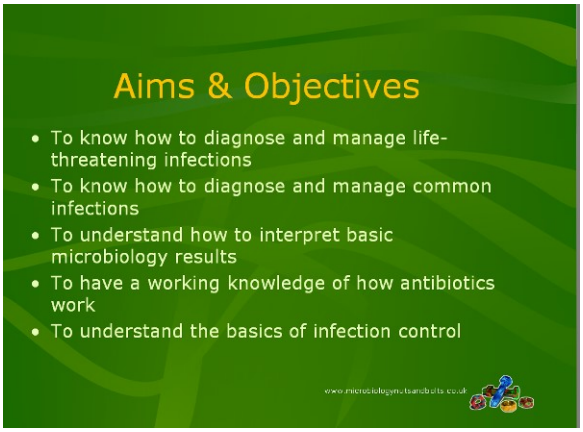
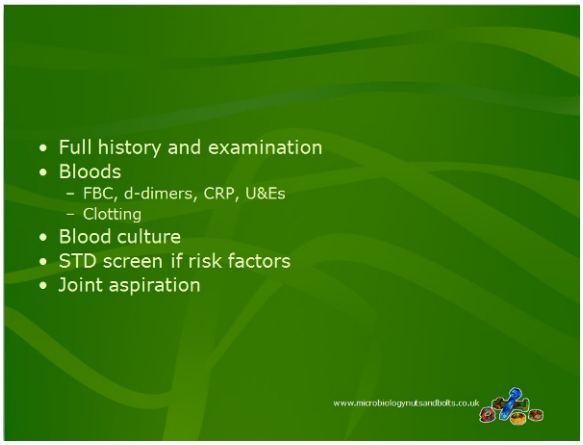
Microbiology Nuts & Bolts: Session 2: Skin, Bone and Joint Infections



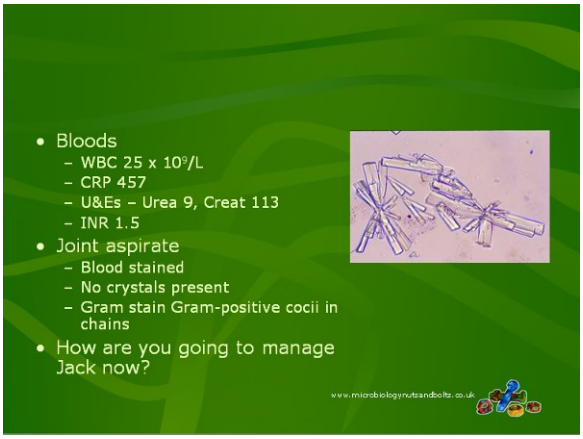
- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common 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 acutely swollen joints 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
- Given that Jack has both an acute inflamed joint and a fever, an infection is a definite possibility and should be the main focus of attention

- 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



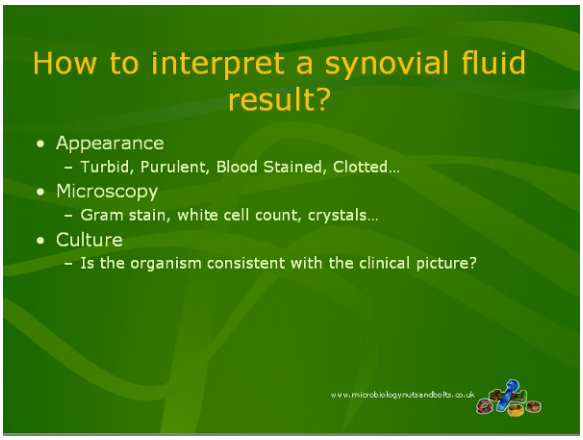
- It is essential to know the normal values of all tests within your hospital
- Full blood count (FBC)
  - The total white blood cell count can go up or down in infection
  - The differential white blood cell count can help to point to the type of organism but nothing is 100% (neutrophils = bacteria/fungi, 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
- Clotting
  - The INR (International Normalised Ratio) is basically a comparison of the time it take a persons blood to clot compared to a standard time
  - It is a ratio and therefore has no unit
  - Normal is 1 +/- 0.2
  - The INR increases if a patient is on Warfarin, in disseminated intravascular coagulation (DIC), liver failure and also with invasive Group A Beta-haemolytic Streptococcal infection (Streptokinase)
  - A high INR indicates that a patient is more likely to bleed with a minor traumatic injury or even spontaneously
- Joint Aspiration
  - The presence of white blood cells indicates inflammation and possible infection
  - Crystals indicate either gout or pseudogout but do not rule out the possibility of infection
  - A positive Gram film is always significant and indicates infection because synovial fluid should be sterile



