An Echocardiogram will show if the ICD is definitely infected as will serial blood cultures
- If the ICD is the source it will need to be removed, but this is often easier said than done



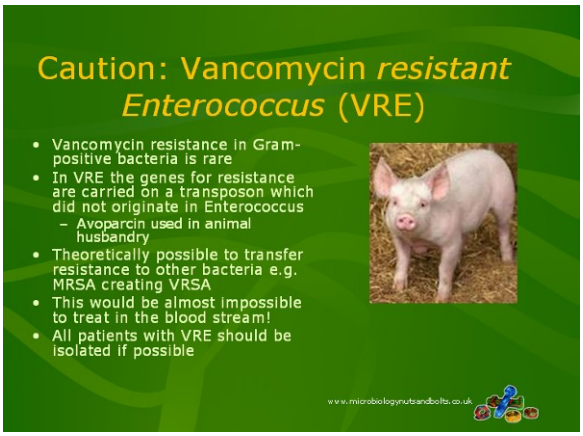
- The diagnosis is confirmed and the treatment has been started
- The Teicoplanin is only dosed every 72 hours because the patient is in renal failure and it will take him much longer than normal to clear the antibiotic from his blood
- From a treatment perspective this doesn't matter, he will remain therapeutic throughout

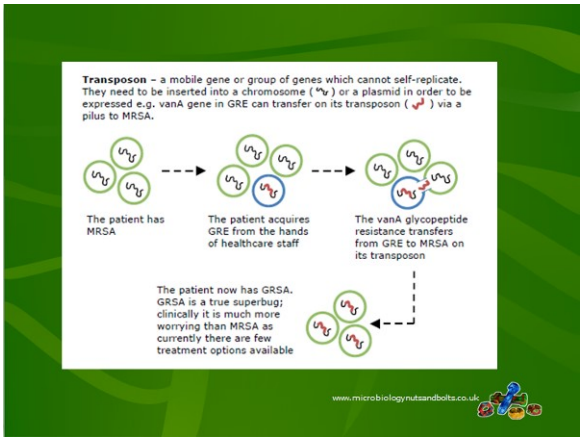


- Most antibiotics are affected in some way by renal failure
- Where doses are concerned it is important to use a calculated GFR because eGFR does not take body mass or even ethnic origin in to account and so can be very different from an actual value
- It is safest to use a calculated GFR to aid the prescribing of antibiotics in renal failure and to consultant renal dosing guidelines

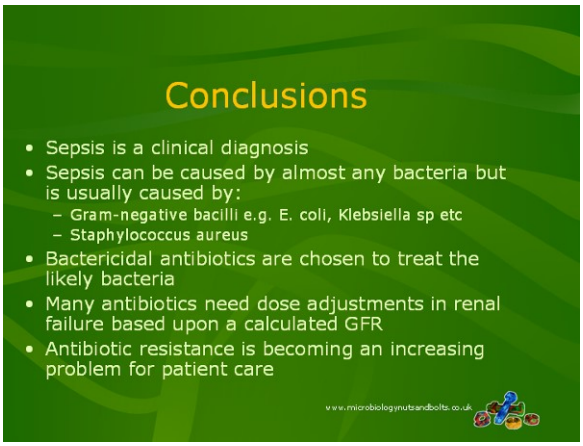


- Unsurprisingly with the correct treatment Geoff got better
- It is really important to keep an open mind about a diagnosis and not to be afraid to question what is happening, that is good medical practice





- Vancomycin Resistant Enterococcus (also known as Glycopeptide Resistant Enterococcus) has a resistant mechanism on board which is capable of transferring to other bacterial species
- As a result it is capable of making an organism like MRSA resistant to Teicoplanin or Vancomycin which are the current mainstays of treatment with these bacteria
- Since VRSA/GRSA would cause severe diseases with a high mortality we isolate patients with GRE in most UK hospitals
- GRE itself doesn't cause many infections and is pretty low grade even when it does
- GRE is thought to have arisen through the previous unrestricted use of the glycopeptide Avoparcin in the swine industry, and is a clear link between our bacterial flora and the food we eat



- Sepsis is a clinical diagnosis and a medical emergency
- There are lots of potential causes and it is important to try and diagnose the underlying cause in order to try and treat patients effectively
- Sepsis requires aggressive treatment with antibiotics but these may need dose adjustment if the patient is in renal failure
- Antibiotic resistance is an increasingly problem and has recently been put on the UK National Risk Register by the Chief Medical Officer (CMO) as a mark of just how serious the problem is