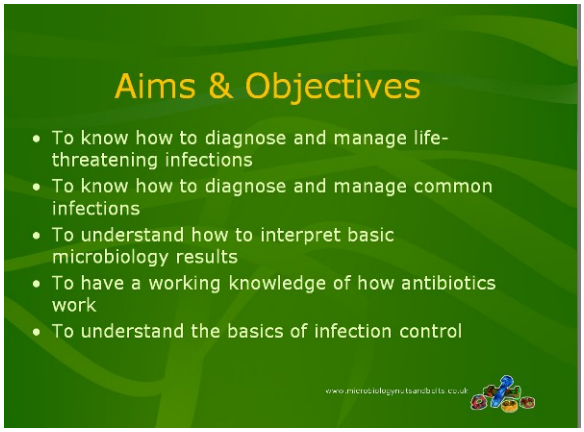
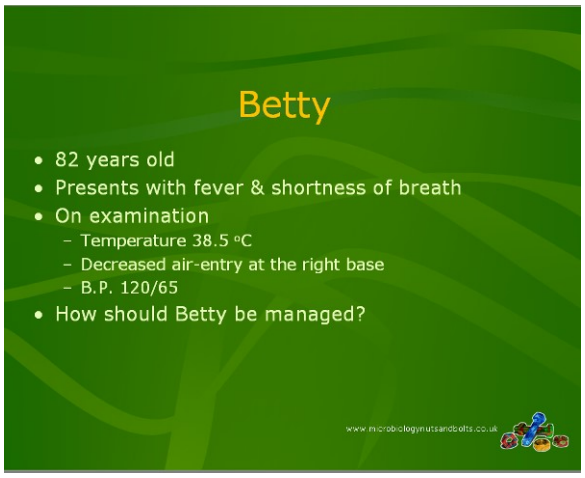
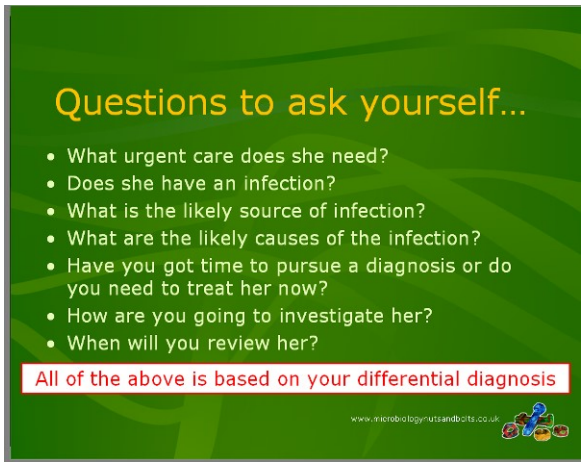
Microbiology Nuts & Bolts: Session 2: Urinary Tract Infections



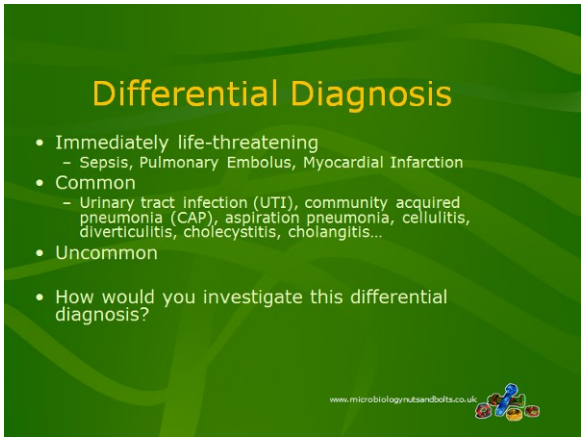
- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common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