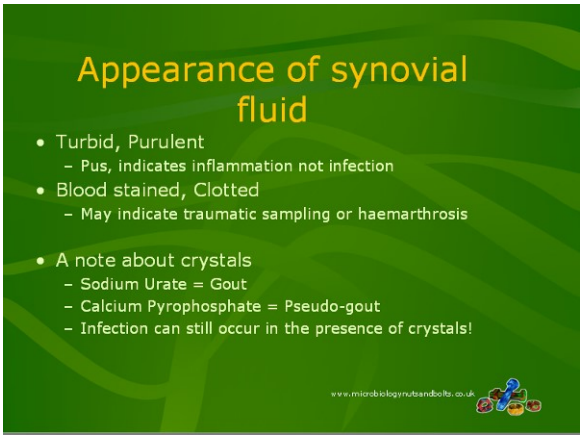
- Patient has raised high white blood cells and CRP indicating a significant inflammatory problem and therefore a likely infection
- U&Es shows a degree of renal failure and may make antibiotic dosing problematic
- The joint fluid sample contains bacteria confirming an infection but given that it is blood stained it may or may not be in the joint itself
  - This is not too important acutely as the antibiotic choice is likely to be the same in a sick patient
  - Gram-positive cocci in chains indicates the presence of Streptococci
- The INR of 1.5 is worrying and makes Group A Beta-haemolytic streptococcus a definite possibility
- Jack should be seen by a senior orthopaedic surgeon with regards a probable septic arthritis and possible invasive Group A Beta-Haemolytic Streptococcal

infection

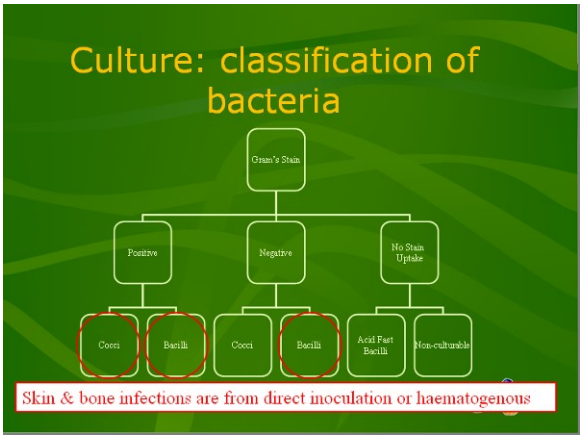
- Antibiotics should be targeted at the Streptococcus but at this stage it is also worth continuing to ensure cover is adequate for Staphylococci as these can occasionally be hard to distinguish in fluid samples and are also a common cause of these types of infection
  - A combination such as Benzylpenicillin PLUS Clindamycin would be the best choice



- As with other tests it is important to have a system for looking at microbiology results
  - Synovial fluid samples are first assessed to see if there is any obvious inflammation on appearance
  - Microscopy will indicate a potential pathogen if present and if performed a white cell count can help diagnose infection in prosthetic joints
  - Culture will indicate if one of the common bacterial causes of septic arthritis has been isolated or not
- The presence of any organism is the Gram film is significant and it is essential that any antibiotics given target these bacteria
- The most crucial information on the request is the clinical details as this dictates what tests are done
  - If you say the patient has a prosthetic joint the lab staff will look for additional bacteria which can cause infections of prosthetic material but which otherwise could potentially be skin contaminants e.g. Coagulase negative Staphylococci

