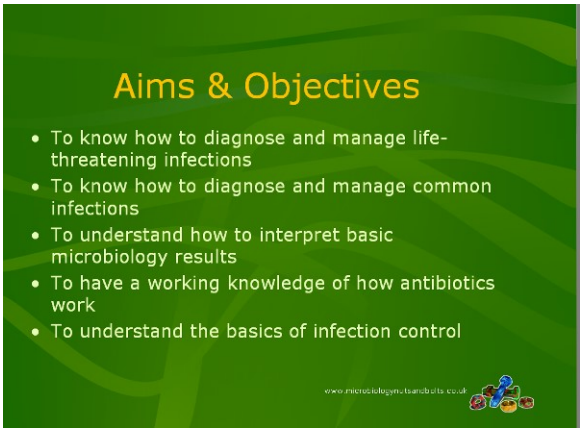
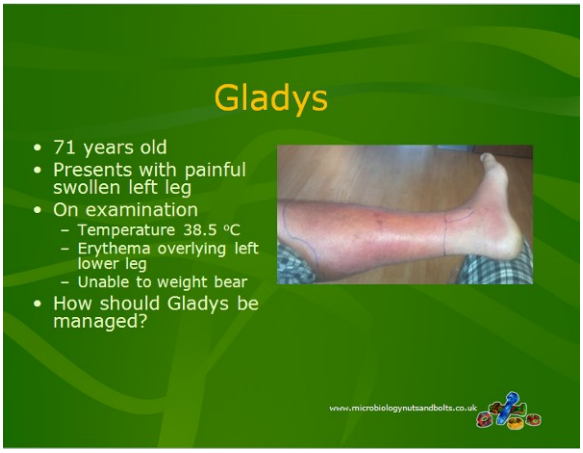
Microbiology Nuts & Bolts: Session 4: Skin, Bone and Joint Infections

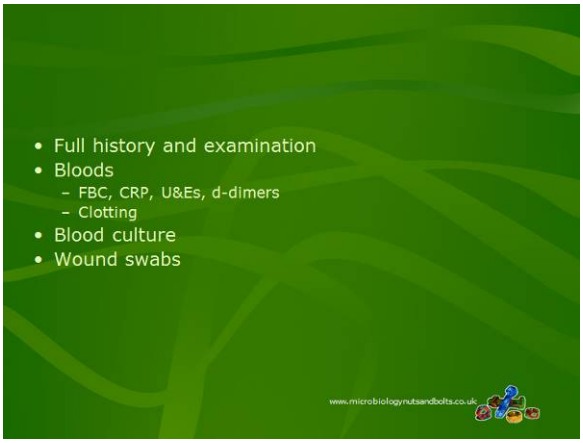


- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common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

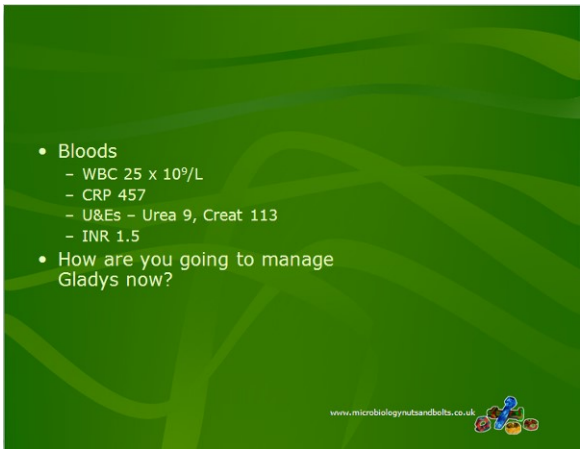


- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for acutely legs therefore it is important not to become too fixated on a diagnosis without considering all possibilities
- All doctors should know the limitations of the tests they do including 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 Gladys has both an acute inflamed leg and a fever, an infection is a definite possibility and should be the main focus of attention

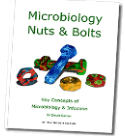
- Formulating a differential diagnosis appears to be going out of fashion but it is essential if diagnoses are not to be missed
- A systems approach (e.g. respiratory, cardiac, Gastrointestinal, genitourinary, neurological, skin, bone, joint, etc) can be fitted to a template of life-threatening, common, 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

