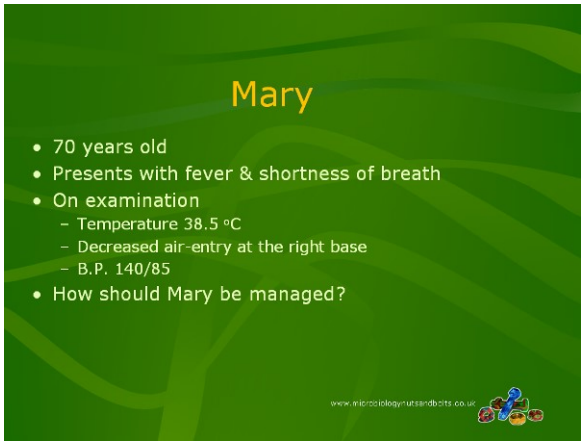
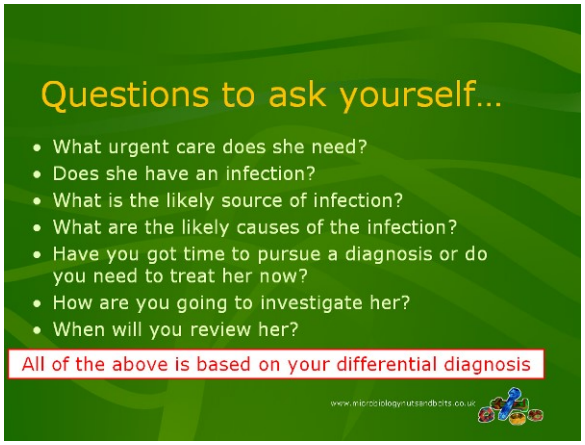
Microbiology Nuts & Bolts: Session 1: Respiratory

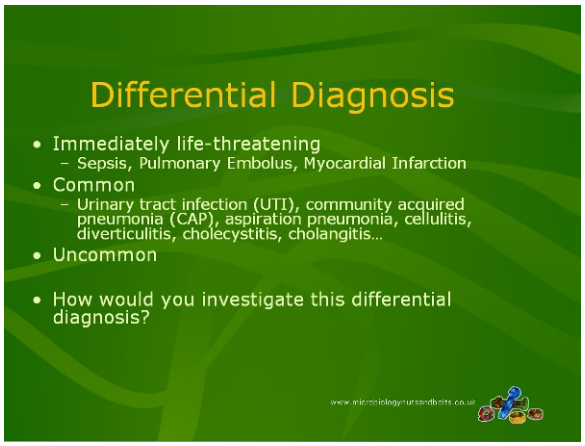
- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common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



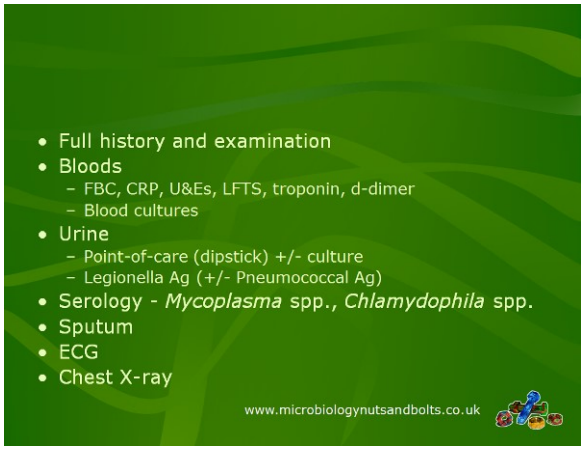
- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for fever and shortness of breath therefore it is important not to become too fixated on a diagnosis without considering all possibilities
- All doctors should know the limitations of the tests 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
- Decreased air entry is more in keeping with either fluid or collapse of the lung than infection which when giving rise to consolidation leads to bronchial breathing (a harsh breath sound)
- One off values of blood pressure can be valuable if very abnormal but trends are usually more informative and knowing if the patient is normally hypo/hypertensive (helps to look at the medications)
- After emergency care (ABC) the next step is to take a full history and perform an examination in order to produce a differential diagnosis