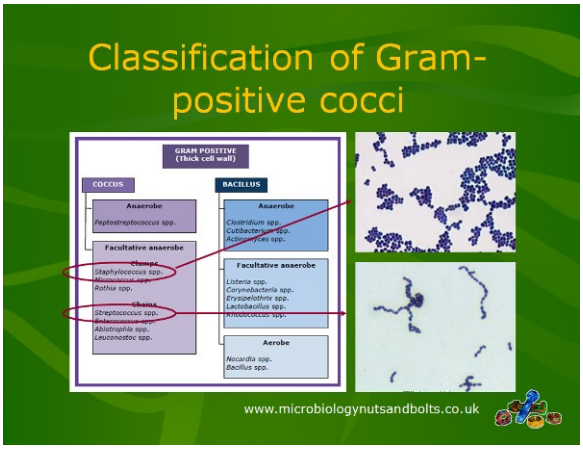


- It is important to remember that gouty joints become infected just as readily as non-gouty joints and so the presence of crystals in itself does not rule out a diagnosis of septic arthritis

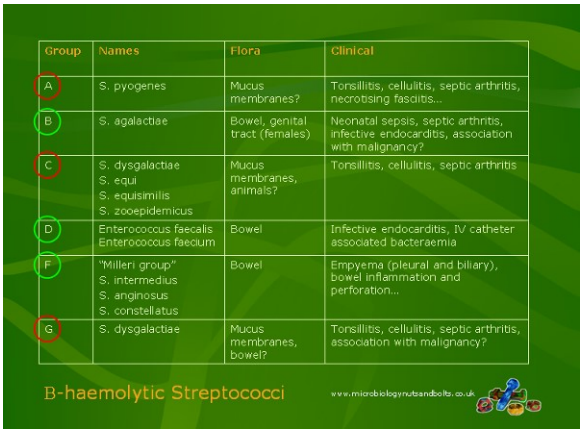


- The majority of skin, bone and joint infections are haematogenous in nature, that is they seed the skin, bone or joint via the bloodstream
- Occasionally prosthetic joint infections occur with direct inoculation of the organism into the joint at the time of the prosthetic joint operation but this is unusual because there are many processes put in place to prevent it e.g. antibiotic prophylaxis, special theatre ventilation
- Gram-positive cocci are the most common causes of cellulitis, septic arthritis and osteomyelitis
- Gram-negative bacilli can be a cause of bone and joint infections in the elderly, especially females because UTIs are more common and therefore so is Gram-negative bacteraemia
- Gram-positive bacilli occasionally cause prosthetic joint infections by direct inoculation as they are commonly

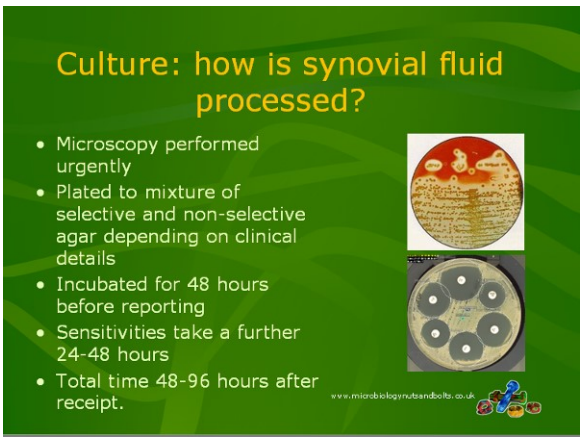
found on the skin e.g. Diptheroids, Propionibacterium sp.



