Medical Committee
The University of Jordan

PHARMACOLOGY

Lecture No.: 1

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Pharmacology

Pharmacology is considered to be a difficult subject due to the abundant amount of new drugs created every year; as we need to know each and every one of them. To be honest we do not need all of the drugs that are found in pharmacies since they are there to bring up a net profit for pharmaceutical companies.

New drugs are not necessarily better than old drugs. For instance if a new colleague joins our class it does not mean that he is better than us nor he is worse than us as we do not know anything about him yet. So be careful about new drugs as we know little about them especially their side effects. As they (research centers) did not have enough time or enough sample of people to test the new drug and its Adverse or Side effects on them. This is very important for the future as you start practicing medicine some people will come and tell you that this new drug has no side effects. This is a **big lie**, as we don't know about new drugs yet, we know little about them.

Basic Definitions of Pharmacology:

1-Pharmacology: a- Pharma- : drugs

b- cology- :- science

Thus **pharmacology** is the science of drugs. A **drug** is a chemical substance that that affects living processes and modifies an already existing function. It changes the function by an increase or a decrease, stimulates or suppresses, enhance or block a living process which is usually a biochemical or a physiological function without creating a new function. As there is no new function created by drugs; if you don't speak no drug will let you speak. If you have a genetic abnormality and you have an absence of enzyme or enzymatic pathway, no drug can restore that enzyme or pathway for you. Thus drugs don't create new functions but only modifies already existing biochemical or physiological functions.

Pharmacology deals with almost everything about the drugs starting from the history of drug (how it started), source (most of drugs originally came from plants but now they are synthesized in the labs, some are natural in source but modified in the labs; drugs are synthetic and semi-synthetic), physical and chemical properties of the drugs that are very important, the absorption (entrance of the drug into the body and circulation), distribution (how it goes into different tissues and organs of the body), metabolism (biotransformation; how it is transformed from one chemical substance to another), how it is excreted out from the body, the action of the drug in the body, the adverse reactions (actions that are not desired), the toxic effects of the drugs, and the therapeutic uses of the drug all of these come under the science of pharmacology.

Some part of pharmacology does not deal with you; as they do not aim to affect any function in your body but rather aim to attack and stop growth of or destroy microbes and cancer cells or. These are also considered as a part of pharmacology.

There is a difference between adverse effect and Toxic effect. The adverse effect is the effect that we do not like about the drug and it is also called side effect. However the doctor does not like the word "side effect" as it creates a mentality in patients that these unwanted effects are not important however some of them (adverse effect) in some cases can cause death. Now the toxic effect is also undesirable effect however it is the effect which occur if you exceed the therapeutic dosage (doses that are suitable for treating the disease). Now despite of using the therapeutic dose you may have adverse effect as these are expected from the pharmacological effect of the drug itself, however when you tale a higher dose exceeds the dose limit you will get effects called toxic effects which are dangerous. In other words if you take too much of the drugs it will become a toxin rather than a drug. All drugs are toxins but not all toxins are drugs, as most of toxins are not drugs.

2- Medical (clinical) Pharmacology: "this is what concerns you as a doctor in the future" Drugs that are used for three areas which are diagnosis, prevention, and treatment of diseases.

Drugs are used in diagnostics when facing a two possibility situation (i.e. certain cancer cardiac arrhythmia) where if you use a drug and a patient improves then you know that you are on the right track or if the patient momentarily gets worse or exaggerates its effects you will know that the patient has the other diagnosis but this exaggeration will not last long because the half-life is short. They usually use drugs with very short half-life in order to limit the bad effects if the occur.

Also drugs are used for diagnostics in myasthenia gravis or the complication of myasthenia gravis. Sometimes the disease and its complication of the same disease caused by the drugs have the same symptoms and in order to differentiate between them we use clinical drugs. They administer a short half-life drug to a patient if he improves then it was caused by the disease, if he gets worse then it will be the effect of the drug but it will not last long.

3- Toxicology: Is part of pharmacology. It is the aspect of pharmacology that is concerned with the adverse effect of drugs, toxic effect induced by drugs, household, environmental toxins, industrial toxins, poisonous animals and plants. It is identifying symptoms, naming the toxic and finally after diagnosis starting a treatment. Clinical toxicology it is the treatment of disease in humans. General toxicology could be on animals...etc.

There are two general principles that we need to know about:-

1- All substances can under certain conditions be toxic.

There is no such thing of a harmless drug or adverse free drug, these who claim such a thing are liars. Even water which is essential for our bodies if it was taken at excessive amounts and wasn't being eliminated at a fast rate it would accumulate in your body causing hypotonicity in the blood causing lysis of RBCs and you may die. Moreover it may cause edema, accumulation of fluid

in the brain increasing the intracranial pressure which will press against the nerves and it may cause death. Another example is oxygen as if the O2 intake was more than 21% (normal oxygen concentration in the air) it will cause oxidation of the lungs thus destroying of your lungs.

This also applies on drugs as there is no 100% safety on drugs. However there is a drug that is safer to a certain patient with certain medical condition due to certain characteristics. The same drug would be considered less suitable for another patient. Thus there is no absolute safety on drugs.