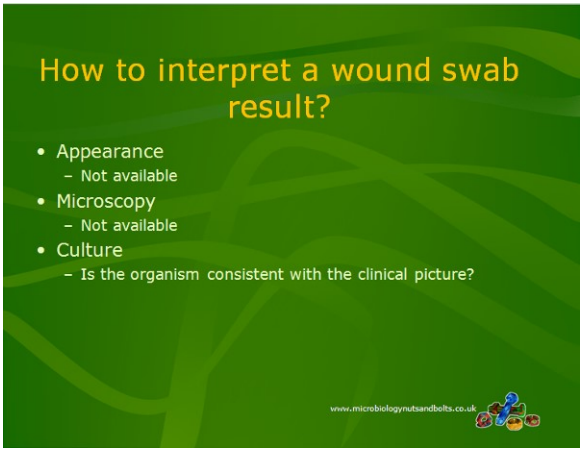


- It is essential to know the normal values of all tests within your hospital
- Full blood count (FBC)
  - The total white blood cell count can go up or down in infection
  - The differential white blood cell count can help to point to the type of organism but nothing is 100% (neutrophils = bacteria/fungi, 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
- Wound swabs
  - The diagnosis of a wound infection is clinical based upon the symptoms and signs of acute inflammation e.g. pain, swelling, discharge, redness
  - A wound swab should only be taken if an infection is suspected otherwise there is the risk of over treating colonising bacteria rather than the causes of an infection

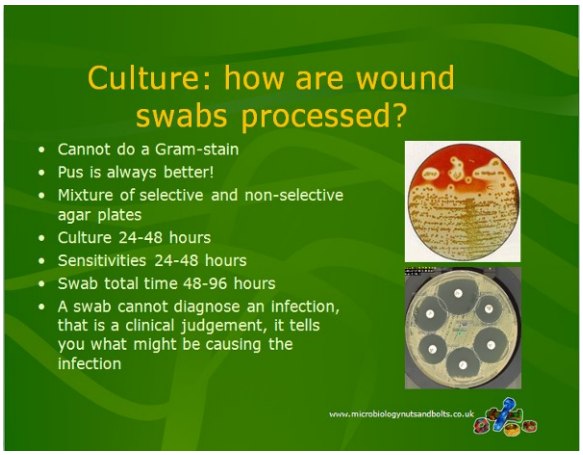


- Patient has raised high white blood cells and CRP indicating a significant inflammatory problem and therefore a likely infection
- U&Es shows a degree of renal failure and may make antibiotic dosing problematic
- The INR of 1.5 is worrying and makes Group A Beta-haemolytic streptococcus a definite 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 causes of cellulitis such as Staphylococcus aureus and the Beta-haemolytic Streptococci
  - Flucloxacillin or Teicoplanin would be suitable choices

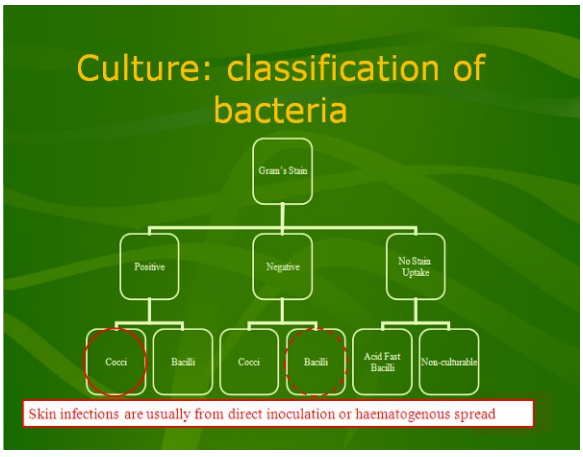




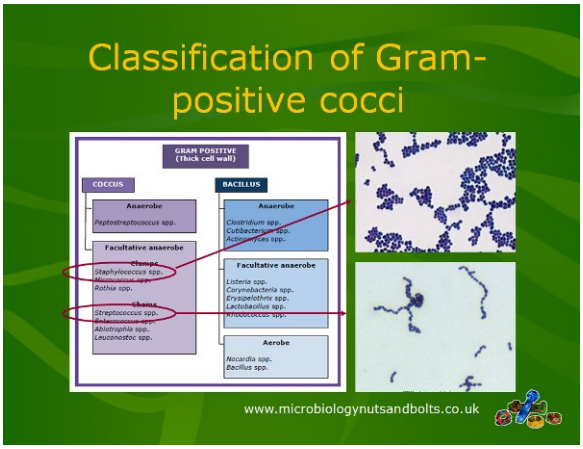
- The most crucial information on the request is the clinical details as this dictates what tests are done
- For wound swabs the only result available is the culture result, and the interpretation of this is dependent on the clinical picture of the patient
- In the absence of the signs of acute inflammation, any growth is likely to indicate colonisation rather than infection
- It is common for swabs from the legs to grow enterobacteriaceae e.g. E. coli, Proteus spp. etc, however these are colonising bacteria not causes of skin infections