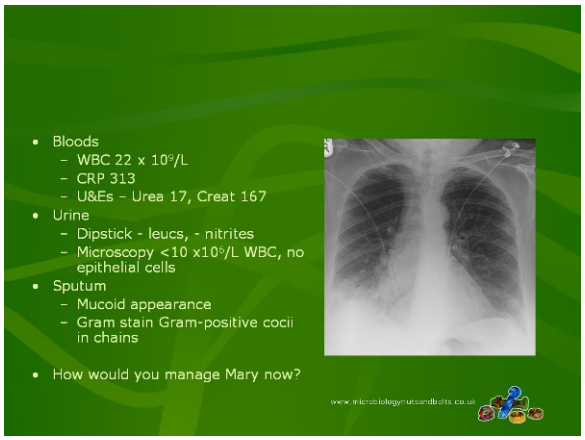
- If Mary is septic then she needs urgent care, for every hour delay in giving effective treatment the mortality increases by 7% up to approximately 40% by 6 hours
- If she is very unwell then she will need frequent and regular review in order to ensure she is improving or to spot any deterioration as early as possible
- The differential diagnosis is a list of possible reasons for a patients illness which can then narrowed down through careful questioning, examination and investigation until a single unifying diagnosis is proven



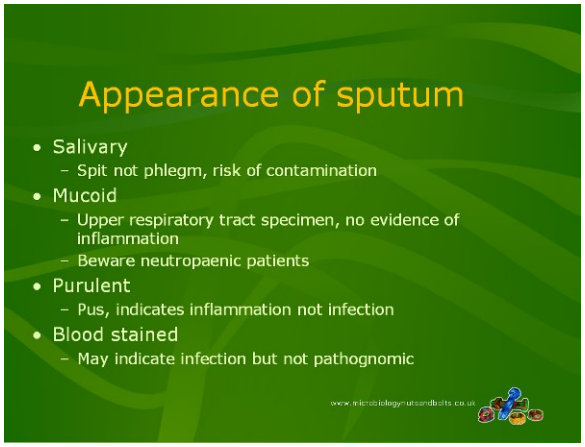
- Formulating a differential diagnosis appears to be going out of fashion but it is essential if diagnoses are not to be missed
- A systems approach (e.g. respiratory, cardiac, Gastrointestinal, genitourinary, neurological, skin, bone, joint, etc) can be fitted to a template of life-threatening, common,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



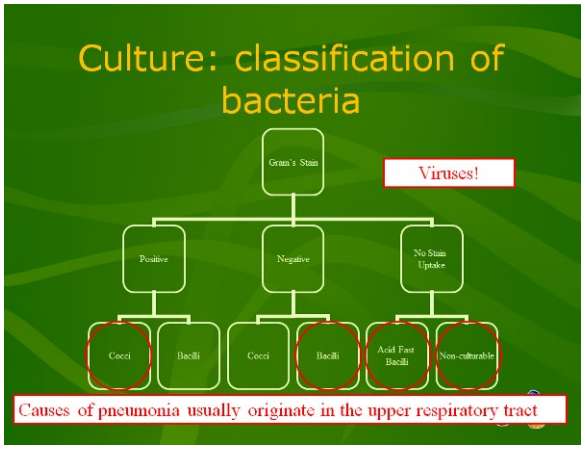
- The list represents a common "septic screen" within the hospital setting to which is added respiratory specific tests
- The history is the most important aspect where infection is concerned but it is a skill that has to be learnt and practiced to become good at it
- It is essential to know the normal 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
  - Urea and Creatinine can be markers of severity of infection e.g. Urea in community acquired pneumonia and creatinine in Clostridium difficile
- Chest X-ray is required by the British Thoracic Society in order to diagnose pneumonia in hospital
- Respiratory tests to look for the cause of the patients pneumonia include Legionella and Pneumococcal Antigen tests on urine and Mycoplasma and Chlamydophila serology



