Microbiology Nuts & Bolts: Session 3: Gastrointestinal Infections

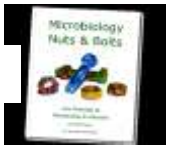
- 30-40% of patients admitted to hospital will receive an antibiotic
- It is critical to pick out those with life-threatening conditions in order to manage them appropriately and correctly in order to give them the best chance of survival
- It is also important to know how to diagnose and manage common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

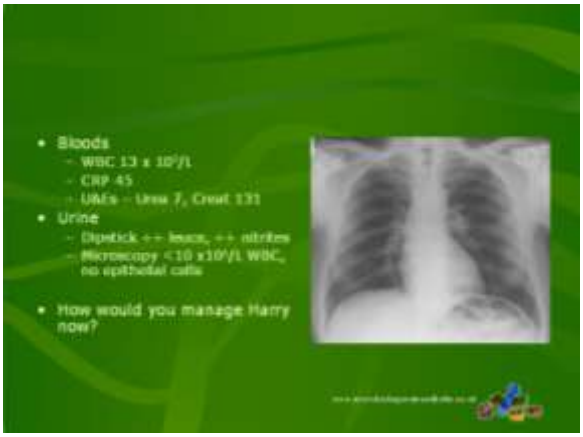
- A vague history but allows the process of diagnosing the patient to begin
- There are non-infectious reasons for abdominal pain therefore it is important not to become too fixated on a diagnosis without considering all possibilities, especially when the temperature is within normal range
- All doctors 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
- 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
- In this case we do not know the cause of Harry's pain, what the nature of his allergy is and therefore whether the choice of antibiotic is appropriate or not

- If Harry is septic then he needs urgent care, for every hour delay in giving effective treatment the mortality increases by 7% up to approximately 40% by 6 hours
- If he is very unwell then he will need frequent and regular review in order to ensure he 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
- In this case we have no evidence that Harry is very unwell and it would probably have been better to try and work our what was going on before rushing in with antibiotics

- 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
- Liver Function Tests and Amylase
  - These are essential to investigate for possible biliary infection or pancreatitis, both of which may require antibiotics or specific surgical management
- 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 only slightly raised high white blood cells and CRP, which are non-specific and are not consistent with an acute bacterial infection
- 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 normal white blood cell count on microscopy makes a diagnosis of UTI unlikely
  - The absence of squamous epithelial cells suggests the urine has not been in contact with the skin of the perineum making contamination less likely
- This chest X-ray is normal, and in particular given the history of abdominal pain there is no air under the diaphragm to indicate a perforated viscus
- At this point in time there is little to support a diagnosis of infection

- Harry is now becoming very unwell
- In addition to new nausea and diarrhoea his blood tests now show an inflammatory response and acute renal failure
- The abdominal X-ray shows dilated loops of large bowel, a condition known as megacolon
- There are very few causes of megacolon, the most likely in this case is Clostridium difficile because the patient is elderly and has been given a high risk antibiotic, Ciprofloxacin
- Harry needs a senior review, his Ciprofloxacin should be stopped immediately and he should be started on treatment for C. difficile even though otherwise he should be kept nil by mouth
- He should be isolated in a side-room in order to protect other patients
- He will need supportive care with fluids and he should be assessed by a surgeon

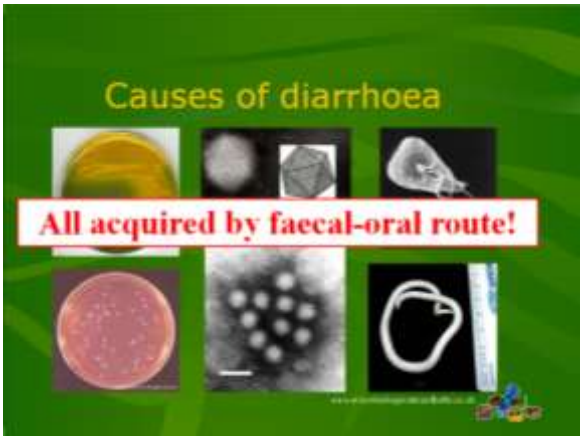
- As with other tests it is important to have a system for looking at microbiology results
  - Stool samples are first assessed to see if the patient actually has loose stool
  - Microscopy will indicate if a parasite has been seen
  - Culture will indicate if one of the common bacterial causes of diarrhoea has been isolated or not
- Too many patients get treated for what is essentially normal flora and this is a mistake!
- The most crucial information on the request is the clinical details as this dictates what tests are done and also protects the laboratory staff handling the pure cultures from the specimen
  - If you say the patient has been abroad then the lab staff may look for Cholera as well as taking care not to acquire typhoid or paratyphoid themselves

