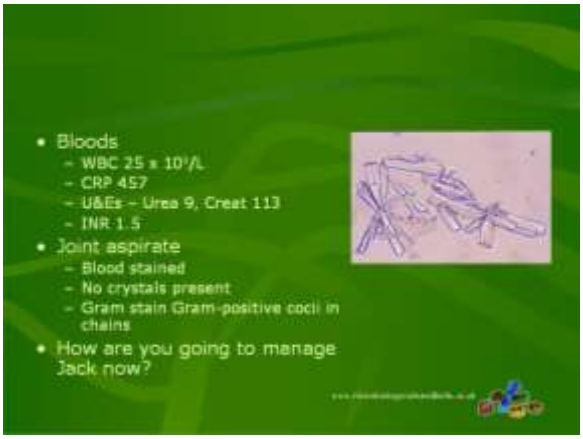
Microbiology Nuts & Bolts: Session 5: Skin, Bone and Joint Infections

- 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^{o}C to 37.5^{o}C
  - Often a tympanic temperature which is actually a peripheral temperature not a core temperature
  - Can vary from core by up to +/- 1^{o}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

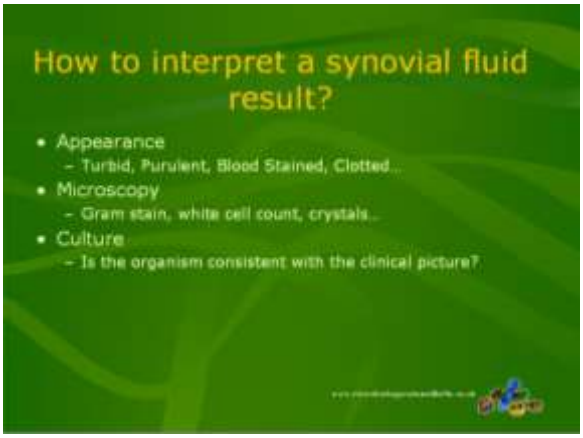
- It is essential to know the normal values of all tests within your hospital
- Full blood count (FBC)
  - The total white blood cell count can go up or down in infection
  - The differential white blood cell count can help to point to the type of organism but nothing is 100% (neutrophils = bacteria/fungi, 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

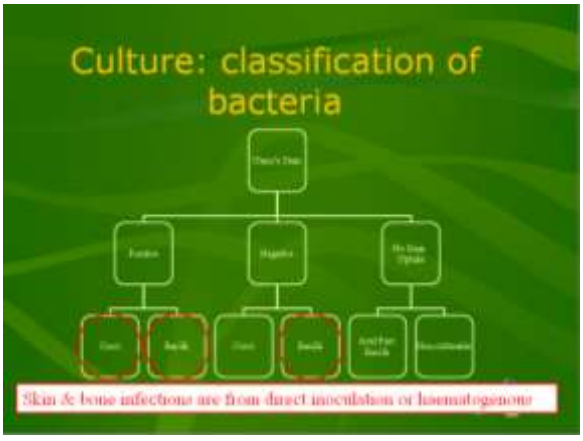
infection

- 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



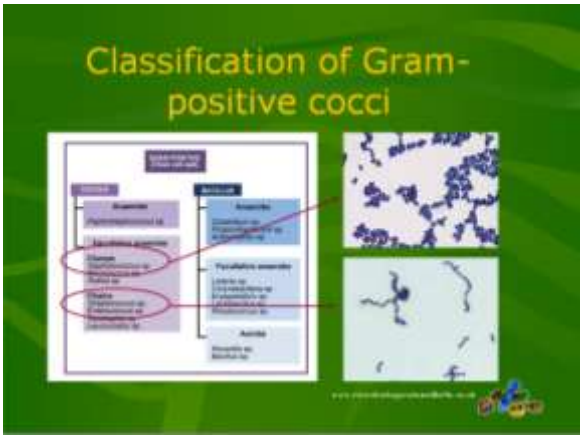
- As with other tests it is important to have a system for looking at microbiology results
  - Synovial fluid samples are first assessed to see if there is any obvious inflammation on appearance
  - Microscopy will indicate a potential pathogen if present and if performed a white cell count can help 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

