Drug excretion

Renal clearance: → Volume of Plasm Clear of Drug

- One method of quantitatively describing the renal excretion of drugs is by means of the renal clearance value for the drug.
- Renal clearance can be used to investigate the mechanism of drug excretion:

إذا الدوا ماعمله Secretion و reabsorbtion لازم ال Clearance إله لشخص الطبيعي ما تقل عن 120 mL/min

A- If the drug is filtered but not secreted or reabsorbed the renal clearance will be about 120 ml/min in normal subjects. GFR

B- If the renal clearance is less than 120 ml/min then we can assume that at least two processes are in operation, glomerular filtration and tubular re-absorption. يرجع من البول الى الدم

C- If the renal clearance is greater than 120 ml/min then tubular secretion must be contributing to the elimination process. → يرجع من الدم الى البول

GFR * اجيب دوا معين واشوف

⊛ عشان يزيد ال Clearance :-

Base أيّنِي ← Acid → ionized يكون Polar وسهل يخرج

Acid أحمِض ← Base

Drug excretion

Renal clearance is then:-

$$CL_{renal} = \frac{\left(\text{filtration rate} + \text{secretion rate}\right) - \text{reabsorption rate}}{Cp}$$

تركيز الدوا في الدم ← Cp

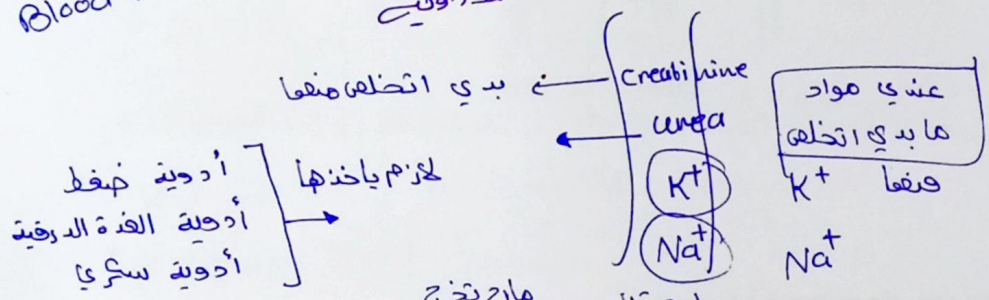
$$\text{Renal Clearance} = \frac{\text{Rate of Excretion}}{\text{Plasma Concentration}}$$

في البلازما

Factors Altering Renal Drug Clearance

Renal drug clearance is lower [therefore you must reduce dose] in:

- Elderly and Newborn
- Women (20%) than men
- Kidney and Heart Disease
- Patients taking drugs which block secretion (aspirin, probenecid)



Drug excretion

Hemodialysis:

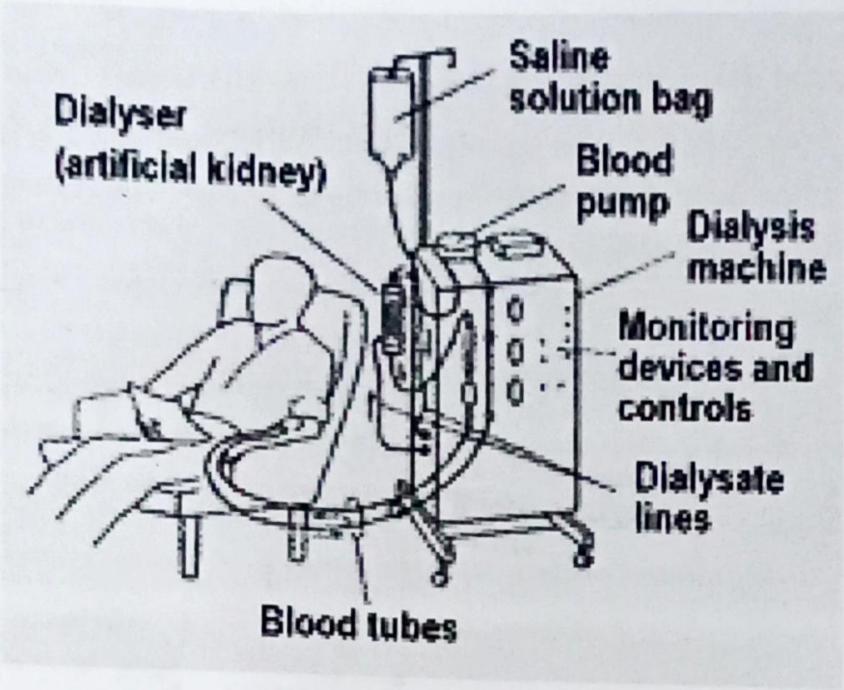
- Hemodialysis or `artificial kidney' therapy is used in renal failure to remove toxic waste material normally removed by the kidneys.
- In the procedure blood is diverted externally and allowed to flow across a semi-permea membrane that is bathed with an aqueous isotonic solution. Nitrogenous waste produc and some drugs will diffuse from the blood, thus these compounds will be eliminated.