- 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)

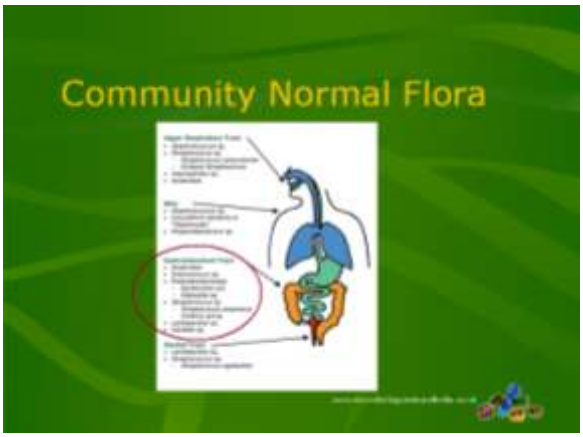
- It may sound like an odd thing to do but the development of the Bristol Stool Chart has made a major impact on the management of diarrhoea
- It provides an objective classification of whether a stool sample can be graded as liquid or not
- Types 6 and 7 are those that concern us the most

- Stool samples are technically the most demanding samples sent to a microbiology laboratory
- The laboratory are trying to find particular pathogenic strains of bacteria amongst what is about 1/3rd dry weight bacteria of a similar appearance
- It helps if the lab have an idea of what they might be looking for and clinical details are essential for this
  - The lab do not routinely look for all pathogens but are guided by the clinical history, especially the travel history e.g. if travelled to India they will look for Cholera etc
- The clinical details also help protect the lab from potentially dangerous pathogens which are easily acquired when grown in pure culture e.g. typhoid, paratyphoid
- Culture can take up to 96 hours for some bacteria such as Campylobacter sp. which are fastidious and slow growing

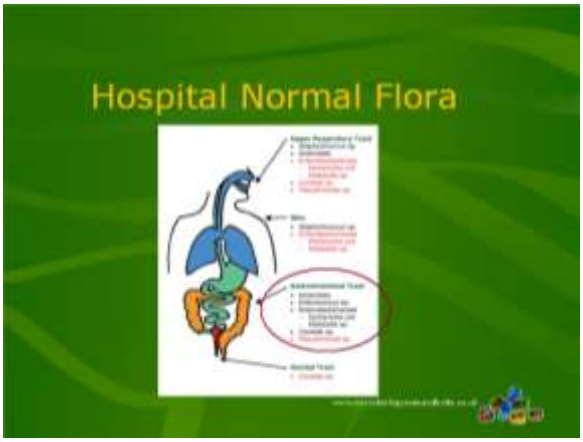
- The types of organisms that commonly cause gastrointestinal infections are commonly viruses, bacteria and parasites
- The speed of onset is usually fast for viruses and bacterial toxins and slightly longer for other bacteria
- Parasites often give prolonged symptoms
- Outbreaks in the developed world are often caused by viruses which are highly infectious and not readily killed by alcohol hand gels
  - There are 10 million infectious doses of virus in each gram of stool from a patient with Norovirus or rotavirus