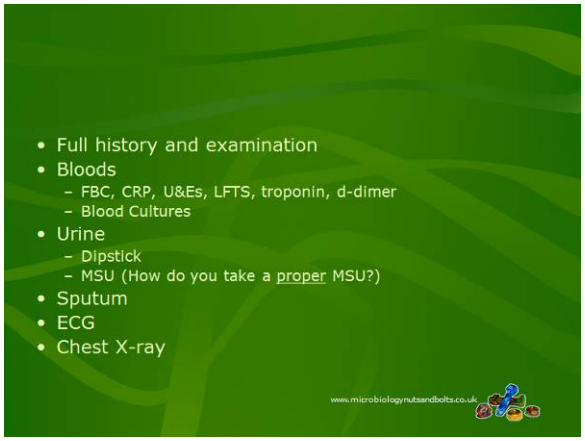
- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for fever and shortness of breath therefore it is important not to become too fixated on a diagnosis without considering all possibilities
- All doctors should know the limitations of the tests 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



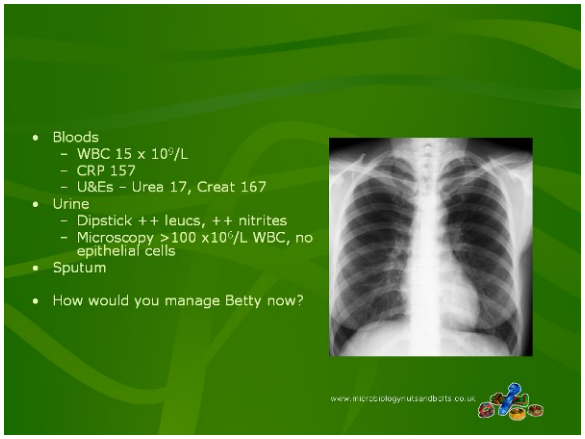
- If Betty is septic then she needs urgent care, for every hour delay in giving effective treatment the mortality increases by 7% up to approximately 40% by 6 hours
- If she is very unwell then she will need frequent and regular review in order to ensure she is improving or to spot any deterioration 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



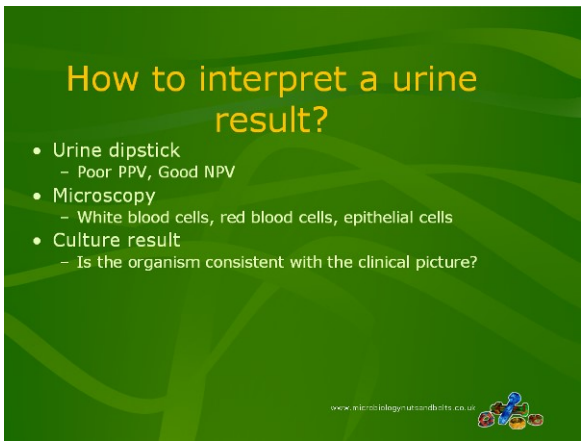
- Formulating a differential diagnosis appears to be going out of fashion but it is essential if diagnoses are not to be missed
- A systems approach (e.g. respiratory, cardiac, Gastrointestinal, genitourinary, neurological, skin, bone, joint, etc) can be fitted to a template of life-threatening, common,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



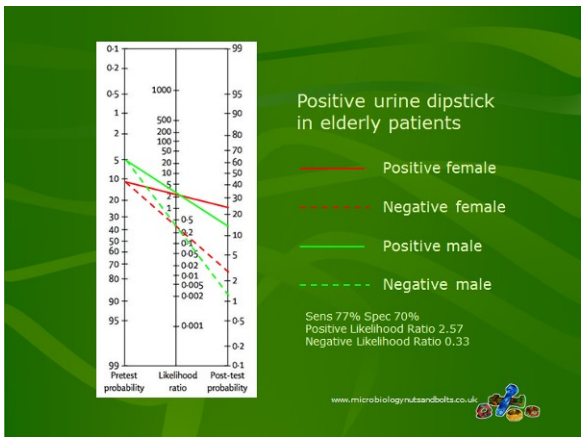
- The list represents a common "septic screen" within the hospital setting to which could be added a lumbar puncture if a neurological diagnosis was possible
- It is essential to know the normal values of all tests within your hospital
- Full blood count (FBC)
  - The total white blood cell count can 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
- 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