- This technique is particularly important with drugs which:-

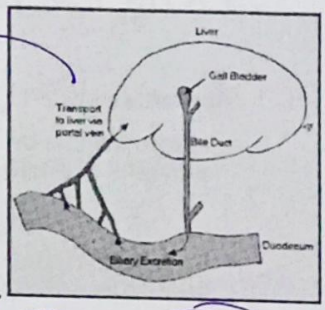
1) have good water solubility;
2) are not tightly bound to plasma protein;
3) are smaller molecular weight; and
4) have a small apparent volume of distribution.

- Drugs which are tightly bound or extensively stored or distributed into tissues are poorl removed by this process.

Haemodialysis



Drug excretion



Active ←

2.Fecal excretion:

Elimination of toxicants in the feces occurs from two processes: → من خلال الـ bile أو من الـ intesten

A- excretion in bile:

- Some heavy metals are excreted in the bile, e.g., arsenic, lead, and mercury. However, the most likely substances to be excreted via the bile are comparatively large, ionized molecules, such as large molecular weight (greater than 300) conjugates e.g. morphine and chloramphenicol (as glucuronide).

زرنيخ → مواد تخرج مع البراز

① ② في الـ intestin

bile تتكسر glucuronid و يرجع على الأمعاء و يمتصه و جزء منه يروح في urine و تخرج تلفا

- The biliary secretion is active since bile/plasma concentrations maybe as high as 50/1. There can also be competition between compounds.

الأدوية تركيزها في الـ bile أكثر ←

Bile تركيز المواد في أعلى بـ 50 مرة من تركيزها في البلازما

Drug excretion

- Once a substance has been excreted by the liver into the bile, and subsequently into the intestinal tract, it can then be eliminated from the body in the feces, or it may be reabsorbed.

- Since most of the substances excreted in the bile are water-soluble, t are not likely to be reabsorbed as such. However, enzymes in the intest flora are capable of hydrolyzing some glucuronide and sulfate conjuga which can release the less-polar compounds that may then be reabsorb This process is known as the **enterohepatic circulation.**

- The effect of this enterohepatic circulation is to prolong the life of the d in the body.