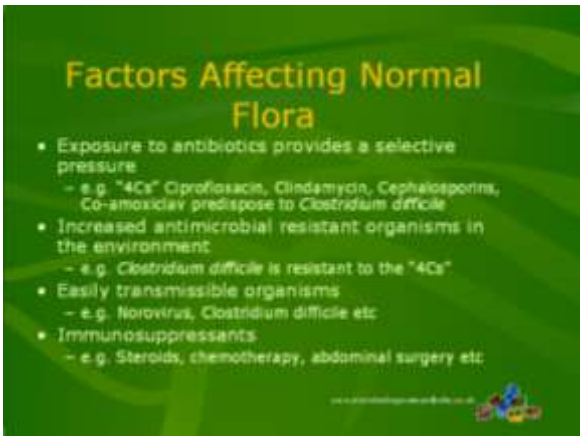
- Whilst there are many organisms that can cause gastrointestinal infection, what they all have in common is that they are acquired by the faecal oral route
- The pictures are:
  - Left – top Cholera, bottom E. coli O157
  - Middle – top Adenovirus, bottom Norovirus
  - Right – top Giardia, bottom Ascaris (roundworm)



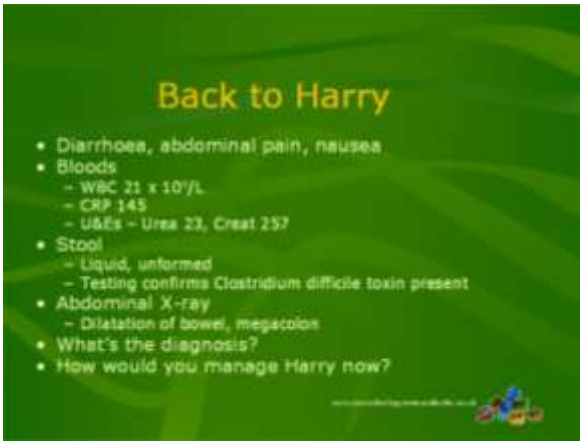
- The normal flora of a human body consists of 10^{14} bacteria (that's approximately 15,000 times the number of humans on the Earth!)
- Knowing the common bacteria that colonise the human body allows:
  - Prediction of the causes of infection from any body site because 85% of infections are caused by 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 or allowing resistant ones to colonise
  - This is how antibiotics predispose to Clostridium difficile infection
  - C. difficile is resistant to the antibiotics which predispose to it and so is able to exploit the ecological niche left behind by the antibiotic
  - C. difficile then starts to produce toxins which cause the diarrhoea
  - The highest risk antibiotics at the moment are known as the "4 Cs"
    - Ciprofloxacin (and the quinolones)
    - Clindamycin
    - Cephalosporins
    - Co-amoxiclav

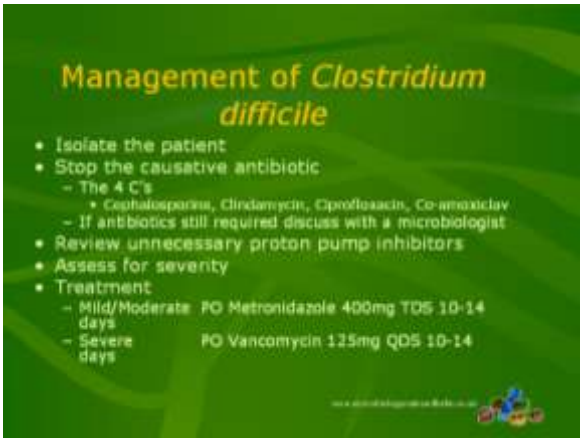


- Harry stool tests positive for Clostridium difficile toxin and so his diagnosis is Toxic Megacolon secondary to Clostridium difficile
- This is severe C. difficile and so in addition to the measures mentioned earlier the antibiotic choice to treat him is normally PO Vancomycin 125mg QDS
- Severity markers are presented later but in this case they are:
  - His age
  - High white cell count and CRP
  - The presence of toxic megacolon

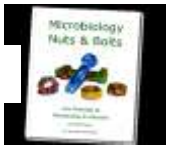
- There are many gastrointestinal tract related infections and only detailed history taking and targeted investigations can separate them

