Medical Committee
The University of Jordan

PHARMACOLOGY

Lecture No.: 25

Doctor Name: Dr. Malek

Written By: Areej Jaber

SHEET

SLIDES

DONE BY: ISSA KHASHAN

ANTIBIOTICS

**** This Sheet Will Cover Slides From 1-15 ****

You have done with Dr. Yacoub the autonomic nervous system, which is the best ever system you can do .Because the **ANS** is part of all systems and it is gonna be repeated and repeated and repeated all over again.

You're gonna take it in **cardio**, **respiratory**, **gynecology**, **urinary tract infection** and even in **GI** system.

You have to master it; If you don't understand it, you will get problems in pharmacology later. Understand it well from now; study it from the book or from anywhere else to be good in ANS.

Away from the pharmacology, we can go to sth called the chemotherapy.

The **chemotherapy** isn't a real pharmacology; because the stories of homology (tissue specific issues and tissue specific receptors) >> all aren't ideals .

We have different targets, and the different targets can be either bacteria, virus, fungi or even cancer cells .All of these have structures that **differ** from human cells.

So this drives us to something called **chemotherapy** and it isn't a "chemo – " . All the Antibiotics, anticancer and antivirals are called chemotherapy.

At the end of the day, in the Introductive Pharmacology, we're gonna speak about Antiviral, Anticancer and Antibiotics.

Antibiotics are very **important**; actually you cannot be a doctor without dealing with antibiotics, because infections can be related to any disease. Whenever the Immunity goes down, the patient will be manifested with many infections .so you need to deal with it.

The problem in dealing with bacteria , virus or fungi that they **can manipulate themselves.**

So the way we do it today will not be the way we do it the next five years. At the time you will be graduated from JU, after 4 years insha2allah, may be the things we're gonna talk about them now, they're gonna be **changed**.

Written by Areej Jaber

Why it might be changed or it might be different?

- Because the **resistant** is getting more and more.
- And if you know **NATURE** "the best ever scientific journal .There is a big , big title always there which is " We are losing the battle against the microorganisms"

Ebola is one of the stories :

We are producing **new strains** of microorganisms , and those new strains need **new drugs** , and the drugs we are dealing with now will not be used any more after 15 years

>>This is the **beauty of antibiotics** , so you need to **understand** it **VERY WELL**.

We are not here to memorize drugs (unfortunately ,you are compelled to memorize them ://) ,We need **to set the principles of antibiotics treatments** .That's why you need to be here even if there is no marks for attendance "7o9'or & 3'eyyab" .

Antibiotics will not be given to you any more next years, so you need to know them very well. So let's deal with them **step** by **step** .. ☺

Antibiotics

Antibiotics : drugs & compounds that **destroy structures** within bacteria (you have done some of them in microbiology) , and they don't really attack anything in the host.

And that's give the Antibiotics a **"wide-therapeutic window**" so usually you don't have side effects of antibiotics EXCEPT diarrhea (the next minutes we will know why) .

Logically speaking ,We don't have these issues of receptors because the receptor "structure" that will be attacked by the antibiotic is not found in our bodies (in the host) ,but rather in the microorganisms , so they " antibiotics" destroy things present in bacteria not present in human.

**** You have to understand two other words, which are very important to you as a doctors : **Disinfectants** & **Antiseptics** .

❖ What is the difference ?

Simplly , **Disinfectant** is the smell you will get whenever you get to hospitals . This is almost phenol ; you will smell phenol.

- →Something called phenol based disinfectant: it is a liquid that is used to disinfect floors, walls, machines and benches. We need to disinfect these things.

As for **Antiseptics** ; you have hygiene (many of you use it) that it is an antiseptic , so you have either iodine or alcohol that you use to disinfect your skin .

In clinical practice, as a doctors, we really need to use both of these "**disinfectants** & **antiseptics**" ; the disinfectant isn't your job , it is the job of the cleaners & hospitals. But antiseptic is your job.

If you enter any hospital, you will find bottles of antiseptics. You really need to use them " those bottles" for **two reasons** :

1- to avoid cross contamination .

2- to reduce the contamination to your patient " not to contaminate your patient with your hands" .so you really need to use them.

In theater (in surgery) : we apply this (after a lot of studies in the university of Jordan , al hussain center and everywhere), we apply things for disinfection protocols ; the number of the survivals were more as a result of using disinfectant and it had a good impact on the health of the patients.