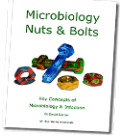
- Patient has an inflammatory process going on with high white blood cells and CRP
- U&Es shows a degree of renal failure and if this patient has pneumonia then the U of CURB-65 is fulfilled with a urea > 7mmol/L
- The urine has no leucocytes or bacterial nitrites which has a high negative predictive value of 97%, i.e. the patient does not have a UTI
  - The absence of squamous epithelial cells also suggests the urine has not been in contact with the skin of the perineum making contamination less likely
- It is important to have a system for looking at Chest X-rays, one such system is:
  - Most obvious abnormality first
  - A = Airways and lungs including hilum
  - B = Bones
  - C = Cardiac outline and blood vessels
  - D = Diaphragm and air under it
  - E = Everything else including lines, NG tubes, ETT tubes etc
- This X-ray shows right basal consolidation

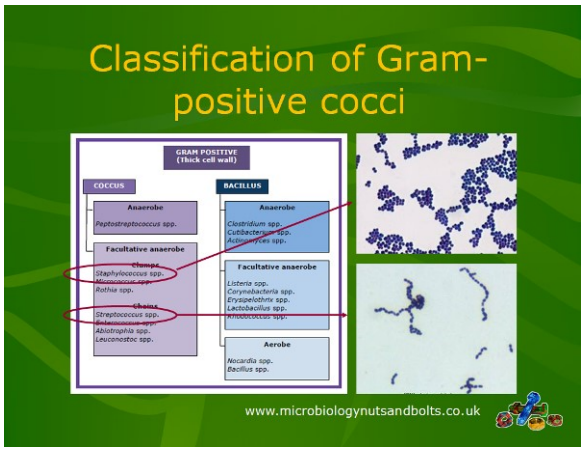


- As with other tests it is important to have a system for looking at microbiology results
- Microbiology results should be looked at in the following order if available:
  - Appearance
  - Microscopy
  - Culture
- For sputum results the appearance gives guidance on the likelihood of any cultured bacteria being from the upper respiratory tract or not
- Too many patients get treated for what is essentially normal flora and this is a mistake!

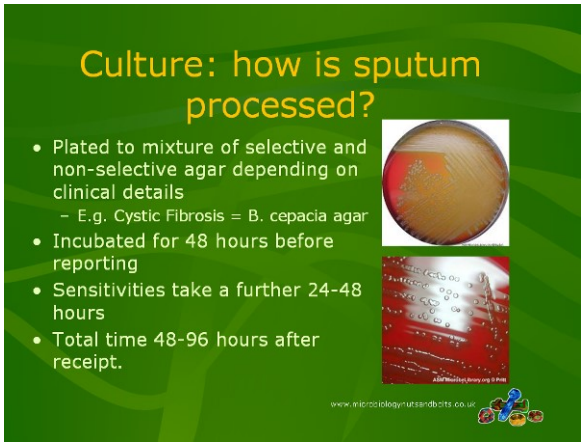


- The types of bacteria which commonly cause community acquired pneumonia usually originate from the upper respiratory tract
- Gram positive cocci
  - *Streptococcus pneumoniae*
  - *Staphylococcus aureus*
- Gram negative bacilli
  - *Haemophilus influenzae*
- Non-culturables ("atypicals")
  - *Mycoplasma pneumoniae*
  - *Chlamydophila pneumoniae*
  - *Legionella pneumophila*
- Acid fast bacilli
  - *Mycobacterium tuberculosis*
- Don't forget that the 2nd most common cause of pneumonia are the viruses such as *Influenza Virus*, *Respiratory Syncytial Virus* and *Adenovirus*

