University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

PHAMACOLOGY

● SHEET ○ SLIDES

LECTURE # : 

TITLE: Introduction for Antibiotics

PROFESSOR: Dr. Malek Al-zohlof - 1

DATE: 4.12.2012

DONE BY: Dana Qasrawi

M.D Class of 2018

PRICE: .....

DESIGNED BY WASEEM KAMAL

groups/Doctor2012
http://medstudygroup.weebly.com

- Before we start, please note that:
  - You need to be able differentiate between gram +ve & -ve bacteria and their meaning to understand the coming lectures.
  - The doctor insisted that you must attend all the lectures (around 7) as they're linked together; and what you learn now is what you'll carry to your practice.

(يعني ما رح ينعاد هاد الحكي في السنوات الجاي)

- Antiseptic vs. disinfectant :

Antiseptic	Vs.	Disinfectant
Example: the hygiene that you use. Very imp. in many cases (Eg: in surgeries).		Not allowed to be used on the skin. Used on floor, benches …… Example: phenol (which can be smelled once you enter a hospital)

- Antimicrobial therapy includes the following drugs:

  Antimalarial , Antiprotozoal , antifilamentic , antiviral therapy and Antibiotics .

- Antibiotics: (the only one we'll include in this semester)
  - Are drugs that work on and destroy bacteria in a selective way.
  - They target the differences between bacterial & human cells. (structures found in bacteria not humans).
  - E.g.
    - bacterial cell wall (not found in human cells).
    - bacterial protein machinery (which is different from humans).

- Normal flora vs. Infectious organisms:

  Generally speaking, we have normal micro - flora living in our system (Eg: bacteria in GI & Respiratory tract), which doesn't produce infection.

- What distinguishes normal flora from infection?

  No. of microbes….. If the no. increases in a way that immune system can't control, then it's an infection.

- What is the sign of infection?
  - Inflammation (which involves many things in the body especially the immune system).
  - E.g.: if u have an infected wound, u can notice swelling (which is caused by penetrating neutrophils that produce infection).

- What happens if a patient comes to u with an infection?
  - You should take a swab and send it to the in order to identify the infection (causative agent).
  - (very basic steps , must be done in all patients).
  - Note : In U.K. a doctor is not allowed to prescribe an antibiotic before sending a sample for culture and indentifies the microbe. While here in Jordan, it can be simply prescribed over the counter: without a prescription (gives u *Zithromax* (azithromycin) → 11 JD's to make profit)

(الصيدلاني بيعطيك الدواء عكيفو بدون وصفة طبية، بتقوت عالصيدلية وقبل ما تخلص تحكي شو مالك بكون معطيك الدواء وبكون غالي عشان يربح) .

- Why to differentiate the type of microbe?

- To prescribe the drug with the narrowest spectrum so that u target the microbe without targeting the whole micro flora. (If you disrupt the flora, u will disrupt your body's homeostasis). So the drug with narrowest spectrum should be administered.
- Even if u give a broad spectrum drug it might not cover everything (y3ne it usually covers everything BUT THERE'S ALWAYS AN EXCEPTION).

- Remember that types of antibiotics :

- Narrow spectrum: act only on single limited group of microorganisms.
- Extended spectrum: covers more gram +ve & -ve BUT NOT EVERYTHING.
- Wide/broad spectrum:
    - Works on: both gram +ve & -ve bacteria. That's why :
    - Side effects : are more sense it work on normal flora too causing :

    a) Severe diarrhea .
    b) Super infection (Most Imp) : since it's killing all weak bacteria except the strongest which will survive causing another type of infection.

    - No. of dif microbes it works on: covers most of the bacteria not all. (E.g. MRSA which is resistant for all antibiotics except some like vancomycin).

- How does super infection happen ? (A Slide containing a cartoon about super infection)

Simple story: you're giving a strong/broad spectrum antibiotic → all weak guys without hats will die BUT ones with hats will survive → after 1-2 days of treatment they'll proliferate/divide (since the treatment is not affective against them) → causing another infection.

So what u did here is that u selected for this bacteria to live since u killed the competition, and now instead of treating this simple infection by this drug, U caused another infection on top of the previous infection.

- To sum up:

  administrate drug → kills normal flora → increases in no. of pathogens a resistant bacteria → Super infection.

- So how does super infection usually happen ?

  When u take a drug haphazardly. (اعتباطا، عشوائيا :P) .

- Examples to such cases :

  - Give a patient with simple tonsillitis an antibiotic (and he doesn't stick to it) :

    3rd day: kills weak microbes (but stronger survives).

    5th day: stronger microorganism causes super infection which is stronger than the first.

  - Clostridium difficile: (causative agent for pseudomembranous colitis)
    Now : no infection (high competition → low difficiles no.)
    Give antibiotic: infection (low competition → high no.)