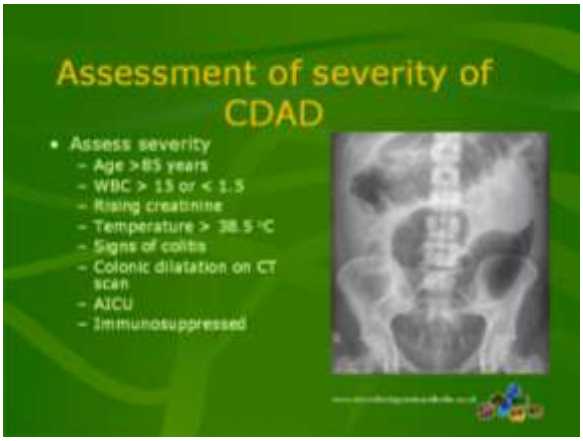
- Over treatment with antimicrobials is a common and serious problem
- There are a number of common reasons for this:
  - The patient does not have a bacterial infection
  - Clinical signs are over interpreted
  - Treatment is trying to target normal flora
- Many of these instances can be avoided by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

- Most gastrointestinal infections do not require antibiotic treatment
- The exceptions are:
  - Clostridium difficile – where treatment reduces morbidity and mortality as well as the duration of symptoms and the risk of transmission to others
  - Typhoid & paratyphoid – which are actually systemic infections associated with a high mortality and are usually treated with either Ceftriaxone or Ciprofloxacin
  - Parasites – which often tend to cause chronic infections and nutritional problems if not eliminated

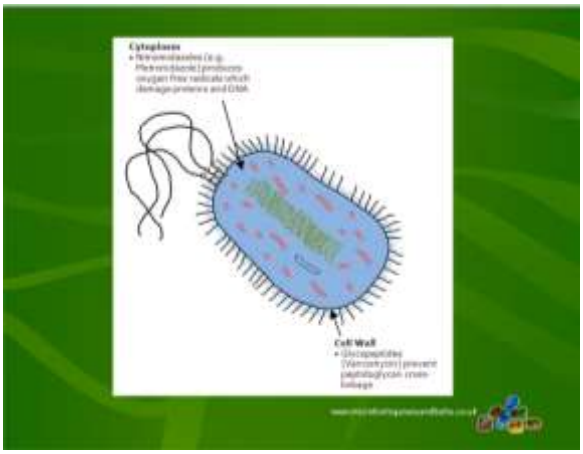


- All patients with Clostridium difficile should be reviewed urgently by a Doctor and assessed for severity of disease
- They should be isolated in a side-room and protective isolation implemented
- The offending antimicrobial should be stopped or discussed with a Microbiologist
- They should be started on appropriate treatment for the severity
- If severe it is a good idea to get a gastroenterology or surgical assessment urgently

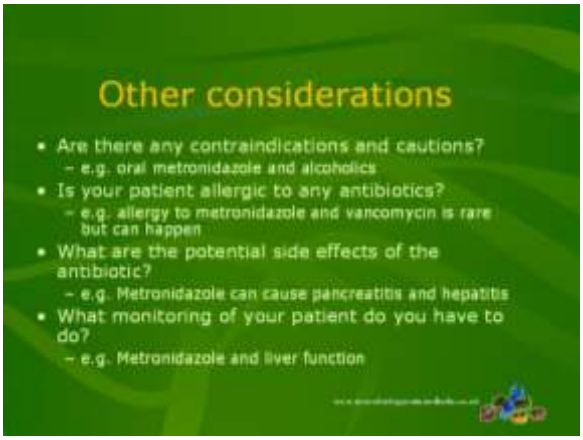




- Clostridium difficile is a potentially life threatening infection which needs careful management