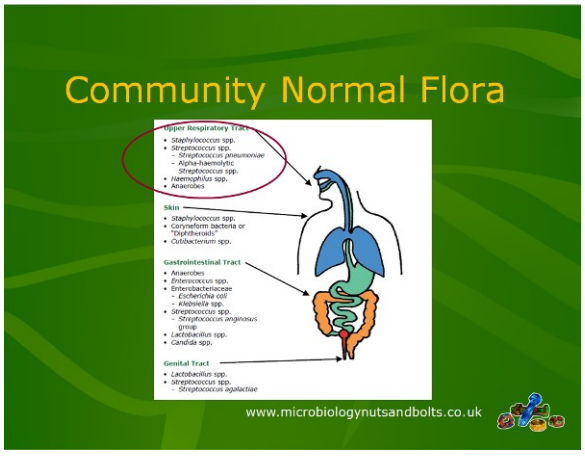




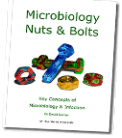
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Staphylococci from Streptococci but these are of no use to ward doctors
- In practical terms Gram-positive cocci can be distinguished by:
  - Staphylococci form clumps
  - Streptococci form chains

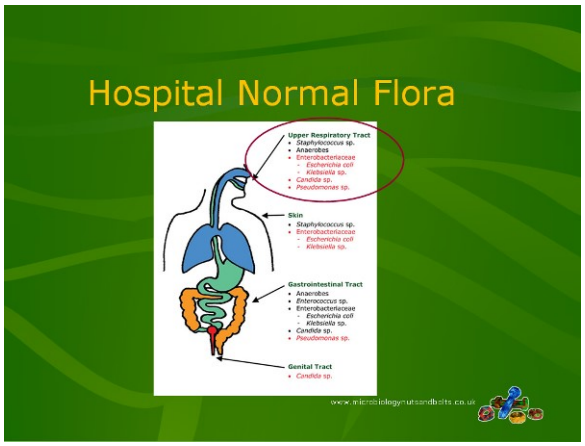


- Most microbiological tests are based on the clinical information on the request card
- If adequate clinical information is not provided the correct tests may not be done e.g. if the request card does not say cystic fibrosis the lab will not look for *Burkholderia cepacia*
- In addition, clinical information allows the lab to spot high risk samples that may be hazardous to the health of the laboratory staff when they are processing them
- Sputum samples can take up to 96 hours to give a result which is only helpful in the event of either de-escalating antibiotics or knowing what to change to if the patient does not respond to initial treatment

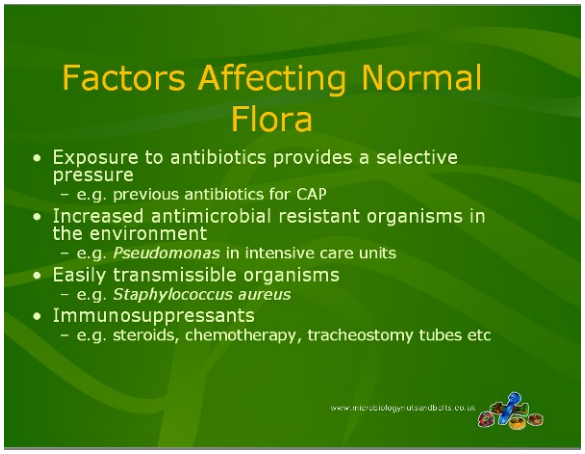


- The normal flora of a human body consists of 10^{14} bacteria (that's approximately 15,000 times the number of humans on the Earth!)
- Knowing the common bacteria that colonise the human body allows:
  - Prediction of the causes of infection from any body site because 85% of infections are caused by the patients own flora getting in to a site it should not be e.g. pneumonia caused by bacteria from the upper respiratory 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