Always remember : Always try to disinfect yourselves

So always you need to use **1**-Disinfectants ,**2-** Antiseptics and **3-** Antibiotics. Remember these **three** words very well ☺ .

:: BACK to the base of science ::

Science says that **1-** antibiotics are an indication to treat bacterial infection ..

2- we have many microorganisms that live in all over our bodies; in GI tract , for example, there are millions , billions of microorganisms . Also in respiratory tract and in urinary tract we have a lot of microorganisms .

Why we don't get infected with those microorganisms ?

Simply , we have to understand the world of load ; **load** is the **limit** (الحدّ) . if those microorganisms are multiplying more than the load "it reflects how much your immune system can deal with microorganisms " ;if you exceed that limit " load" , you will get an infection . And the size of infection usually returns to have an inflammation (BY IT : you gonna get fever , pain and swelling)

If bacteria multiply faster than the body's defenses can destroy them, *infectious disease develops with inflammatory* signs, e.g. wound infection or urinary tract infection.

SO the **real reason** is , because the number of those microorganisms in our body is very low " below the limit or the load ", so the immune system can deal with them. If the number is high ,then infections will occur .

Another thing we really need to touch , which is **ideality** or **ideally**

- We , in Jordan, are far far away from ideality :O , Why ?!

Some of you have antibiotics in their bags

- In US , England , Canada , anywhere else ; an antibiotic to be prescribed you need to send a **culture to the lab** and prove that you have sent that culture to the lab.

Simply speaking I will read "from slides" :

- **Ideally, before beginning antibiotic therapy, the suspected areas of infection should be cultured to identify the causative organism and potential antibiotic susceptibilities.**

- Antibiotics are NOT over the counter drugs (drugs that don't need prescription)
- **I**n Jordan, **Antibiotics** are over the counter(**OTC**) drugs (or even they are under the counter :P you can find it in the safeway :O) antibiotics , here, are **everywhere** where ever you go , it is like a food of every day !! :P .
- This is bad ,so we are trying hard to make the antibiotics prescribed , we tried with pharmacies and doctors so as not to give antibiotics without prescription . But all fights against you that is because of money !!
  { **Money Talks And Nobody Walks** }
- **C**ulture will change the way , the resistant of the microorganisms in our countries , we will see why later .
- So **Don't prescribe Antibiotics without prescription** except you do a culture or if you are sure that your patient has a bacterial infection.

:: Back again to the micro :: this is the beauty of pharma "touching everything ".

We have **different types of Antibiotics :**

- **N**arrow spectrum : very simple , works on limited number of microorganisms { for example, 5 G+ve , or one G-ve }
- **B**road spectrum : more wide , working against G +ve & G –ve .
- **E**xtended spectrum : working against a lot of microorganisms including mycoplasma , spirochetes , G+ve , G –ve .

The **Question** is : <u>how this is releated to pharmacology</u> ?

- The *more the extended* spectrum antibiotics we use , the *more the side effects* you're gonna produce
  Here the side effects are different from other drugs, they are **linked to two things** :

1- the more extended spectrum antibiotics we use , the **more diarrhea** we have . (because antibiotics cause disturbances to normal flora which cause diarrhea) [a lot of you have took Augmentin or any other antibiotics , but only 20% of you might have diarrhea; but the more you use Augmentin , the more you have diarrhea]

2-the more extended spectrum antibiotics we use , the **more the antibiotics we lose** " we lose the bottle against the microorganisms "so microorganisms will win over us if we use the extended spectrum antibiotics more and more.

In hospitals , when dealing with infected patient , the easiest way to treat a patient is to prescribe the most extended spectrum antibiotic :O ??! so by this way of thinking we cover a lot of microorganisms and that's the **worst** way of thinking.

- **Why** is it the worst ? → **Because** we are producing more resistant microorganisms in the future .

Dealing with microorganisms is a **community problem** ,it is a world problem . An example is **E**bola and its Bad effects . Also **S**almonella , past year, in the north of Saudi Arabia.

In Jordan , before one month a lot of people got Gastroenteritis .Now **E.coli** , in Jordan, is resistant to many antibiotics because of taking antibiotics *without prescription* .