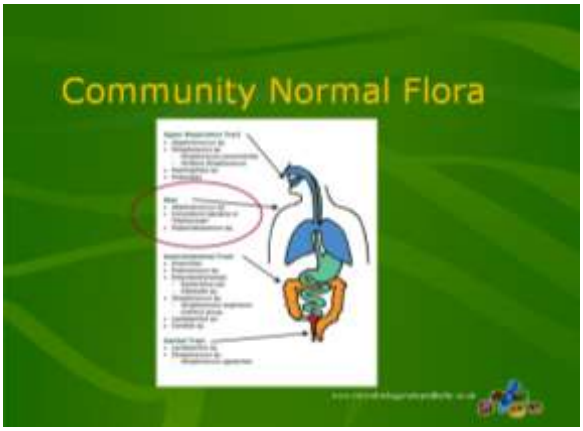
found on the skin e.g. Diptheroids, Propionibacterium sp.



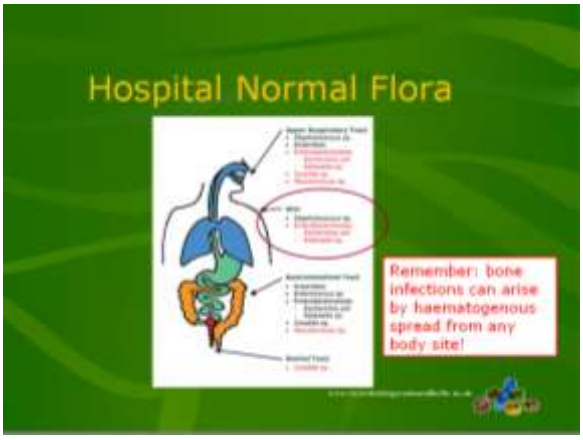
- Most skin, bone and joint infections are caused by Gram-positive cocci, notably Staphylococcus aureus and the Beta-haemolytic Streptococci
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Staphylococci from Streptococci but these are of no use to ward doctors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

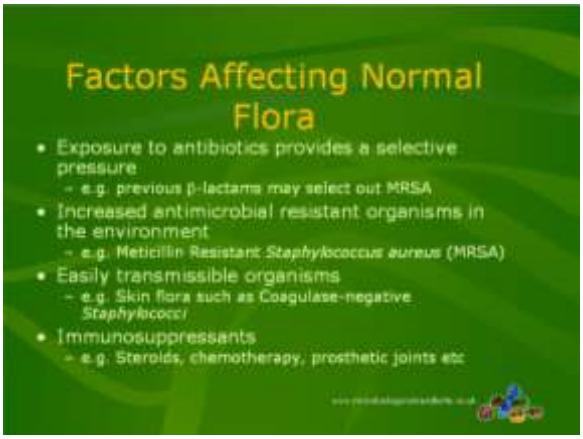
- Most microbiology laboratories have an out-of-hours service with the biomedical scientist oncall from home therefore if an urgent sample is taken it is essential to let either the lab or BMS know it is coming after it has been taken
- Most microbiological tests are based on the clinical information 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



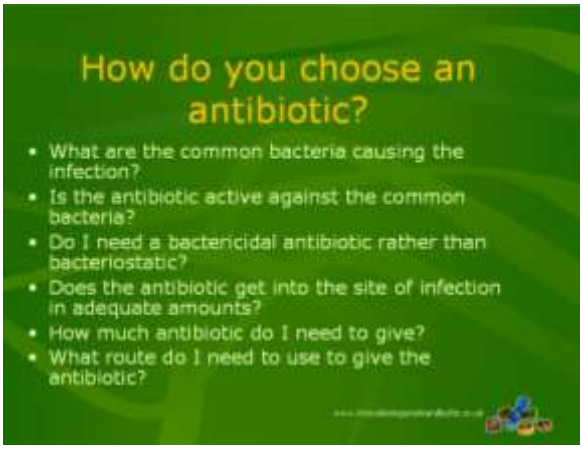
- There are many circumstances that can affect a patients normal flora
- Understanding how this happens can allow predictions to be made as to how the flora will change and therefore how this will influence the types of bacteria causing infections
- Antibiotics will tend to remove sensitive bacteria 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 rapid spread of the erythema should ring alarm bells and suggest a need for urgent re-evaluation
- The most important infection to consider at this point in time is necrotising fasciitis secondary to Group A Beta-haemolytic Streptococcus (S. pyogenes), a severe soft tissue infection and surgical emergency