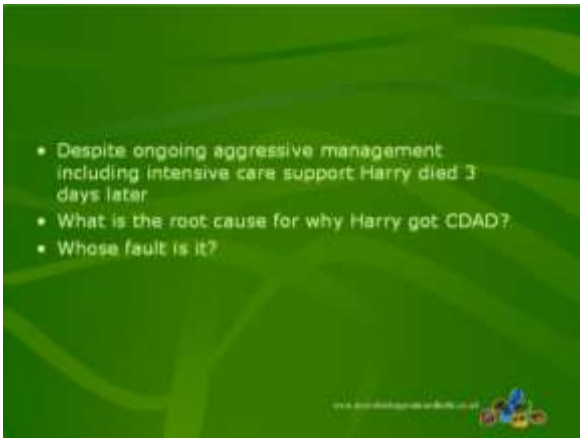


- The mechanisms of action of antibiotics causes a lot of confusion (and the similarity of names makes it even worse – anything ending in "mycin" is derived from a fungus and has nothing to do with the class of the bacteria!)
- It can helpful to split them into groups as this at least reduces the list 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 (Clostridium difficile is a Gram-positive bacillus)
  - Mainly act in the cytoplasm
    - Metronidazole is a nitroimidazole which kills anaerobic bacteria by producing oxygen free radicals which they are unable to deal with and which therefore interact with intracellular processes



- Patients given metronidazole should be warned about the harmful interaction with alcohol
  - Metronidazole causes a disulfiram-like reaction with alcohol which can be potentially fatal
- 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

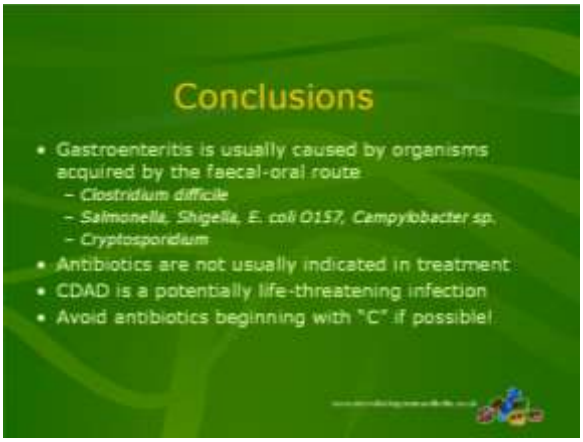
- The Ciprofloxacin is stopped because it is almost certain that it has predisposed him to Clostridium difficile associated disease and if it continues he will continue to get worse
- Oral Vancomycin is started for what is a severe infection
- Harry has progressed to one of the consequences of severe C. difficile infection with perforation of his bowel requiring surgery



- This is a disaster
- Harry came in with one problem and as a result of his treatment he died
- Root Cause Analysis (RCA) is the process by which we investigate incidents and errors in order to see if there are lessons which can be learnt to prevent them happening again (there can be more than one)
- In this case the root causes are:
  - Inadequate history, examination and investigation to find the cause of his symptoms
  - Incomplete history of allergy to decide if Harry really was allergic to penicillin
  - Unjustifiable use of a high risk antibiotic in a high risk patient
- In terms of who is responsible in this case it is likely to be the Doctor who initially managed the patient incorrectly as well as the Senior who reviewed the patient the next day

- RCA is a powerful tool if used correctly leading to real change to prevent recurrences of problems

- Infection control is the responsibility of everyone who works in the health service at every level
- Everyone has a responsibility to protect our patients from harm, including the acquisition of infections within the hospital or other healthcare settings
- Hand hygiene is the single most important aspect of this process (for gastroenteritis this should be with soap and water, alcohol gel is not effective)
- Infection control evaluation is a continuous process and if patients clinical conditions change so should their infection control precautions
- Careful prescribing of antibiotics is essential
  - You must be able to justify every prescription you right
  - There should be clear guidance on the prescription of why the antimicrobial has been prescribed and how long you intend to continue it for
  - This allows someone to come after you and stop the antibiotics as appropriate or evaluate clinical response after the event



- Gastroenteritis is caused by organisms transmitted through the faecal oral route
- Antimicrobials are rarely indicated in otherwise fit and healthy individuals
- Clostridium difficile Associated Disease is often preventable and can be life-threatening
- There are a number of infection control related measures to prevent the spread of CDAD:
  - Hand hygiene with soap and water
  - Isolation of patients with diarrhoea whatever the cause
  - Careful antimicrobial prescribing
  - Early treatment of patients with infection