:: We Avoid Prescribing Extended Spectrum Antibiotics :: To Avoid Producing What Is Called ' **SUPERINFECTION**' or SUPRAINFECTION

➔**W**hat **i**s **m**eant **b**y **Super Infection** ?

First the doctor want to explain ' **competence**' , For example : if we 'all' were sitting to eat from one tray or one dish of mansaf , every one of us might get one or a half of bite ONLY .

And , back to microorganisms, this 'competence' will keep them down , lazy, there is no food ,So when we give antibiotics most of those microorganisms are gonna die , and resistant microorganisms will stay alive and multiply more and more and infect us.

- ☒ so **Dealing with microbes with antibiotics will not work** :: An Example that will simplify this ::
  if you are taking an antibiotic " extended one- broad spectrum" , you will kill the normal flora & lead to Over Growth Of **Clostridium difficile,** which is resistant to most antibiotics . So you are taking antibiotics for an infection " for

example : respiratory tract one ; like tonsillitis or sinusitis " and you will end up with another infection ' usually worse one' **Why** ??

- **B**ecause you are **S**electing toward the Resistant and produce **C. difficile** that can cause diarrhea and life-threatening bowel inflammation. This is superinfection .

::Another example :: is the administration of broad-spectrum antibacterial drugs can select for the overgrowth of fungi .

Food is there , so Fungi ,spirochetes and bacteria all they **compete**. so if you're killing the microorganisms , one of the resistant type (means that antibiotics doesn't work against it) "fungi for example" will be more dominant and produce what is called **Candida** [thrush in mouth will cause it].

::**Another example**:: In Postpartum "after delivery" we give a Broad spectrum (Not Extended) antibiotic which will kill the microorganisms , that's because there is a wound and we want to prevent the infection in it (by giving antibiotics) . Those antibiotics will kill even the normal flora in the vagina , simple ? this will lead to a problem :

Which is vaginitis , it is called **postpartum vaginitis** "because it is caused by the antibiotics that kill the normal flora resulting in dominance of fungi". But you don't have other choice , you need to give antibiotics .

Vaginitis, here, is an example of **Superinfection** that happens because of **loss of competence.**

- to reduce the super infection frequency we need to deal with the narrowest spectrum antibiotics . **So, the most narrow-spectrum agents appropriate to the infection should be administered .**

Narrowest Spectrum Antibiotic **LEADS TO** Less Microoganisms You Kill **LEADING TO** Less Competence You Lose .

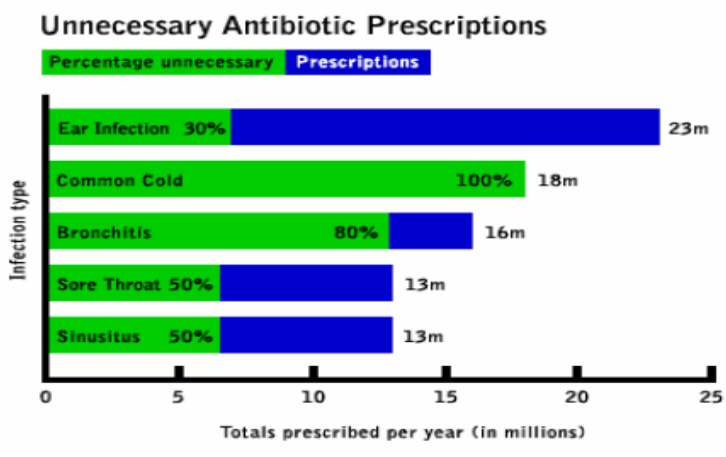
Antibiotic Misuse :

We **don't abuse** the antibiotics to get euphoria. We use it **not intentionally** we want to use it . We want to use it in the proper way, but we lack knowledge.

:: **For Example**:: Common **FLU** is found everywhere in the community and it is **99%** due to **viral** infection.

But the problem that 80% of Jordanian community are taking Antibiotics for viral Flu .

Look at this , in USA .. This is how they prescribe drugs according to the culture



More than 50 million unnecessary antibiotic prescriptions are written each year in the United States for patients outside of hospitals, according the the Centers for Disease Control and Prevention

According to **common cold** : they have 18 million prescription every year of unnecessary antibiotic . This is what we really do ,here in Jordan also .And we must avoid this prescription ; WHY ? because common cold is mostly a viral infection ..