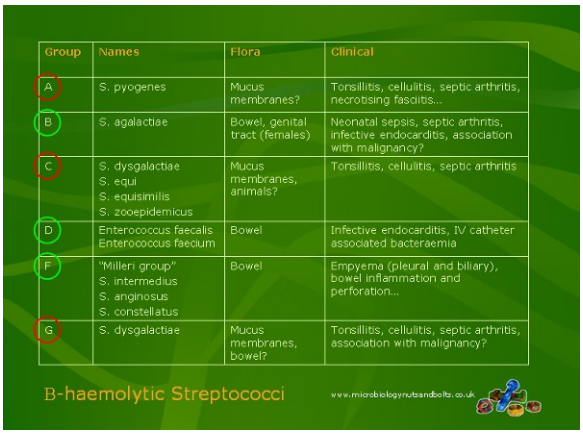
- Swabs take up to 96 hours to give results
- Swabs do not diagnose infection but rather indicate the presence or absence f bacteria
- Skin infection is a clinical diagnosis not a microbiology laboratory diagnosis



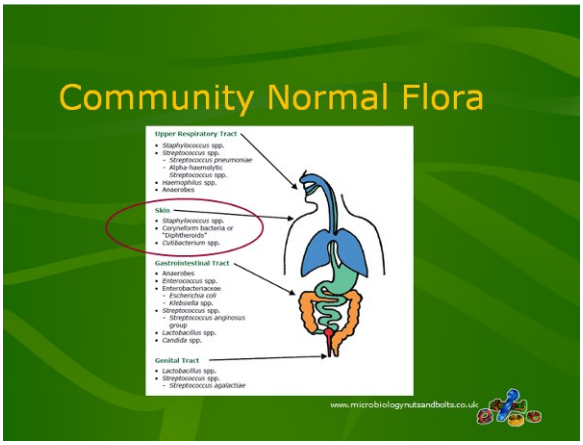
- Skin infections can be haematogenous in nature, that is they seed the skin via the bloodstream, or from direct invasion from outside, e.g. infected ulcers
- Gram-positive cocci are the most common causes of cellulitis
- Pseudomonas aeruginosa is a rare cause of skin infections, and is usually only implicated in skin grafts, burns and occasionally in diabetics



- Most skin 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 simpler 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



- 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

Factors Affecting Normal Flora

- Exposure to antibiotics provides a selective pressure
  - e.g. previous β-lactams may select out MRSA
- Increased antimicrobial resistant organisms in the environment
  - e.g. Meticillin Resistant *Staphylococcus aureus* (MRSA)
- Easily transmissible organisms
  - e.g. Skin flora such as Coagulase-negative *Staphylococci*
- Immunosuppressants
  - e.g. Steroids, chemotherapy, prosthetic joints etc

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- 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

Back to Gladys…

- Bloods
  - WBC 25 x 10^9/L
  - CRP 457
  - U&Es – Urea 9, Creat 113
  - INR 1.5
- Erythema spreads within the 30 minutes after she was examined
- What is the probable diagnosis?
- How would you manage Gladys now?

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- Gladys' 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

Types & Causes of Bacterial Skin Infections

- Ulcers
  - *Staphylococcus aureus, β-haemolytic Streptococcii*
    - Become colonised with bacteria, especially Enterobacteriaceae that DO NOT need treating in most patients
    - Take samples from "healthy" base after debriding slough
    - Only treat if increasing pain, erythema or purulent discharge
- Cellulitis
  - *Staphylococcus aureus, β-haemolytic Streptococcii*
- Necrotising Fasciitis
  - *Group A -β-haemolytic Streptococcus (S. pyogenes), Clostridium perfringens, Synergistic gangrene*

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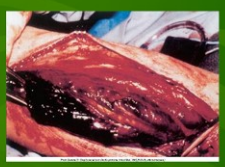
- Too many patients get treated for bacteria which are colonising ulcers and other breaks in skin without causing an infection
- The diagnosis of an infected ulcer is clinical and based on signs of acute inflammation
- Slough is detached necrotic material and is a great culture media for colonising bacteria, 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 Treatment