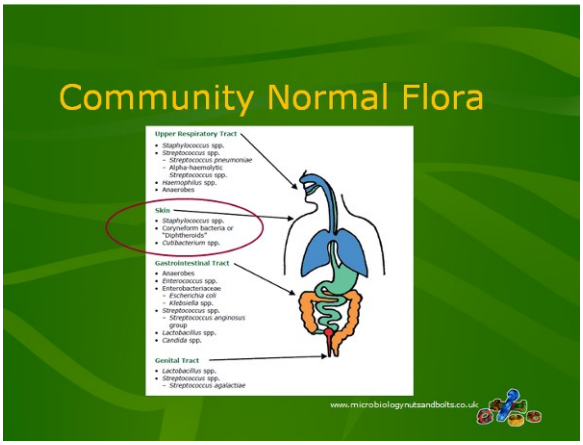
- Most skin, bone and joint infections are caused by Gram-positive cocci, notably Staphylococcus aureus and the Beta-haemolytic Streptococci
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Staphylococci from Streptococci but these are of no use to ward doctors
- In practical terms Gram-positive cocci can be distinguished by:
  - Staphylococci form clumps
  - Streptococci form chains



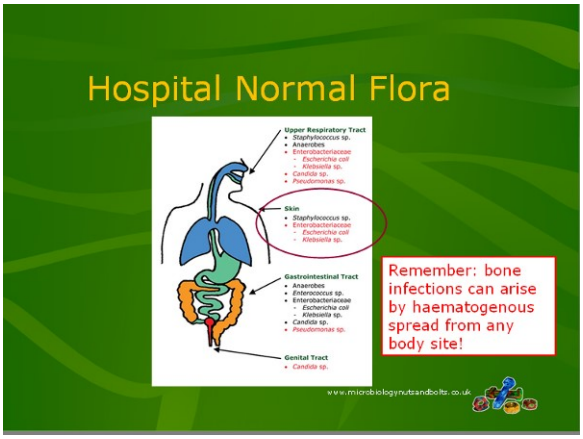
- Beta-haemolytic Streptococcal grouping causes a lot of confusion but can be made simplar by considering different types together
- Beta-haemolysis refers to the type of red blood cell breakdown that the bacteria gives on blood agar in a laboratory, but there are 3 types of haemolysis
  - Alpha-haemolysis = partial haemolysis causing a green discolouration on blood agar (Viridans Streptococci, Viridans means green)
  - Beta-haemolysis = complete breakdown of the blood allowing you to see through the blood agar plate (see image in next slide)
  - Gamma-haemolysis = this is a very misleading term as in fact there is no haemolysis at all (also called non-haemolytic)
- Consider Groups A, C and G together because they all cause very similar infections of the upper respiratory tract, skin, bone and joint
- Consider Groups B, D and F together because they all originate in the gastrointestinal tract



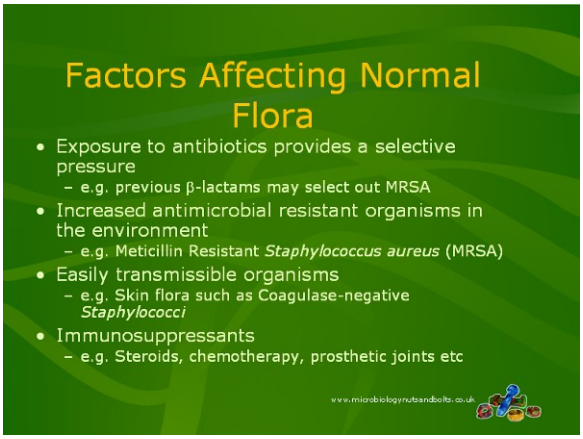
- Most microbiology laboratories have an out-of-hours service with the biomedical scientist oncall from home therefore if an urgent sample is taken it is essential to let either the lab or BMS know it is coming after it has been taken
- Most microbiological tests are based on the clinical information on the request card
- If adequate clinical information is not provided the correct tests may not be done
- In addition, clinical information allows the lab to spot high risk samples that may be hazardous to the health of the laboratory staff when they are processing them
- Synovial fluid microscopy results should be available within 2 hours although culture can take up to 96 hours to give a result, however as treatment should already have started this can then be used to evaluate the appropriateness of that treatment and narrow down the spectrum of the antibiotics if possible