  - Vaginal fungal infection: (usually post partum).
    After delivery we usually give an antibiotic → changes normal flora → causes genus Candida overgrowth → fungal infection.

- Antibiotic misuse :

  Don't use drug frequently, X miss doses, U must finish prescription. Because drug misuse is a community problem not a personal one (ALL OF US HAVE TO WORK ON THIS) or else bad infections will spread.

.

- When is it considered misuse?

  When it's not needed, like in viral infection.

- A study done by the center for disease control and prevention in the U.S : (slides)
  - It describes the no. of unnecessary prescriptions. (Green = unnecessary. blue = necessary).
  - Eg:

Common cold	Vs.	Other type which can be viral or bacterial:
*Viral infection which is common nowadays in Jordan. *People take antibiotic and they think they feel better but in reality it does nothing (with or without it your cold will stay for 1 week). *common cold: u shouldn't be allowed to prescribe drugs thought the patient will insist making u too shy to tell him that he doesn't need .		*Diagnosis: It comes to the good doctor to decide if this is viral or bacterial infection (by taking good history). * This also applies to (bronchitis, sore throat, sinusitis, ear infection) → usually is bacterial but can be caused by viral infection * EAR infection: Usually allowed to prescribe antibiotic because (70% bacterial),

- Drug prescriptions :
  - Canada / Australia / U.K. → drug X cannot be taken over the counter but with prescription.
  - Here → Over the counter and the drug might not be really needed because it's a viral infection (like common cold).

- 3 problems regarding drug misuse :

    - Saving the drug for future illness: next time you're ill ….. you look in the cabinet for any antibiotic and just take it without knowing it's type or the right time to take it or even if u can or can't take it.
    - Sharing someone else's drug (like taking it from your friend if you have sore throat).
    - Stopping the drug once you feel better (and that might be after the 2nd or the 3rd dose) and by not exposing the bacteria to this antibiotic for enough time you're selecting for the resistant type.

- So why is it imp to stick to the schedule? (if the doctor for example told u to take amoxicillin/augmentin/julmentin 2 or 3 times daily)

  Imp to reach the correct drug C_{ss} (steady state concentration) that is high enough to kill both (Weak + Strong) bacteria.

  Usually we give patients 4 to 8 times of MIC (minimal inhibitory concentration of bacteria : the concentration that will kill 50 % of the population of bacteria or the IC50 → measurement of the effectiveness of the antibiotic).

  So if we send a culture to the lab and the results were that the MIC for amoxicillin 50mg/ml we give the patient (50 X 8) = 400 mg /ml .

- Why to give (MIC * 4 to 8) not simply MIC ?

    - To keep the drug's concentration in the patient high enough to suppress any resistant organisms since they differ (but still having same general characteristics)….. keef y3ne?

      Eg: all staph aureus microbes (strains) have the same general characteristics but differ in their susceptibility to antibiotics from 1 person to another , or from a year to year.
    - To prevent a super infection that might be caused by the resistant type. If we give a low dose, we will keep the strong organism alive. This causes a superinfection.

- So warn the patient :
    - He must adhere to the drug's schedule (adherence) ….If he doesn't stick to the schedule he'll disrupt the curve of reaching the C_{ss} and will mess up his normal flora.
    - E.g. if the 2nd day he felt good (especially if it's bacterial infection) , he misses 2 doses → curve goes down → takes the drug again next day → this curve must be rebuilt from scratch→ and if he misses another dose the cycle is repeated. → So this fluctuation will never reach the correct C_{ss} and this will select for the strongest bacteria to survive.
    - Remember: it takes 5 T1/2 to reach C_{ss} …….. 3 T1/2 to reach 90% of C_{ss}.
    - To sum up: u need to keep the Cs_{ss} 4 to 8 times higher than the MIC (C_{ss} must be kept over MIC).
    - If you miss a dose, the steady state concentration will never be reached. It might be reached, but it will not be maintained. This will cause the drug to be less effective.

- Why is drug misuse a problem?
    - Drug becomes less effective and may not work the next time you use it.
      E.g.: - staph aureus 1940's : was susceptible to penicillin G.
      1950's: became less sensitive /susceptible.
      60's/70's: became resistant.
      Why did that happen? Because of the abuse of penicillin. (The more you use an antibiotic the faster you lose it (you will not be able to use it) → that's why nowadays they advise not to use any of the new drugs unless you really need them.)

        - Livofloxacin , lindzolin , Daptomycin → new & very good drugs .

      Livofloxacin / livoflox : v.good in hospitals and ICU. Now because of its over usage, it's starting to lose its affectivity/ activity , so in 5-10 yrs we might lose it. We can't afford that since we don't have antibiotics in the pipelines (y3ne ma fe backup antibiotics).