1. Surgical
   - Remove all dead or diseased tissue
2. Antibiotics
   - Combination of β-lactam plus Clindamycin
3. Adjuncts
   - Immunoglobulin



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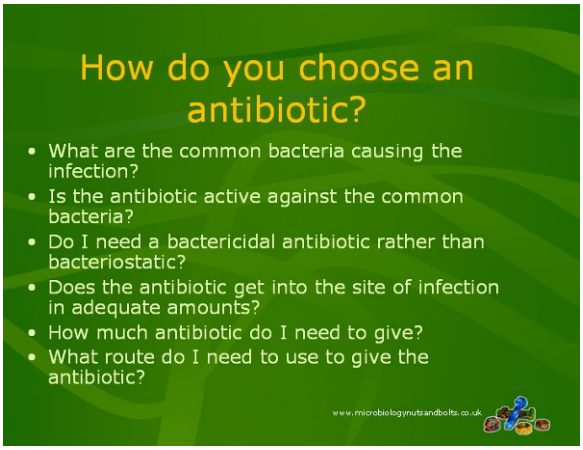
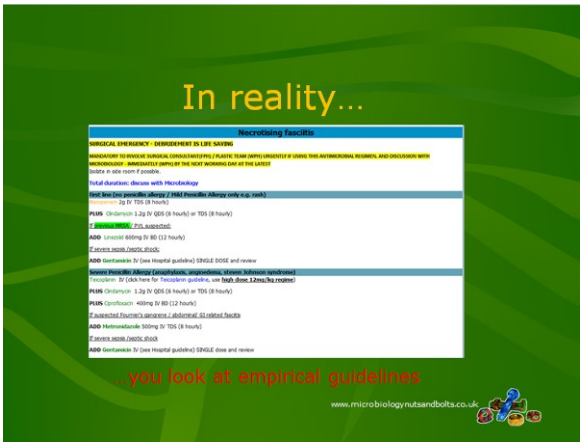
- Necrotising fasciitis is a surgical emergency
- The mainstay of treatment is urgent debridement of all dead and diseased tissue including amputation if necessary
- It is usually a mistake to use CT scans to investigate these patients as there is little pus present because all of these bacteria breakdown 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

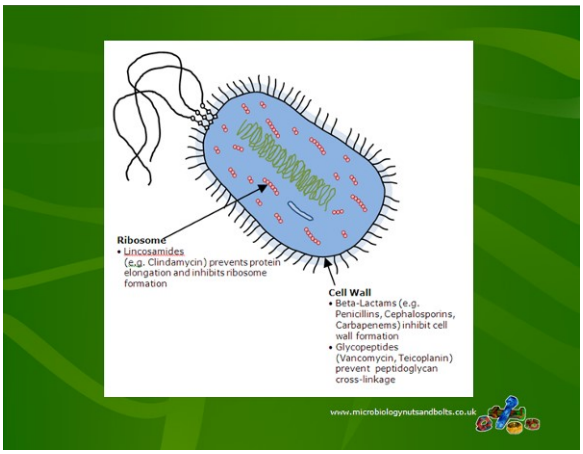
ribosome
- Immunoglobulin "mops up" toxin in the blood stream



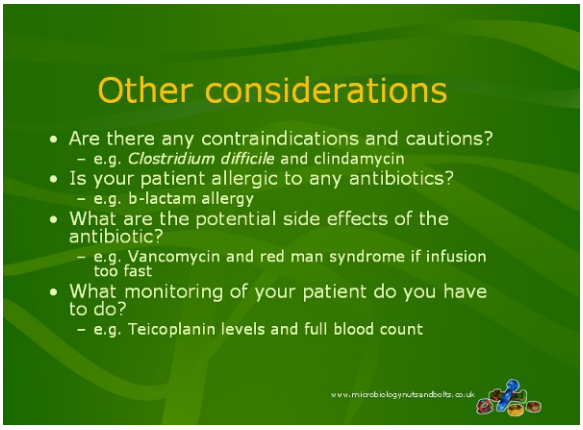
- In this case the patient clearly needs antibiotics
- Because he is so unwell he needs antibiotics that will kill the bacteria as quickly as possible
- The antibiotics should be bactericidal, penetrate soft tissue and synovial fluid, should be given intravenously in the maximal dose possible