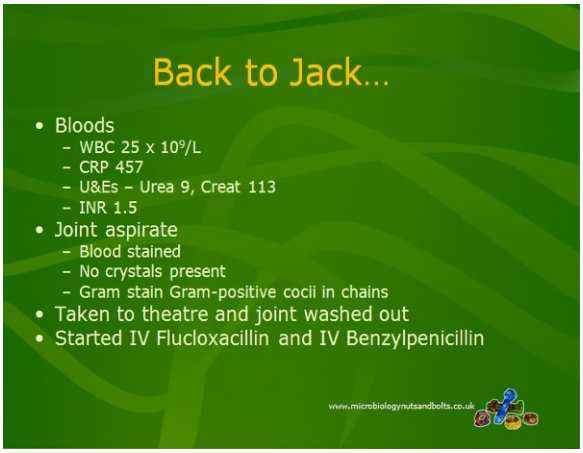
- The normal flora of a human body consists of 10^{14} bacteria (that's approximately 15,000 times the number of humans on the Earth!)
- Knowing the common bacteria that colonise the human body allows:
  - Prediction of the causes of infection from any body site because 85% of infections are caused by the patients own flora getting in to a site it should not be e.g. UTI caused by bacteria from the gastrointestinal tract
  - Prediction of the origin of an infection when a bacteria is found in a normally sterile site e.g. E. coli in blood cultures from either urine, bowel or Biliary tract



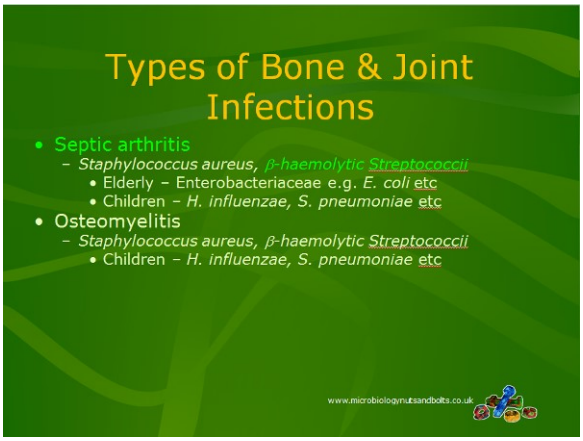
- Unless there is an obvious break in the skin e.g. ulcers, most skin, bone and joint infections are haematogenous in nature



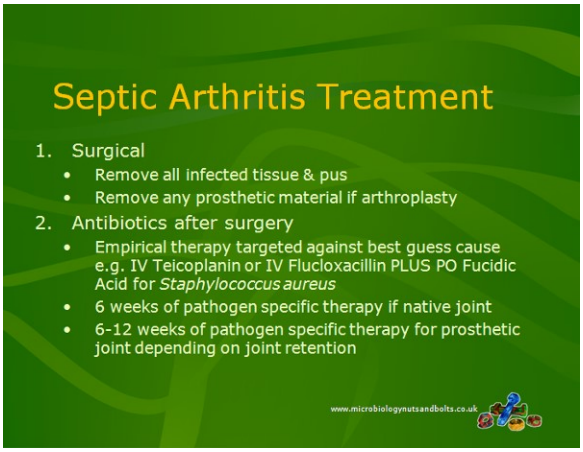
- There are many circumstances that can affect a patients normal flora
- Understanding how this happens can allow predictions to be made as to how the flora will change and therefore how this will influence the types of bacteria causing infections
- Antibiotics will tend to remove sensitive bacteria 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