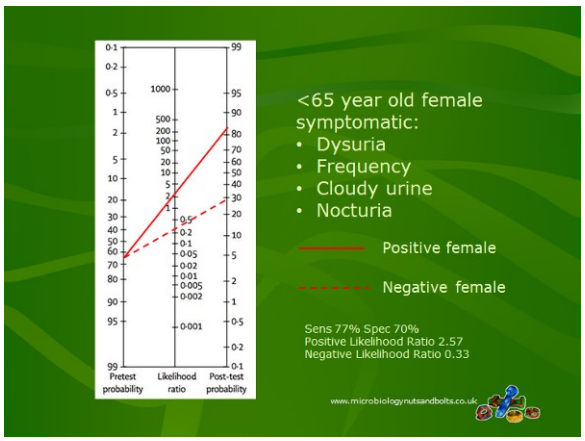
- Patient has an inflammatory process going on with high white blood cells and CRP
- U&Es shows a degree of renal failure and may make antibiotic dosing problematic
- The urine contains leucocytes and bacterial nitrites which has a low positive predictive value of 60%, i.e. the patient may have a UTI but formal microscopy with or without culture is required to investigate further
  - The raised white blood cell count on microscopy confirms an inflammatory process and makes a diagnosis of UTI more likely
  - 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
- This chest X-ray is normal
- It would be sensible to treat Betty for a severe UTI or pyelonephritis given her fever, possible low blood pressure and systemic inflammatory response



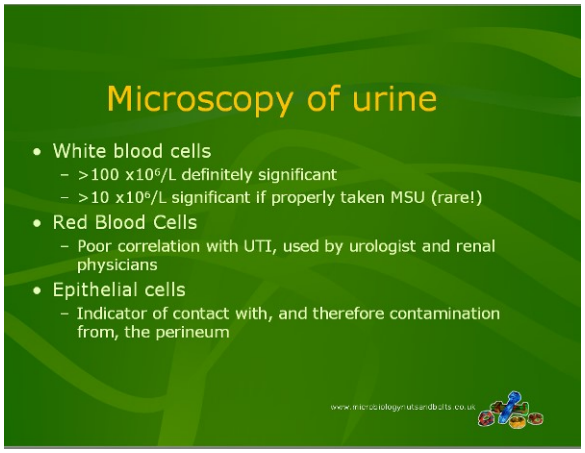
- As with other tests it is important to have a system for looking at microbiology results
- Urine dipsticks are good for excluding UTIs in normal immunocompetent adults but beware patients who cannot mount an immune response or who can have significant UTIs without a white blood cell response:
  - Neutropaenia
  - Pregnancy
  - Children
  - Anatomical abnormalities of the urinary tract
- Too many patients get treated for what is essentially normal flora and this is a mistake!



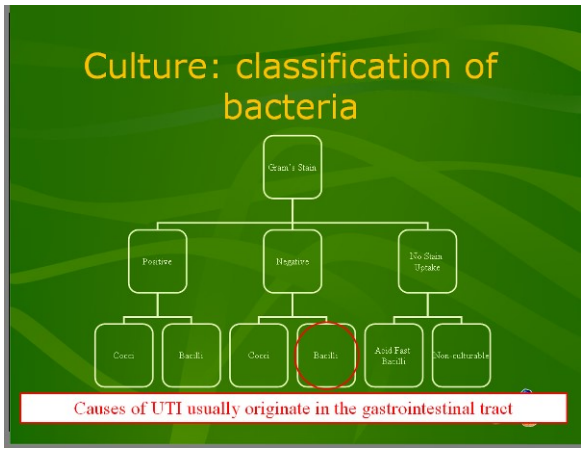
- The Fagan Nomogram is a statistical tool for evaluating the effectiveness of a test
- A positive urine dipstick in an elderly female patient with a fever is only about 25% predictive of a UTI; that means 75% of patients with a positive urine dipstick DO NOT HAVE A UTI
- A negative urine dipstick in the same type of patient means that 97% DO NOT HAVE A UTI
- Urine dipsticks are a screening test for ruling out a diagnosis of UTI, they are not a diagnostic test for proving a patient does have a UTI