- Too many patients get treated for bacteria which are colonising ulcers and other breaks in skin without causing an infection
- The diagnosis of an infected ulcer is clinical and based on signs of acute inflammation
- Slough is detached necrotic material and is a great culture media for colonising bacteria, swabs from here will always grow something
- The presence of Pseudomonas is commonly over treated but remember, Pseudomonas will colonise any moist site (including a wet ulcer) it is only rarely a cause of infection

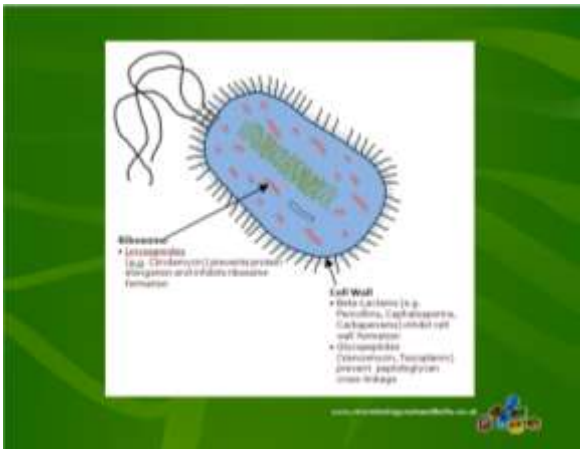
- Necrotising fasciitis comes in three main forms depending on the underlying bacteria
- Group A Beta-haemolytic Streptococcus
  - Usually on a limb, aggressive, rapidly spreading infection with pain out of proportion to clinical signs, mainly toxin mediated damage
- Clostridium perfringens (gas gangrene)
  - Usually on a limb following tissue damage or ischaemia, gas (crepitus) usually felt in the tissue, mainly toxin mediated damage
- Synergistic gangrene (Fournier's gangrene)
  - Usually abdominal or pelvic caused by extension of bowel bacteria into soft tissue, often as a result of a perforated viscus or rectal malignancy

- Necrotising fasciitis is a surgical emergency
- The mainstay of treatment is urgent debridement of all dead and diseased tissue including amputation if necessary
- It is usually a mistake to use CT scans to investigate these patients as there is little pus present because all of these bacteria breakdown the white blood cells leaving only a serosanguinous discharge and so you can be lulled in to a false sense of security and the scan just delays taking them to theatre
- Antibiotics and immunoglobulins are adjuncts to the surgical debridement
- Clindamycin is often added for its "anti-toxin effect" by interfering with protein formation by the bacterial ribosome
- Immunoglobulin "mops up" toxin in the blood stream

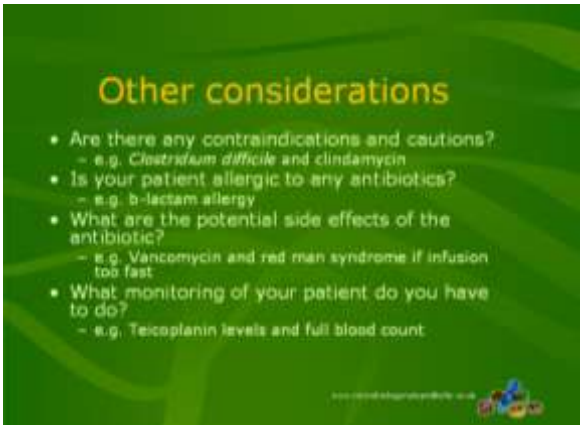


- In this case the patient clearly needs antibiotics
- Because he is so unwell he needs antibiotics that will kill the bacteria as quickly as possible
- The antibiotics should be bactericidal, penetrate soft tissue and synovial fluid, should be given intravenously in the maximal dose possible