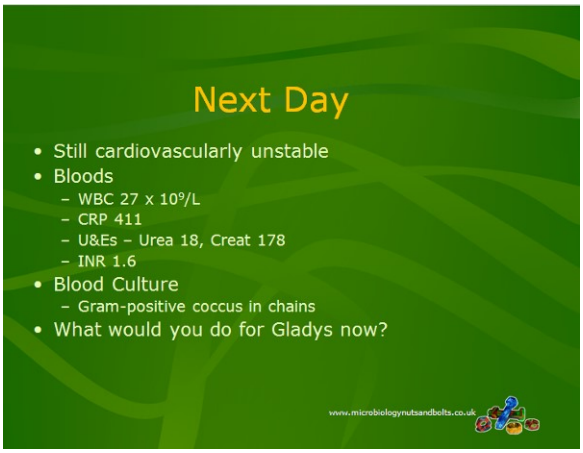
- Empirical antibiotic guidelines vary a little between hospitals based upon local epidemiology, therefore it is important to know your own guidelines
- They are empirical, that is they are designed to initiate treatment when the cause is unknown, they are not definitive for a specific cause
- Once the 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



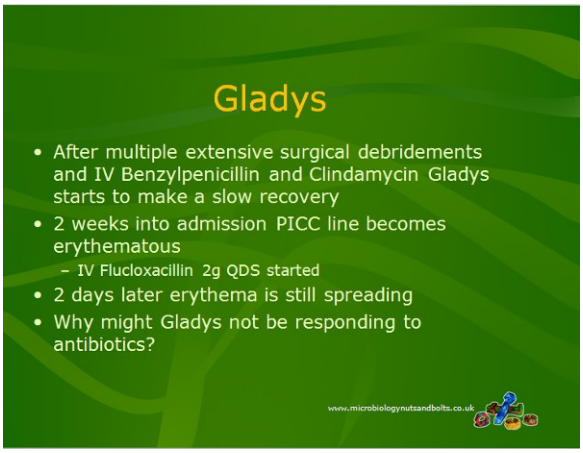
- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list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

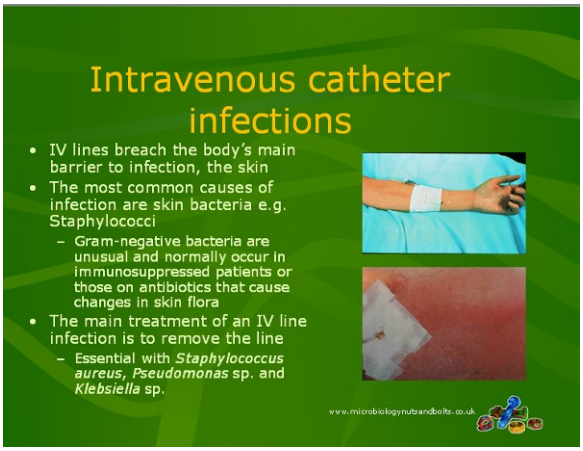


- This patient is still clearly very unwell, her bloods show an ongoing inflammatory response and his INR is still raised
- She has ongoing, uncontrolled infection
- She needs to go back to theatre for further surgery, wash out and excision of dead or diseased tissue

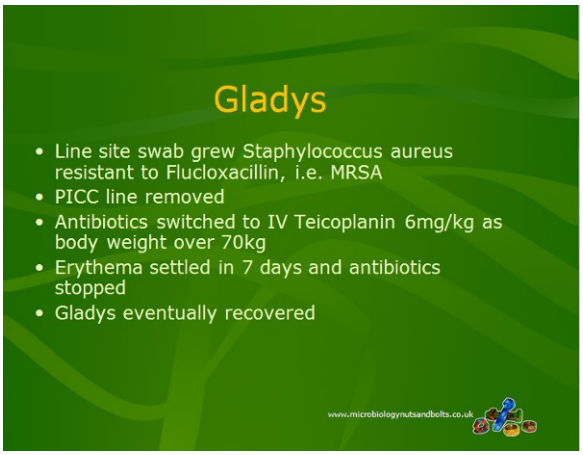


- Complications of treatment do occur, but central venous catheter infections should be very rare
- Most infectious in patients with normal immune systems are usually Staphylococcal
- Flucloxacillin is not an appropriate empirical treatment for Gladys because she has already had lots of antibiotics, 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 Gladys' 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 she responded well to treatment

- Gram-positive cocci are the most common causes of skin infections
- 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