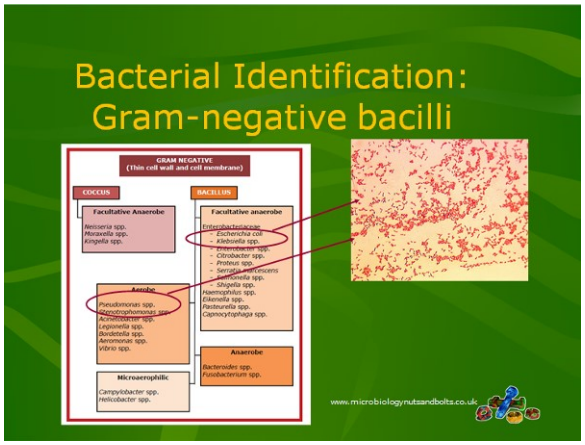
- In comparison to the urine dipstick above, the combination of dysuria, frequency, cloudy urine and nocturia in a female < 65 years old is better at predicting a UTI than a positive urine dipstick.



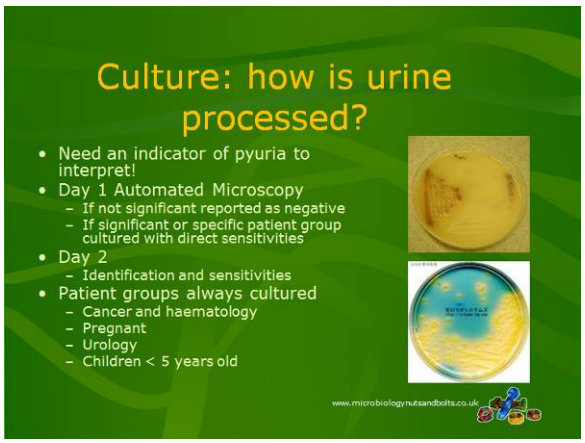
- A high WBC in the urine is consistent with a UTI but other systemic inflammatory conditions can give rise to pyuria e.g. pneumonia, appendicitis, etc
- The presence of epithelial cells in a urine sample indicates that the urine has not been taken correctly and has been in contact with the skin of the perineum with the risk that anything that has grown may actually be a contaminant from the perineal flora
- Positive bacterial culture in the presence of epithelial cells or the absence of white blood cells is consistent with possible contamination and should be regarded with caution when planning patient treatments (it may be better to repeat these samples with a carefully taken specimen)



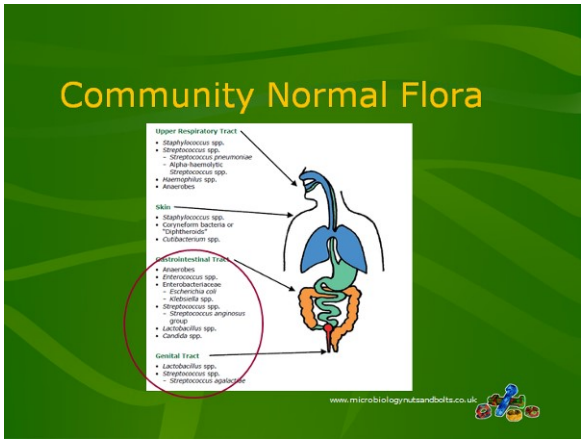
- The types of bacteria which commonly cause urinary tract infections originate in the bowel and enter the urethra from the perineum by "swimming" within the column of urine
- Gram negative bacilli
  - *Escherichia coli*
  - *Klebsiella* spp.
  - *Enterobacter* spp.
  - *Proteus* spp. (associated with urinary tract stones)
  - *Pseudomonas* spp. (if catheterised)
- Proteus breaks down urea in to water and ammonia and therefore alkalinises urine, which in turn helps precipitate out the chemicals which then form urinary tract stones
  - Patients with recurrent Proteus UTIs should be investigated for the presence of stones as they will be unlikely to be cured until the stones are dealt with