- 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

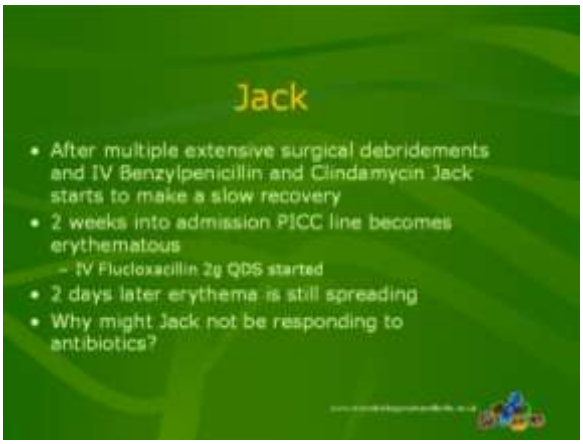


- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list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



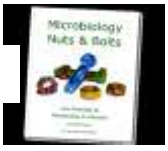
- Patients given clindamycin should be warned about the risk of Clostridium difficile, however this should not stop you using it if the patient needs it
- It always worth checking if a patient is allergic to whatever drug you are going to give them although be sure they are describing an allergy not 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

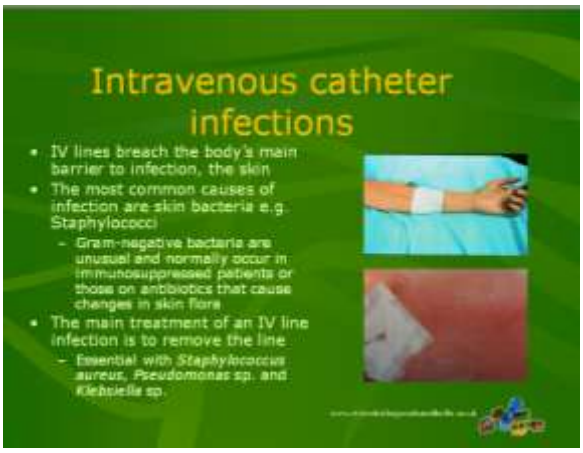
- This patient is still clearly very unwell, his bloods show an ongoing inflammatory response and his INR is still raised
- He has ongoing, uncontrolled infection
- He needs to go back to theatre for further surgery, wash out and excision of dead or diseased tissue



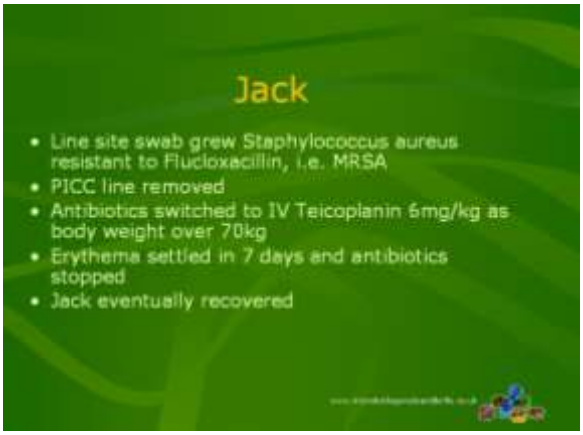
- Complications of treatment do occur, but central venous catheter infections should be very rare
- Most infectious in patients with normal immune systems are usually Staphylococcal
- Flucloxacillin is not an appropriate empirical treatment for Jack because he has already had lots of antibiotics, whatever is causing the infection is likely to be resistant to these

- There are a number of questions to run through if a patient is not responding to antibiotics before getting to the point of having to change the antibiotic
- Antibiotics tend to get changed too quickly without checking for simpler problems first such as whether they have actually been given them





- Most IV catheter infections are caused by bacteria either go in to the line or around the line
- As a result most are caused by skin bacteria
- Occasionally there are unusual bacteria on the skin such as the Gram-negative Enterobacteriaceae and Pseudomonas sp. and these can cause severe line infections and sepsis
- The most important treatment for a line infection is to remove the line because most of the time bacteria in biofilms in lines do not respond to antibiotics alone
- Biofilms are layers of bacterial slime containing colonise of bacteria in a reduced metabolic state which therefore do not respond very well to antibiotics



- Unsurprisingly Jack's swab has grown a resistant bacteria, which is the most likely organism to break through his other antibiotics
- Teicoplanin or Vancomycin (both glycopeptides) are often used as the main treatment of Meticillin Resistant Staphylococcus aureus (MRSA)
- Having removed the line and given the antibiotics he responded well to treatment

- 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-emrging 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