So when we can prescribe antibiotics ? in **otitis media** infection , for example. Because it is mainly caused by bacteria so there's no problem in giving antibiotics .

In the case of **Bronchitis** we shouldn't prescribe antibiotics , because it is mainly caused by viruses ; but we do unfortunately.

As for **sore throat & sinusitis** , they are 50% prescribed unnecessarily ; and those are related to pathology ,we will deal with them later .

Simply speaking ,that most of our community infections doesn't really need an antibiotic >> This What Called **MISUSE**

:: **Another problem**:: of misuse , related to the kinetics of antibiotics is that : we need it but we're taking it incorrectly ' Not in the Ideal Way ' .

--- Go to your small pharmacy in your house & take any of the antibiotics that is taken before; You will find out that you've stopped the medication without finishing the whole coarse :O

- **stopping the medicine when you feel better - not finishing the prescription**

For sure you will feel better , because you have viral infection and it needs 3-5 days to disappear ;and you will start taking antibiotic at the 3rd day and at the 4th day you will feel better , so you will think this is because of the antibiotic and you will stop taking it .{this is a community problem and some of you are doing like this }

- **saving antibiotics for a future illness**

This a problem mostly in western countries because they can't take antibiotics without prescription , so they get it once by prescription and keep it for next time . but ,here in Jordan, we get it easily without any prescription.

- **sharing or using someone else's medicine**

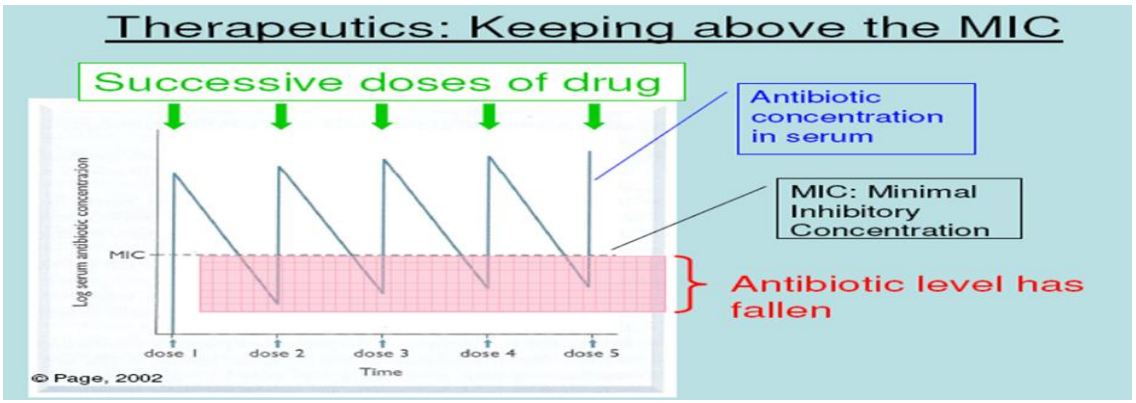
:: In a scientific way ::

In Science there is sth called **MIC**

'**M**inimal **I**nhibitory **C**oncentration'

We need to keep the drug in the blood over the MIC , over By how many times? it depends ; sometimes we give it over 4 times Greater than the MIC OR sometimes by 8 times , it depends .

- ✓ It **depends on** how much the resistant subtype is frequent in your community.



:: **For example** :: you go to the pharmacy and tell the pharmacist that my baby has an otitis media {you already have a prescription from the doctor , which is to give your baby Augmentin '800 mg' } , but you found in the pharmacy that there is 675 mg , 375 mg , 800 mg.