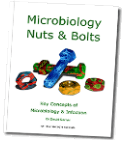
- Most microbiology text books list numerous biochemical tests to aid in distinguishing Gram-negative bacteria
- In practical terms Gram-negative bacilli can be distinguished by:
  - Enterobacteriaceae e.g. *E. coli, Klebsiella* spp., Enterobacter sp. grow in both aerobic and anaerobic cultures (i.e. both blood culture bottles)
  - *Pseudomonas* spp. only grows aerobically
- The distinction is important because Pseudomonas sp. are inherently resistant to many antibiotics used to treat UTIs such as Amoxicillin, Co-amoxiclav, Trimethoprim, Nitrofurantoin, Cefuroxime, Cephradine and Cefaclor

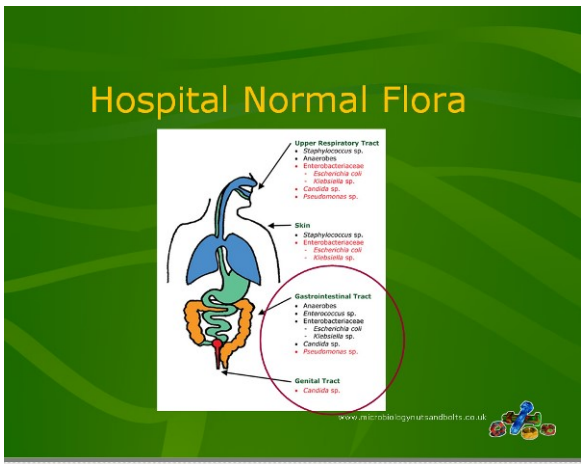


- Most microbiological tests are based on the clinical information on the request card
- If adequate clinical information is not provided the correct tests may not be done e.g. if the request card does not say that the patient is pregnant then a full culture may not be performed
- In addition, clinical 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
- Most laboratories receive urine samples in boric acid containers which helps to stabilise bacterial growth and the white blood cell count for 24-48 hours before being tested however if less than about 8mls of urine is put in these containers then the concentration of boric acid may be high enough to actually kill the bacteria
  - If you are submitting a small volume sample e.g. from a child, use a normal sterile white universal and indicate this on the request form

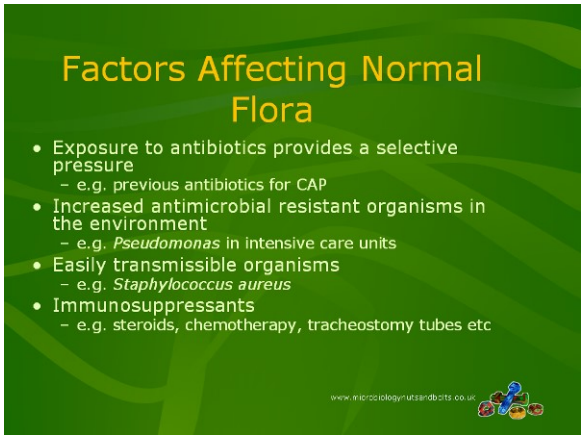


- The normal flora of a human body consists of 10^{14} bacteria (that's approximately 15,000 times the number of humans on the Earth!)
- Knowing the common bacteria that colonise the human body allows:
  - Prediction of the causes of infection from any body site because 85% of infections are caused by 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



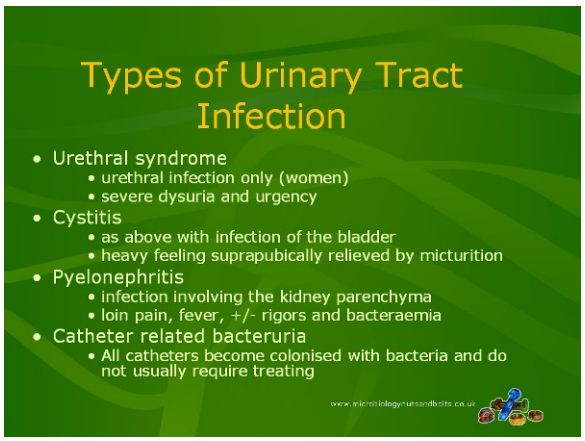


- The normal flora of a patient changes in hospital around 4 days after admission