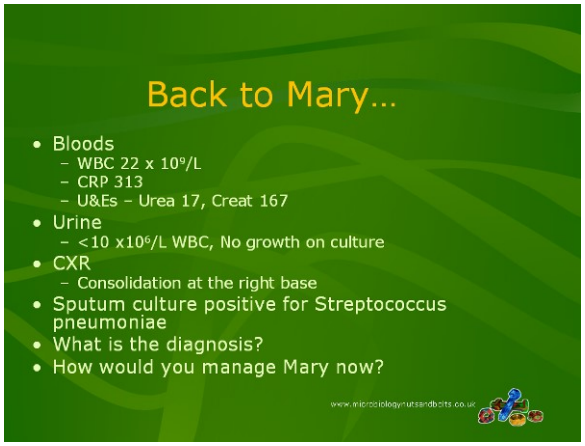




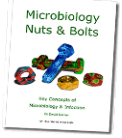
- The normal flora of a patient changes in hospital around 4 days after admission
- The upper respiratory tract becomes colonised with Gram-negative bacteria from the bowel
- This is the reason that different antibiotics are used to tract hospital acquired pneumonia (HAP) from community acquired pneumonia (CAP), NOT because one is more sever than the other
  - Note – it is also not correct to escalate from CAP antibiotics to HAP antibiotics because the causes are different and the antibiotics are chosen to treat these different antibiotics, they are different clinical conditions

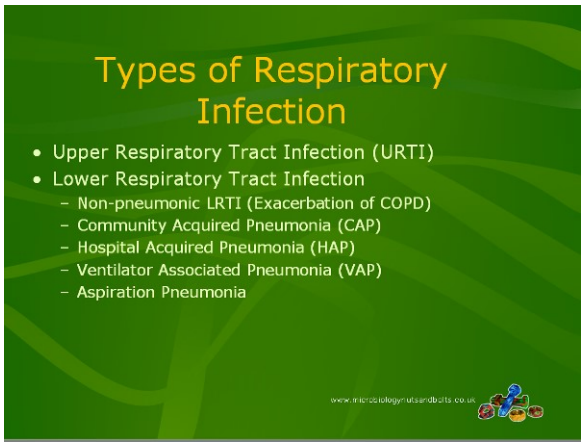


- There are many circumstances that can affect a patients normal flora
- Understanding how this happens can allow predictions to be made as to how the flora will change and therefore how this will influence the types of bacteria causing infections
- Antibiotics will tend to remove sensitive bacteria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



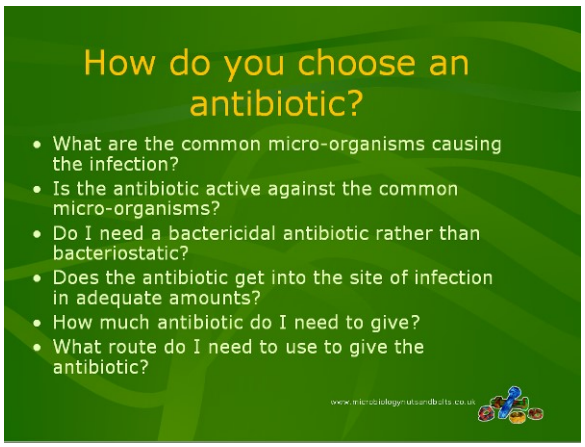
- The chest X-ray proves a diagnosis of Community Acquired Pneumonia
- Whilst Streptococcus pneumoniae is one of the most common bacterial causes of pneumonia it is also part of the normal flora of the upper respiratory tract and therefore if this is a heavy growth in a purulent sample it is likely to be the cause of the pneumonia, otherwise it could be a contaminant
- Mary's treatment would be based upon an assessment of her CURB-65 score:
  - C = Confusion (new onset)
  - U = Urea > 7mmol/L
  - R = Respiratory Rate >30/min
  - B = Blood pressure <90mmHg systolic or ≤60 mmHg diastolic
  - 65 = Age >65 years
  - A CURB-65 score of 3 or more is considered severe



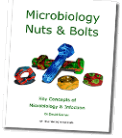


- There are a number of different definitions for respiratory infections.
- CAP = pneumonia occurring in the community of within 48 hours of admission to hospital
- HAP = pneumonia occurring more than 48 hours after admission to hospital AND not incubating at the time of admission
- The incubation comment in HAP is because some causes of CAP have incubation periods of up to 10 days e.g. *Legionella pneumophila*