2- All dietary supplements and all substances promoted as health-enhancing should meet the same standards of efficacy (effect and safety) as drugs.

Sometimes when you enter a pharmacy you may hear that some substances of plant origins set at high prices claiming to be directed at certain diseases and are better than drugs since the latter are chemicals while the former is natural thus there are no adverse effects that can come from it. Again this is a big lie. There is no such thing as plants are safe as there are some poisonous plants. Moreover, drugs are usually tested giving that a drug to reach the market would require 15-25 years of research and experimentation in test tubes and on animals and then humans. Never the less, we still don't know all of its adverse effects.

These processes don't happen with dietary supplements at all. It comes For instance fro, some person saying that pumpkin seeds are suitable for prostate so they will concentrate that material and would store it in a capsule form and set it up at high prices in pharmacies without any evidence for its action. There should be researches and studies to back up their claims and to identify their adverse actions. Also they are not registered as drugs in any country.

3-Pharmacotherapeutics: Is the use of drugs in the prevention and treatment of disease (or the medical uses of drugs).

4-Chemotherapeutics: Is the use of drugs to stop the growth or kill microorganisms or cancer cells.

5-Pharmacogenomics: The relation between the individual's genetic makeup to his/her response to specific drugs (entire genome).

6-Pharmacogenetics: Interindividual variation in drug response that is due to genetic influences (specific gene).

In both last cases it is the response of different people to the same drug. As one would benefit the other would not have any effect on him while a third person may be harmed with it. If the response differences of a person to a drug are controlled by the whole genome then it is called pharmacogenomics while if it is controlled by a specific gene it is called pharmacogentics. Individualization of patient therapy depends on this topic.

What is individualization of patient therapy? To give the dose that is suitable for the patient.

For instance a certain drug leaflet may recommend 250-500 milligram every 6 hours. We do not take the average of the recommended dosage but rather each person benefits from a specific dose and that depends on variable factors such as size, body composition, health, and diseases. Thus we consider what is suitable for this particular patient in order to have therapeutic effects and to avoid adverse effects.

Drugs generally have predictable and unpredictable (unusual) adverse effects. Predictable effects are usually extensions for the pharmacological effects. For instance if you have a drug that is responsible to lower your heart rate within the normal range this is therapeutic effect but if it goes below normal range it cause bradycardia. If the adverse effects are unpredictable to occur from the pharmacological effect of the drug then it is called idiosyncratic reaction. Idio- means strange.

7-Idiosyncratic drug response (reaction):

Unusual response, infrequently observed in most patients. It is usually caused by genetic differences in metabolism of drug, or by immunologic mechanisms including allergic reactions.

We can say that this adverse effect is common when it is one percent and more. When talking about a rare adverse reaction it is less than one percent. It is a serious matter as in the past they would draw all of the drug supply out from the market as it may led to death or aplastic anemia. They found later some of the answer for the causes however they did not figure out all of the reasons behind this though. Sometimes they associate these cases due to genetic abnormalities in metabolism or elimination of the drug and the body won't be able to get rid of the formed products of these drugs and they would accumulate in the body. Thus it may cause a person to form antibodies against them and forming an immunological reactions and allergic reactions and so on. Still there are reasons that we don't know of idiosyncratic reaction, what we need to know is that there reactions are rare, unexpected, cannot be predicted, and could be serious.

8-Tolerance:

Is a decrease in the responsiveness to the drug with continued drug administration. The effect of drug will be reduced and you will need a higher dose.

For instance, you are hypertensive and you use a drug to maintain normal blood pressure, after years of usage of that drug, the usual dose will not be enough then you will either increase the does or change the drug.

9-Tachyphylaxis:

Similar to tolerance but it is more rapid. It is accelerated tolerance (seconds, minutes, few days). However the tolerance is in weeks, months or years.

Each one has its own mechanism which we will discuss later on in the semester.

Another mechanism for tolerance is when you take a drug for hypertension you will have low blood pressure thus the body will retain more water increasing blood pressure. You take a drug that induces heart rate the body will have a reflex to increase the heart rate so that will reverse the effect of the drug. As a reflex mechanism or a compulsory mechanisn in order to correct the situation, as the cells feel that this chemical is foreign and not part of the physiological balance, there is a reflex to the action of the drug and it is usually the opposite to compensate for so you may have the tolerance for the drug. It is a normal response not for every drug however it is for every person; meaning that if person A has tolerance to drug C then person B also will have tolerance towards the same drug. Moreover there are drugs that bodies normally does not create a tolerance towards to thus nobody has tolerance against them.

Areas of pharmacology:

1-Pharmacodynamics: the dynamics or the action of the drug wether we like it or not.

Is what the drug does to the body, which includes the biochemical and physiological effects of the drug, including the mechanism of action, interaction with receptors, pharmacological effects, therapeutic uses, and toxic effects as well as the adverse effects.

2-Pharmacokinetics: movement of the drug.