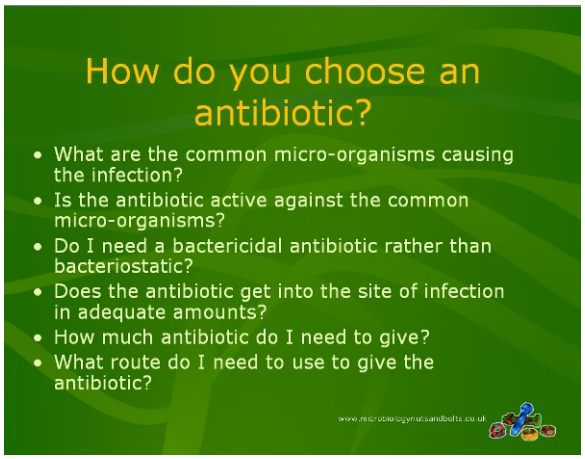
- There are many circumstances that can affect a patients normal flora
- Understanding how this happens can allow predictions to be made as to how the flora will change and therefore how this will influence the types of bacteria causing infections
- Antibiotics will tend to remove sensitive bacteria 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 urine results confirm a UTI
- Respiratory commensals are another name used by laboratories to indicate a mixture of normal flora has been grown
- Betty should be treated for a sever UTI such as pyelonephritis as she has systemic signs of a severe infection

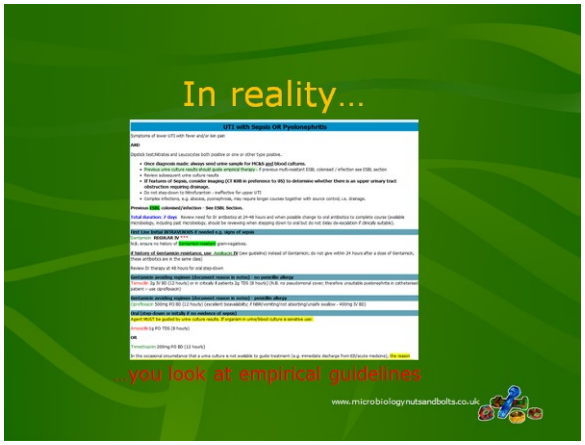


- There are a number of different definitions for urinary tract infections and they have different treatments

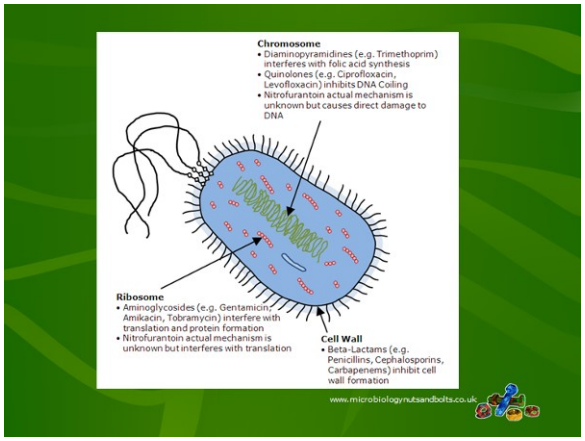
- Over treatment with antimicrobials is a common and serious problem
- There are a number of common reasons for this:
  - The patient does not have a bacterial infection
  - Clinical signs are over interpreted
  - Treatment is trying to target normal flora
- Many of these instances can be avoided by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