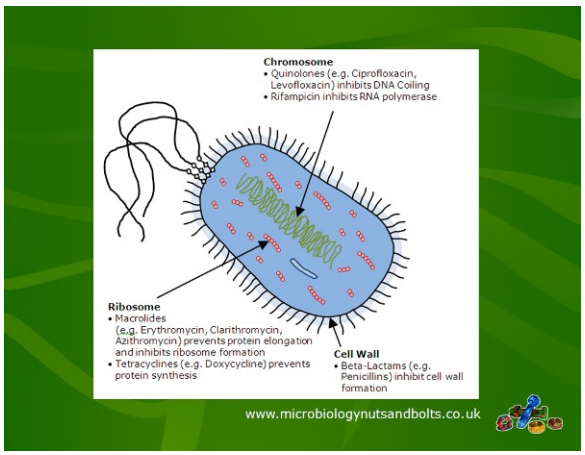
- Over treatment with antimicrobials is a common and serious problem
- There are a number of common reasons for this:
  - The patient does not have a bacterial infection
  - Clinical signs are over interpreted
  - Treatment is trying to target normal flora
- Many of these instances can be avoided by carefully considering the patient and their results before deciding to treat



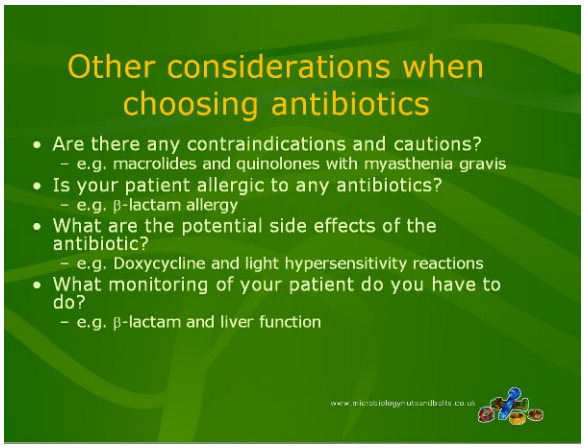
- It is important to understand why different antibiotics are used to treat different types of infections
- It is dangerous to follow guidelines blindly without considering how these guidelines have been produced because mistakes can be made for the few patients whose clinical situation lies outside those guidelines e.g. the guideline says an oral antibiotic but the patient is unable to absorb from their gastrointestinal tract



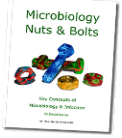
- Empirical antibiotic guidelines vary a little between hospitals based upon local epidemiology, therefore it is important to know your own guidelines
- They are empirical, that is they are designed to initiate treatment when the cause is unknown, they are not definitive for a specific cause
- Once the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



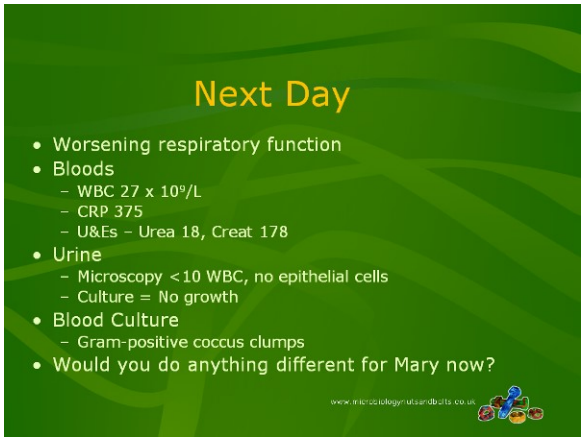
- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list 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 therefore may not be cidal to some bacteria
  - 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