** **W**hich one **S**hould I take ? For sure , **the one the doctor had prescribed**.

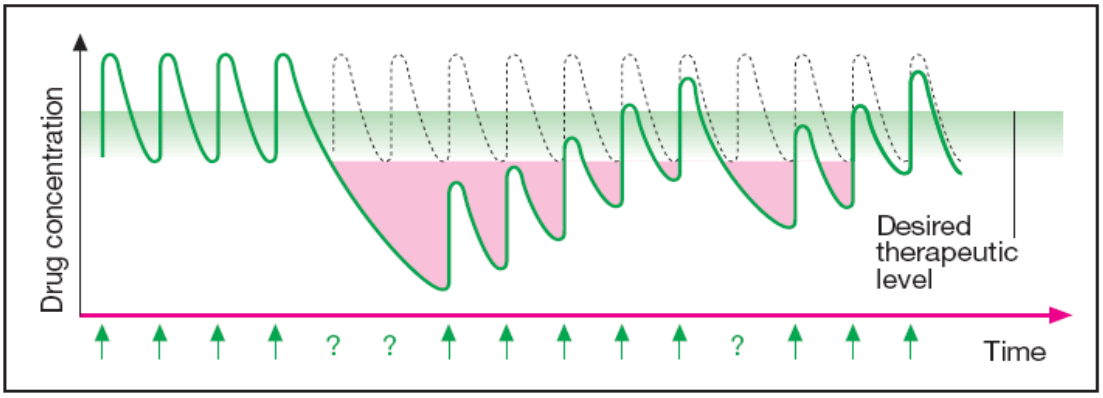
NOTE : why there is high doses ?? >> Because High doses of Augmentin are the only one which are working these days ; those high doses were not present in the past; Because Streptococcus pneumonia becoming more resistant ,

We have to keep **MIC** higher and higher , simple ?

So we kill even the mid resistant not only the totally resistant ; we call it mid-resistant .

[So Our Speaking Now]

We need to keep our level of drug high and high enough according to the situation you are in, but if you miss antibiotic dose , after 4 or 5 half-lives you will lose it , simple ? , why you will lose it because simply if you miss 2 doses the level of the drug within your body is gonna go down. AND trying to rebuild it but if you miss another dose again, so you will be always under The **MIC** and that's how streptococcus pneumonia built its resistant now .



:: **For example** :: people who are taking Augmentin for **streptococcus pneumonia** let's say and they don't take it Longley (as it has been prescribed) . So what are they doing really ? They Are **Selecting** for the **R**esistant type.

**** So** you are killing the weaker type and the resistant one will be kept , and next time the same drug for the same type of infection may be <u>Not Work</u> ! *** This is misuse***

- **A**ccording to the **C**ommunity : there will be spreading out the resistant type; by killing the sensitive type and keeping the resistant type all over

You as a doctor, you need to tell your patient to <u>adhere to the prescription</u> ' whatever it is ; "once or twice daily for example".

So never take 3 tablets together or only once daily "when it is prescribed 3 times daily for example ".

>>> **It Is A Community Issue , A Big Problem** <<<

✓ Why is Antibiotic Misuse a Problem?

(1) Antibiotics become **l**ess **e**ffective and may not work the next time you use them.

(2) **I**mproper use of antibiotics leads to more antibiotic resistant bacteria.

(3) **A**ntibiotic **r**esistant bacteria can be spread throughout the community and from person to person; And this is bad .

::For example ::

Resistance to one of the most widely used antibacterial drugs for the oral treatment of urinary tract infections caused by ***E. coli*** – fluoroquinolones – is very widespread.

Ciprofloxacin is one of the beautiful drugs that is used against the E.coli , and it was mainly found to fight the E.coli but the problem that we really used it widly.

{ so We misused it , use it impropriate } , so we produce →E.coli resistant toward fluoroquinolones .

HOW ?!
By Keeping The pressure on , the microorganisms changed ; also with the story of competence >>All these issues will Kill the good ones and keep the resistant type.

- ✓ The percentage of the **E.coli** resistant to fluoroquinolones in the **UTI** is about 25% even if it isn't that high , it is bad. When the resistant starts to flow it will end with 100% . ** you have to understand it ** .
- ✓ By the time you finish the antibiotic, you will surely have more resistant-for-Ciprofloxacin-E.coli
- ✓ That's why Augmentin will not work on streptococcus of the otitis media

::**Another Example**::

Anthracis are microorganisms , not bacterial ones but have a similar shape to them . After September/11, there had been envelopes sent that have anthracis, and when a person opens the envelope, anthracis will flow on him, causing the him to have an infection and therefore die.

This happened with 2 people in the US. However in a certain state, people there knew that the anthracis can be killed by Ciprofloxacin, so the American community in that state kept on buying flouroquinolones. So Ciprofloxacin got really used in that state, producing high pressure on the E.coli and thus resulting in a wide spread of resistant-to-ciprofloxacin-E.coli in that state, because people there used that antibiotic for like 2-3-6 months.