bile salt

Heavy metal ← ال ← very toxic صعب تخرج من الجسم

تكسر الرابطة بينهم

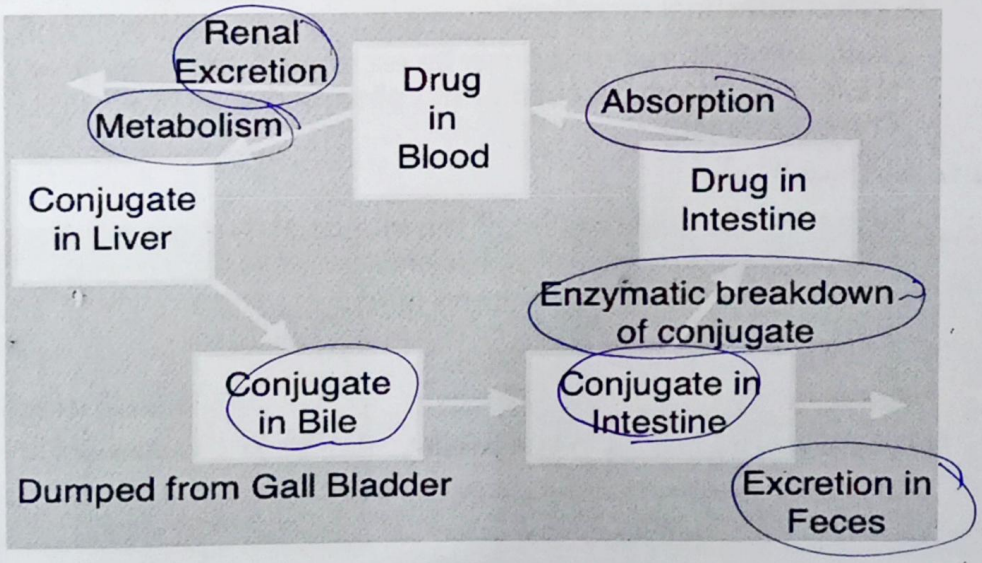
flora → Drug ويرجع الدوا الى الكبد

المادة بتي فسفقا في الـ Phase 2

Drug excretion

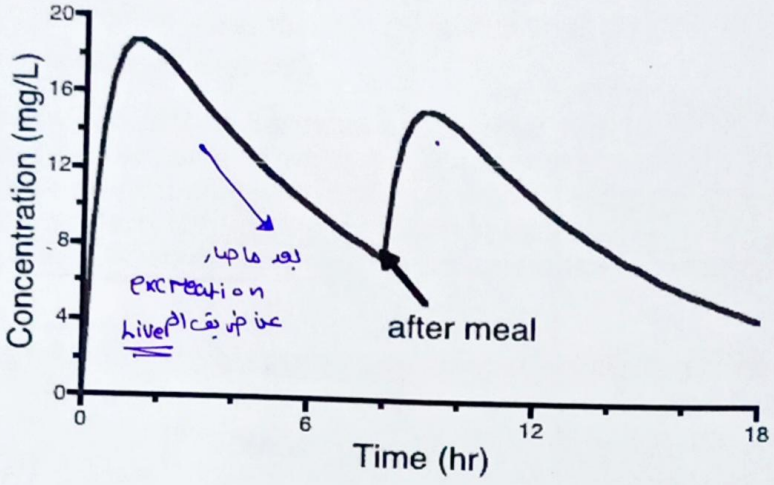
كل لغة احسن من الدوا أقل لهيك الأفضل

Enteroheptic Recycling



Drug excretion

Cp versus Time showing a Second Peak



٪5 تخسرها Bile مع يرتبط Cholestamin ⊖ Bile
Cholestr ↓ N ⊕
Feces ال مع ينزل

Drug excretion

- Another way that drugs can be eliminated via the feces is by:

B- direct intestinal excretion:

- Orally administered drugs may be excreted in the feces if they are incompletely absorbed or not absorbed at all (e.g. Cholestyramine)

لـ الهدف انه مايمتص

- Increasing the lipid content of the intestinal tract can enhance intestinal excretion of some lipophilic substances. For this reason, mineral oil is sometimes added to the diet to help eliminate toxic substances, which are known to be excreted directly into the intestinal tract.

عشان نقلل الكولسترول

Mineral oil (castor oil) تعمل diarrhea

Ketone bodies → hydroxy butyrate مع Aceton مع

Drug excretion

Drugs may be excreted by passive diffusion from:

3. Pulmonary excretion:

- The lung is the major organ of excretion for gaseous and volatile substances. Most of the gaseous anesthetics are extensively eliminated in expired air.

مسكن

4. Salivary excretion:

- Drug excretion into saliva appears to be dependent on pH partition and protein binding.
- In some instances, salivary secretion is responsible for localized side effects. For example, excretion of antibiotics may cause black hairy tongue, and gingival hyperplasia can be a side effect of phenytoin.

Protein bound

Excretion

مضادات

side effect للمضادات الحيوية

Black hairy tongue

penicillin, erythromycin, doxycycline, and neomycin

Gingival hyperplasia

Phenytoin

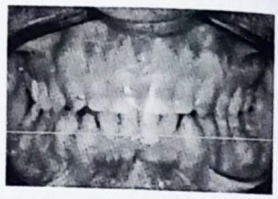
ظهور شعر اسود على اللسان

اللثة تصير غير منتظمة

Drug excretion

Examples of compounds that excreted in saliva:

- Superinfection from antibiotics.
- Dental mottling upon tetracycline ingestion.



5. Skin excretion:

- Iodine, bromine, benzoic acid, salicylic acid, lead, arsenic mercury, iron and alcohol are examples of compounds that excreted in sweat.

- Neonatal jaundice result from sulfonamide interaction with bilirubin.

Drug excretion

6. Mammary excretion:

Both basic substances and lipid-soluble compounds can be excreted into milk.

Basic substances can be concentrated in milk since milk is more acidic (pH ~ 6.5) than blood plasma.

Since milk contains 3-4% lipids, lipid-soluble drugs can diffuse along with fats from plasma into the mammary gland and thus can be present in mother's milk.

-Substances that are chemically similar to calcium can also be excreted into milk along with calcium.

Ethanol and tetracycline enter the milk by diffusion through membrane pores (of mammary alveolar cells).

- Mothers smoking more than 20 to 30 cigarettes a day may induce nausea, vomiting, abdominal cramps and diarrhea in the infant.