It is what the body does to the drug; most of them are foreign to the body so the body will react with them. It deals with absorption, distribution, biotransformation and excretion of drugs.

If you take one dose of a drug it will act for a few hours maybe a day and then it will disappear due to the body metabolizing it and then getting rid of its byproducts. Part of it is compensation and other part of it is natural and follows the law of mass action. Law of mass action is the randomness movement of substances as in dropping an ink in a flask containing water after a while the whole flask would be colored, similarly when a drug is administered in the body it will move randomly if it reaches an eliminating organ

it will be eliminated and if it reaches a tissue (organ of action) with receptors for this drug it will act on it producing it effects. If it goes to the liver the liver would metabolize it. If it goes to the kidney the kidney would excrete it. If it goes to the receptor it will bind to receptor and produce its effects.

1-Absorption: Is the movement of drug molecules from the site of administration into the circulation.

It does not matter how you intake a drug either orally, rectally, subcutaneous, or intravascular. Movement of the drug from the site of administration to the circulation is called absorption.

2-Distribution: Is the movement of drug molecules from the circulation to tissues and between different parts of the body.

For instance, if you take a drug that is lipid soluble it will accumulate in our body fat due to its affinity (lipid soluble), the doctor said :"birds with same color flock together" or . الطيور على اشكالها تقع"

If you stop the administration of the drug then equilibrium reverses it will get out from the fat into the circulation and distribute to other tissues.

3-Biotransformation: Is conversion of the drug from one chemical structure into another by the action of metabolic enzymes (metabolism). When changing a drug structure into another molecule it may lose function because molecules decide the binding to the receptor and they decide the chemical properties of the drug. So when the molecule structure is changed, the effect of the drug in the body will be changed.

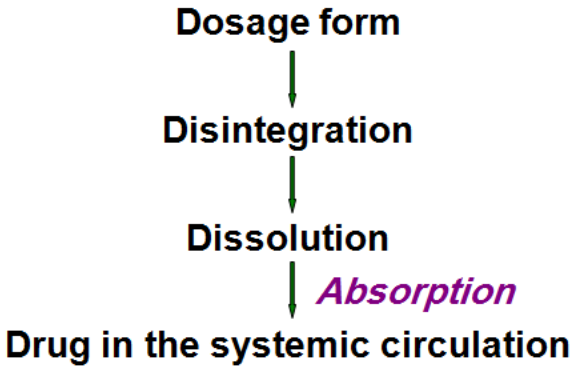
4-Excretion: Is the movement of drug molecules out of the body. For instance it is the elimination of bile and urine.

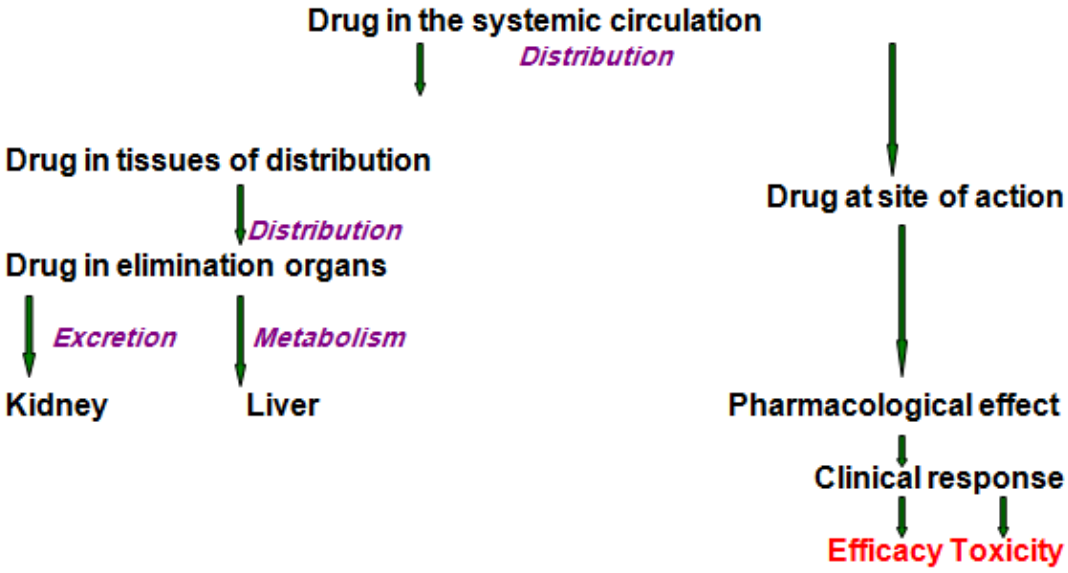
When you take the drug through mouth as an example it is in the solid form called tablet, this tablet is not entirely a medicine; there are additives that make it a tablet and there are preservatives also; the medicine could be dry so they add substances that make it a

tablet and you can't absorb the medicine unless it comes out from the tablet so there are two steps for it to come out;

- Disintegration: the drug should be disintegrated -Dissolution: after disintegrated it dissolves in the fluids of the body.

These two processes could delay the absorption of the drug and if there is something wrong in the manufacturing the drug could not be absorbed completely.





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