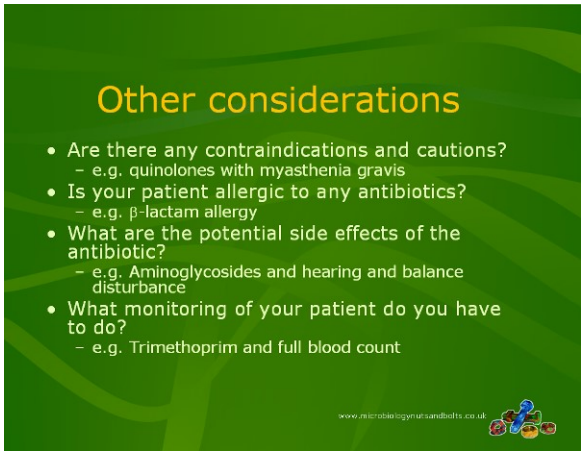
- It is important to understand why different antibiotics are used to treat different types of infections
- It is dangerous to follow guidelines blindly without considering how these guidelines have been produced because mistakes can be made for the few patients whose clinical situation lies outside 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
  - Some other individual action
    - 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
    - Diaminopyramidines such as Trimethoprim prevent folic acid synthesis and therefore are similar to the chemotherapeutic methotrexate!



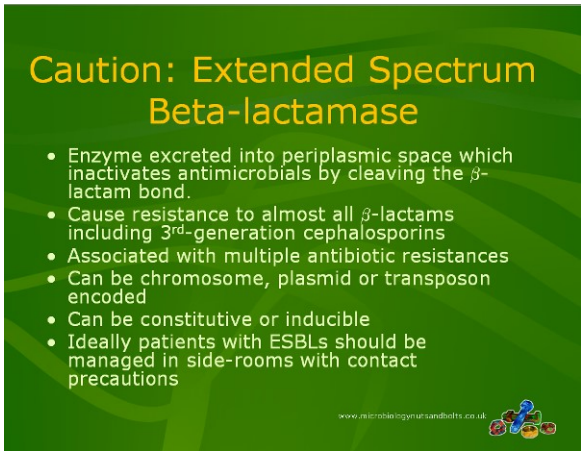
- Myasthenia gravis is a contra-indication to many antibiotics so if your patient has this then check in the British National Formulary (BNF) or with a pharmacist before prescribing
- Mild Beta-lactam allergy occurs in 1 in 20 patients, however severe is rare, only in 1 in 2000 patients
- Some antibiotics 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 antibiotic covers the possible infective bacteria:
  - Gentamicin – *E. coli, Klebsiella* spp., *Enterobacter* spp.
- Gentamicin is often added for septic patients because it is rapidly cidal to bacteria as well as acting synergistically with the Beta-lactams in order to enhance the activity of the other agent

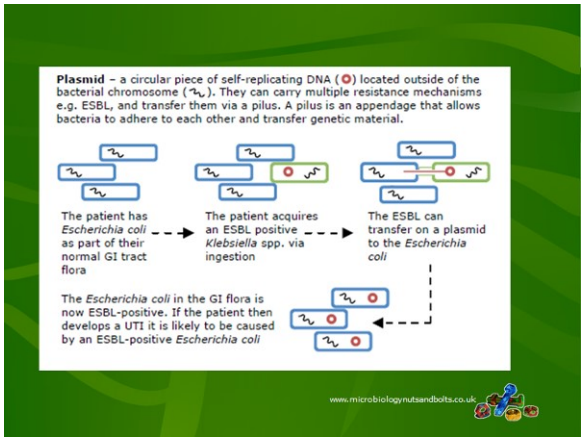
- Although patients can take time to respond to antibiotics occasionally they have resistant bacteria which can require an early escalation of antibiotics
- The blood culture in this instance will probably be the same *E. coli* which is in this patients urine and indicates a severe infection and pyelonephritis
- Most laboratories telephone out all positive blood cultures
- The choice of Temocillin is based upon the observed and predicted resistance of the *E. coli* due to the presence of the extended-spectrum Beta-lactamase (ESBL)
- Temocillin remains active in this situation and is the usual treatment of choice