Therapies

** This is an important ..

What **types** of therapies are **A**ntibiotics ?

1- **Prophylaxis** : the easiest **,**

-A)→ when the patient with 'Endocarditis' goes to the Dentist ; this infection 'Endocarditis' may happen to you by the procedures the dentist will make it to you , so we need to protect your heart by giving you a drug ' an antibiotic ' to keep the load down to prevent infection . We Give 2 gm of Amoxicillin before two hours of the procedure .

-B)→ In a theater surgery , you need to protect your patient by giving him \ her one gm of cefazolin. *names are not important*

-C)→ cancer & AIDS patients , who are immuno-compromised (we Give them bad drugs that kill most of the bone marrow cells → in the case of cancer), so they need to be prophylated against any infection by prophylactic antibiotics , antivirals , antifungal..

Similar to them, are patients who have transplanted a kidney (we already give them an immune-suppressant), so we need also to prophylac them to protect them from getting infected.

** Forget about the names of the drugs , Not Important **

2- Empirical :it means 'blind' ; we don't really know the microorganism & we're gonna use antibiotics . we have 300 or more of antibiotics , which one I will use ?

Empirical Depends on : signs ,symptoms , X-rays . what's really common in the community .

The hospital is the land for microorganisms, so you need to know the abundant microbes in your hospital that may cause that certain infection. So you'll prescribe an antibiotic without knowing the exact microorganism.

When I will know the microorganism ?

when the lab will send you back the result of the culture you have sent it before. and that's gonna take 3 days ; so you now know the microorganism and you have a defined microorganism so you Can Now Give A **Definitiye Therapy** .

3- **Definite therapy**: it is very simple , it is done after culturing and receiving back the lab result. Then you prescribe the antibiotic which showed a positive result on the susceptibility test.

::**For example**:: if I have 5 or 6 microorganisms that cause pneumonia ,then how to treat pneumonia?! >> This Will Differentiate between Good & Bad Doctors ☺

** The medical therapy needs a good , good knowledge of antibiotics , so we need to teach antibiotics ; otherwise you go and read from the book And Memorize Them :O ,,, But Instead We Need these lectures **to understand the medical therapy** .

:: Back to Empirical → we will give the antibiotic by **suspecting** without knowing the real microorganism …

BUT The **Question** Is : Will We Change the therapy when the result come back from the LAB ?

THE Answer is **YES** ☺ ;

Put in your mind that almost **the first therapy** " the empirical one" is **right from the beginning** .

4-**Post-treatment suppression therapy**.

After we treat we suppress ; why we need to suppress ? Because those patients has **a history of recurrence**, especially in the UTI .**For example** : some ladies have UTI every month or more than 3 to 4 times a year .we treat the infection by giving her ciprofloxacin with high doses ; then we

keep her with low doses of it (so as not to produce high selection & to keep pressure on virus) up to 6 months if there is recurrent . So We **Prevent the microorganism to Get Over the Limit "Load".**

Another example is aphthous mouth ulcers [الحمو فى الفم] which are becoming frequent (more than 3 times a year), and we treat it and then we keep administrating low doses of the antiviral.

- Microbes might develop resistance, but we try to prevent this by administrating low doses of the durg.

Bacterial resistance mechanisms

***** you have taken them in micro.....

The four main mechanisms of resistance include:

A. Production of an enzyme that inactivates the drug **: B-lactamases & penicillinases** (extended and narrow)

B. Mutations in the target macromolecule (Receptors): Binding to penicillin change ,in **MRSA** "**M**ethicillin **R**esistance **S**taphylococcus **A**ureus "

C. Induction of mechanisms to reduce accumulation of the drug : it is similar **to P-Glycoprotein** , it will pump the drug to the out of the cell .

D. Multiple drug resistance involving all these mechanisms : it has a combination of all of these , that is really bad we can't treat the patients with this type , that is gonna make them really suffer .

** The spontaneous rate of mutation in bacteria is very low; about 1 in 10 million cells per division will be a mutant. → it **means** : it is not mutated during the therapy . That is good ; except : pseudomonas aeruginosa. We deal with it differently , we need combination of therapy .

Whenever you see green pus in your patient , this is caused by pseudomonas aeruginosa , bad one .

** The clinical difficulty arises when the infecting bacteria are already drug resistant.

GooD LucK