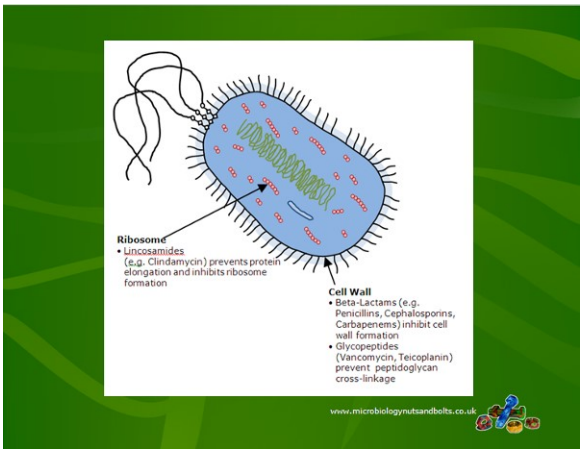
- Jack's tests show a likely infective process with a Streptococcus
- The positive Gram film showing a Streptococcus spp. should prompt the starting of empirical antibiotics for Streptococcal septic arthritis



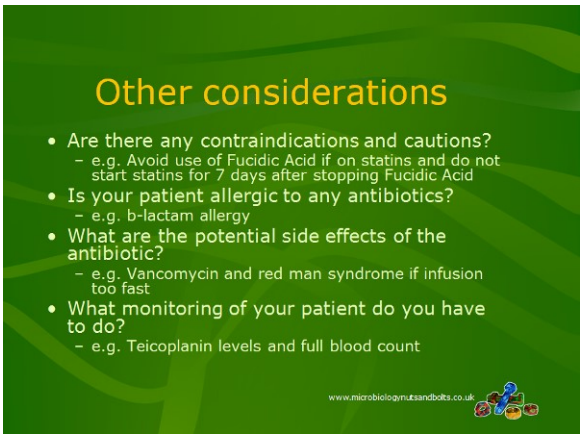
- Most bone and joint infections are caused by Gram-positive cocci from either the Staphylococcus spp. or Streptococcus spp.
- At the extremes of age, in children and the elderly, the causes become a bit more variable
- Elderly patients get Gram-negative infections in bones and joints because systemic Gram-negative infections are more common in these patients e.g. UTI



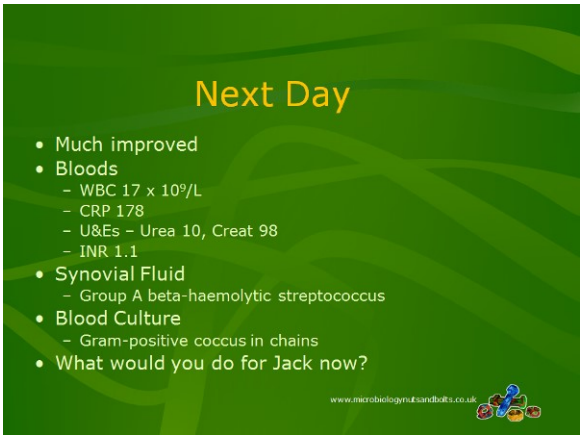
- The management of septic arthritis and osteomyelitis involves the removal of as much infected material as possible
- Not only do antibiotics not get in to bone and joints at very high concentrations, but the acid environment of pus degrades the antibiotics making them less effective, therefore removing as much os this pus as possible makes the antibiotics more effective
- Treatment should be targeted to the causative bacteria whenever possible to give the best outcome, which often requires surgical samples or aspirates to be taken for culture prior to starting antibiotics
- Osteomyelitis and septic arthritis often requires prolonged course of antibiotics



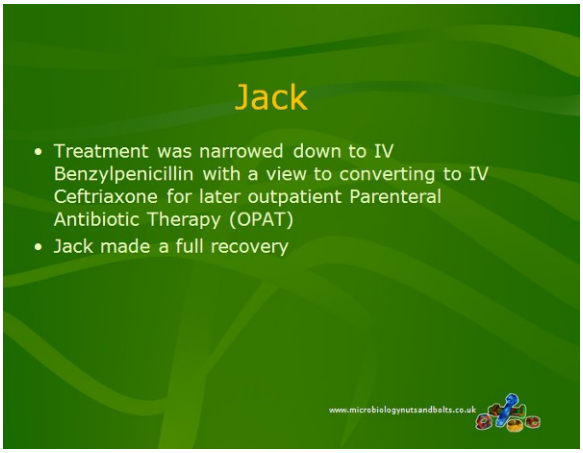
- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list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