- At this stage Betty has shown improvement and a decision could be made about switching her antibiotics from IV to oral
- This would be better for the patient in terms of reducing the risk of IV device associate infections and can also facilitate discharge from hospital
- The problem with these types of bacteria is that they often have other mechanisms of resistance which render oral antibiotics obsolete as is the case for Betty

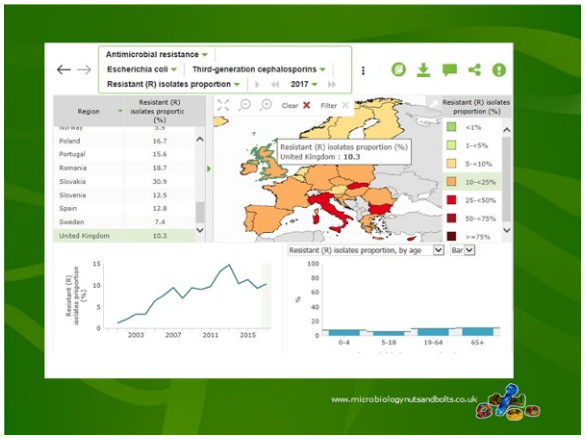
- Fosfomycin and Pivmecillinam Hydrochloride can be used for lower urinary tract infections e.g. cystitis
- The treatment for pyelonephritis is usually 7 days (or 14 days in pregnancy)



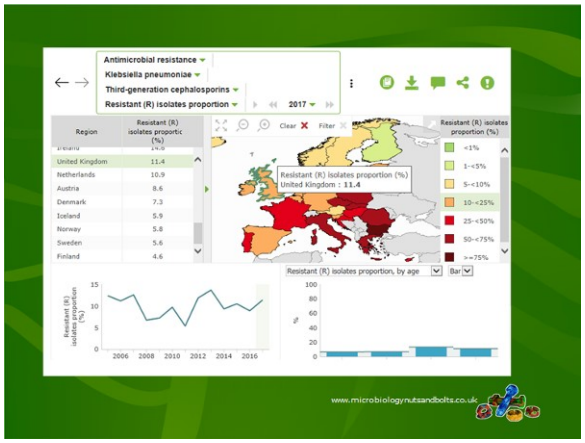
- The extended-spectrum Beta-lactams are the 3rd generation cephalosprins such as Ceftriaxone, Cefotaxime and Ceftazidime
- These enzymes breakdown all of the commonly used Beta-lactams giving resistance to all except the carbapenems such as Meropenem, Imipenem and Ertapenem
- They can be associated with multiple resistance mechanisms
- Constitutive resistance is expressed all the time whereas inducible resistance is only expressed when induced by the presence of the antibiotic
  - Inducible resistance can be difficult to spot on laboratory tests and so a high degree of suspicion should exist when patients fail to respond to what appears to be effective treatment



- Plasmids are mobile genetic elements; they are circular pieces of DNA that sit outside of the bacterial chromosome
- Plasmid transfer is a common mechanism by which antimicrobial resistance can be spread between bacteria



- The presence of ESBL positive bacteria is increasing worldwide with up to 10% of community *E. coli* isolates in UTIs now expressing the enzyme
- It is though that the bacteria may be in the food chain and a number of specific sources have been proposed
- They represent a real public health threat and this is becoming the focus of Department of Health attention with regards to antibiotic resistance



- ESBL positive *Klebsiella* spp. have a similar incidence to *E. coli* in the UK, however in other parts of Europe resistance rates are no in excess of 75%

Conclusions

- UTI is usually caused by bacteria from the lower gastrointestinal tract
  - *Escherichia coli*
  - *Proteus mirabilis*
  - *Klebsiella oxytoca*
- All urinary catheters become colonised, they do not usually require treating
- Antibiotics are chosen to treat the likely bacteria
- All of the microbiology report is important and helps with interpretation of the result
- Multi-resistant bacteria often required infection control precautions

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- UTI is a common diagnosis in both the community and 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 urinary tract infections is available in the pocket guide Microbiology Nuts & Bolts by Dr David Garner