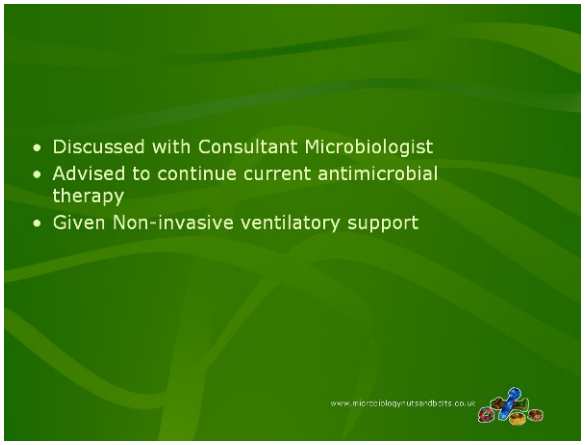
- Myasthenia gravis is a contra-indication to many antibiotics so if your patient has this then check in the British National Formulary (BNF) or with a pharmacist before prescribing
- Mild Beta-lactam allergy occurs in 1 in 20 patients, however severe is rare, only in 1 in 2000 patients
- Some antibiotics 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



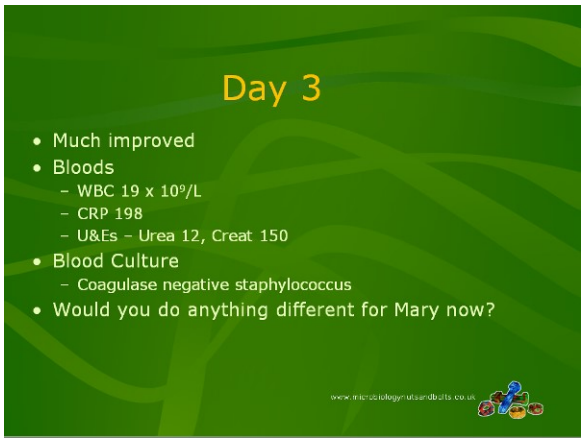
- The antibiotics cover the possible infective bacteria:
  - Co-amoxiclav – *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus*
  - Clarithromycin – *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila*



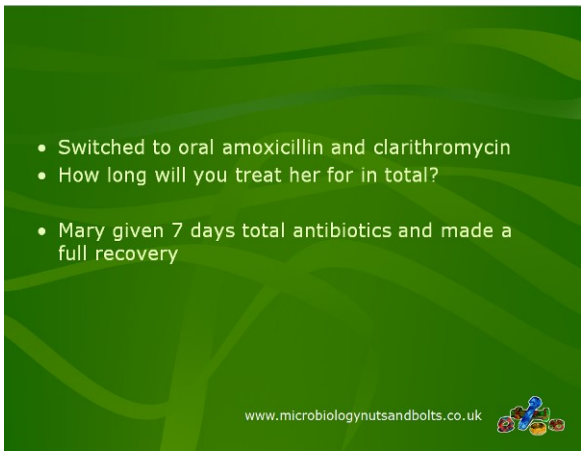
- Patients take time to respond to antibiotics and therefore it is usually not necessary to broaden up cover early
- A common mistake is to "escalate" to HAP antibiotics thinking these are better but this usually involves losing the cover for the non-culturable bacteria
- The blood culture in this instance will be a Staphylococcus, and the majority of these are skin contaminants (Coagulase negative Staphylococci)
  - Most laboratories telephone out all positive blood cultures



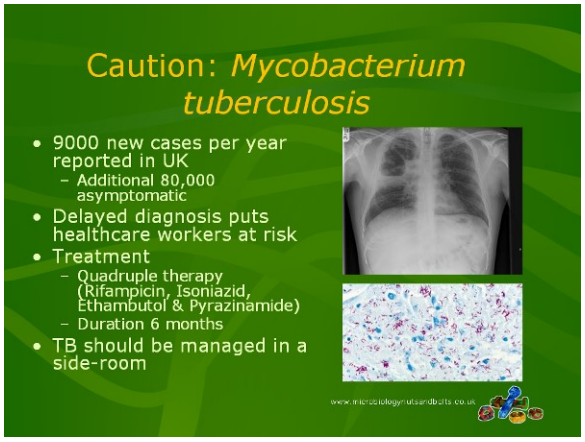
- It is important to remember that antibiotics are not the only treatment for pneumonia, and many hospitalised patients require some form of respiratory support
- Non-invasive ventilatory support essentially means she did not require mechanical ventilation