- Improper use leads to more resistant antibiotic bacteria (the more u use the more u select for the resistant types).
- Antibiotic bacterial resistance can be spread out through the community & from person to person.

➢ Therapies :

Antimicrobial therapies include: antibacterial, anti-filamentic, antifungal …..

➢ Prophylaxis:

Preventing infection (E.g. giving high doses of a drug to your patient before surgery to prevent/ protect him against infection. You don't want the wound to be exposed to a high number of microorganisms.

➢ Empirical (توقعي) : expectation. (we do it without knowing the causative agent)

- E.g.: your patient has tonsillitis , u send a culture to know the specific type of bacteria that caused this infection, but your patient is suffering and you can't wait for 3 days for the results to come , so you write an empirical prescription depending on what you expect to be the causative agent thought u don't really know the cause.
- V.imp in : hospitals where there are life threatening situations :
  - Septicemia or bacteremia
  - Meningitis: the patient might die in 1 -2 days so you have to write an Empirical prescription before (and until) the results come.
- When the culture comes back we change empirical therapy (in 3rd day in case of meningitis) to definitive therapy (where you identified causative agent) and you have the results for susceptibility tests in your hands to use the most effective antibiotic (the one which this bacteria is most susceptible to). The lab will send a sensitivity test. This test should be used to identify the most effective antimicrobial drug against the particular microorganism.

➢ Preemptive/ pre-symptomatic therapy :

- Imp in: viral infections → because treatment is very complicated → so better to give the antiviral drug before symptoms appear.

- Usually for viral infections not bacterial.
- For whom: if a house has an immunocompromised patient and another person that has viral infection. You feel that this immunocompromised person has the infection but yet without any symptoms appearing , so to protect him (or to reduce the symptoms of this viral infection when they appear) u give him the antiviral drug.

➢ Post-treatment suppression therapy: (antiviral – antibacterial – antifungal).

- Reduces the load of the Infection.

E.g.: you treated a patient with viral infection and reduced the no. of particles from 10^12 to 10^3. Although the patient is treated now, you want to make sure that there won't be re-infection.

- For whom? (Patients with AIDS – immunocompromised patients: who take chemotherapy for cancer) since their immune system is weak we want to use another force to prevent re-infection.
- Post –treatment suppression is <u>not</u> common practice for normal patients but for immunocompromised ones.
- Note: Common practice→definitive therapy, empirical therapy, prophylaxis therapy.

➢ Bacterial resistance mechanisms : (Different)

- Changing the target of the antibiotic.
- Producing an enzyme that inhibits the action of the antibiotic.
- Increasing the pumping out machinery (efflux pumps)

(IN DEATAILS)

- Producing an enzyme that inhibits the action of the antibiotic :

E.g. Penicillinase cephalosporinase, wide spectrum beta – lactamases.

- Mutation towards the target of the antibiotic.

E.g. MRSA : won't respond for all penicillins & cephalosporins since it changes their targets (Both antibiotics have the same target →so a small change in the amino acid sequence changes the target).

- Production of machinery to prevent the accumulation of the drug :
    - Usually p-glycoprotein: a Pump found in our bodies that pumps drugs out
    - Also found in microbial cells: once exposed to the drug the no. of those pumps will increase (within the cell wall) → increases pumping out of the drugs.
    - Usually this mechanism is against the antibiotic: tetracycline ➔ most of the microbes are resistant towards tetracyclines) .
    - Not all antibiotics are targets for this pump.

- Are there Multi drug resistant microorganisms ?

  Yes, a lot (they may involve any of the previously mentioned mechanisms) .

- If you are giving a drug which is supposed to be killing all types of microbes and there's no improvement (your patient isn't responding) although susceptibility tests show those microbes are susceptible to this antibiotic …. why?

  He has a form of this multi resistant types in his body, and by giving him the drug you're selecting for this type to increase. ➔ Rare cases.

- Antibiotic targets:
    - Cell wall (penicillinases , cephalosporins, vancomycin ,bacitracin).
    - Protein synthesis (tetracyclines , chloramphenicol , Clindamycin aminoglycosides,erythromycin)→ inhibits protein production
    - Works on RNA polymerase: chloramphempicin , chloramphen → usually in TB.
    - Inhibit Gyrase enzyme in bacteria (similar in the way it works to topoisomerase enzyme in humans which unwinds the DNA): quinolones (most imp group of gyrase inhibitors).
    - Anti metabolites: Inhibit DNA synthesis.

- Why do antimicrobial drugs have very wide therapeutic window?

They target structures not found in human bodies (C.wall , gyrase (dif from topoisomerase), protein synthesis & polymerase & DNA synthesis which are different from humans).
E.g. penicillin: usually you can have up to 10 tablets without having that severe toxicity. (يلا مين يجرب) :P

Sorry for any mistake ☺
"Dana Qasrawi"