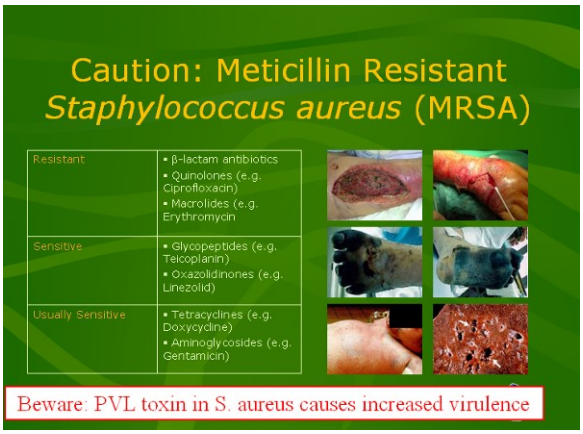
- Patients given Fusidic Acid should not be given statins as this can cause myopathy and rhabdomyolysis
- It always worth checking if a patient is allergic to whatever drug you are going to give them although be sure they are describing an allergy not just a recognised side-effect
- Some antibiotics 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



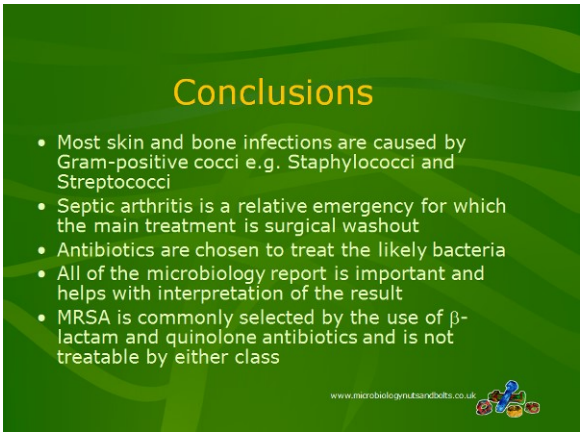
- Following the washout and antibiotics the patient is much improved



- OPAT is Outpatient Parenteral Antibiotic Therapy
- The standard for OPAT is that it should be equivalent to a patient receiving antibiotics in hospital, with the same monitoring and over sight, in order to maintain patient safety
- OPAT allows patients to be sent home where they are more comfortable, where they are less likely to be exposed to Healthcare-Associated Infections (HCAI) and where they can become more mobile and recover faster



- It is possible to predict the pattern of antibiotic sensitivity of MRSA to help guide treatment although it is always useful to check for any specific organism
- An old problem which is re-emerging is the ability of some Staphylococcus aureus to produce a toxin called Panton-Valentine Leukocidin (PVL)
- PVL is associated with recurrent and severe skin and soft tissue infections
- Occasionally PVL is associated with necrotising pneumonia which has a high mortality
- PVL infections should be treated with antibiotics which target Staphylococcus aureus but also have an anti-toxin effect such as Clindamycin or Linezolid
- PVL positive organisms are often shared amongst family members and other close contacts so it is often useful to screen these people and try decolonising them as for MRSA



- Gram-positive cocci are the most common causes of skin, bone and joint infections although in the elderly Gram-negative bacteria can be implicated as well
- Necrotising fasciitis in all of its forms is an emergency requiring urgent surgical management in addition to antibiotics
- If you don't consider all of the microbiology report you will miss significant results and over interpret non-significant results
- When deciding what antibiotics to treat a patient with it is important to consider what antibiotics they have had recently and how these might effect the likely causes of the current infection