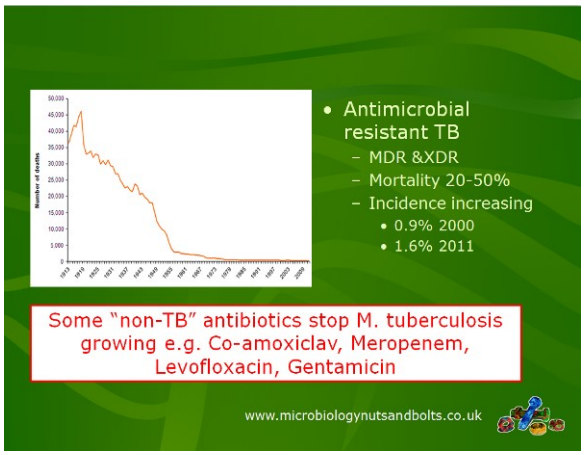
- At this stage Mary has shown improvement and a decision should be made about switching her antibiotics from IV to oral
- This is better for the patient in terms of reducing the risk of IV device associate infections and can also facilitate discharge from hospital
- The blood culture is confirmed as a skin contaminant



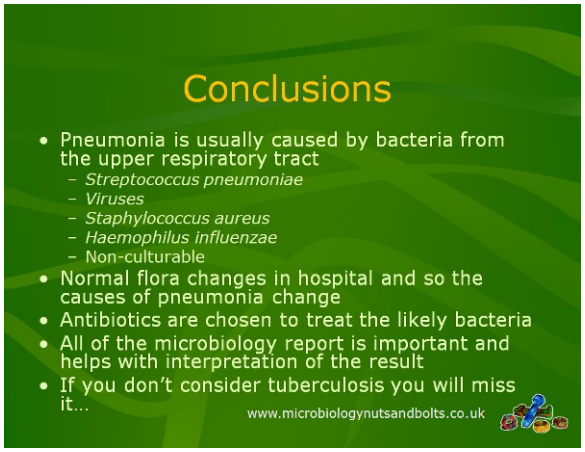
- The treatment for CAP is usually 7 days
- It is important to remember that the patient is unlikely to be back to normal at this and they may still have an abnormal chest X-ray however this is not usually due to ongoing infection but rather the inflammation and damage caused by the infection which may take longer to heal



- Tuberculosis (TB) used to be the third most common cause of death in the UK
- Most patients are asymptomatic however it has been estimated that each untreated person can infect up to 10-15 other people so it is important to diagnose as many as possible
- Many of the patients diagnosed in the UK were born in, or have contact with people from, countries where TB is endemic
- Treatment should be guided by a physician experienced in managing patients with TB because side-effects can occur and compliance can be an issue
- Patients with TB should be managed in a side-room in hospital until they have received at least 2 weeks of treatment or had 3 negative sputum smears for TB



- Multi-drug resistant TB (MDR TB) is resistant to Isoniazid and Rifampicin
  - Treatment requires the use of other cidal agents such as the fluoroquinolones and the aminoglycosides
- Extensively Drug Resistant TB (XDR TB) is resistant to Isoniazid, Rifampicin, fluoroquinolones and Aminoglycosides
  - Treatment is difficult and the mortality is high
  - This requires specialist facilities and experience to treat safely
- If we were to go back to the days when we had no antibiotics for TB then we would see approx. 36,000 deaths/year in the UK (currently 250 deaths per year)!
- Don't forget that some "normal" antibiotics have activity against *Mycobacterium tuberculosis* (MTB) and can therefore make cultures for MTB negative



- Pneumonia is a common diagnosis in hospitals
- In order to diagnose and manage it effectively it is important to understand:
  - The common causes
  - The limitations of the investigative tests used
  - The choice of antibiotics
  - The risk of the cause being something not covered by the common treatments

More information on respiratory infections is available in the pocket guide Microbiology Nuts & Bolts by Dr David Garner