Pharmacology
Team 437

تمت المراجعة
غيداء آل مصمم
&
عبدالرحمن الحيسوني

MED437
KING SAUD UNIVERSITY

Excretion of drugs

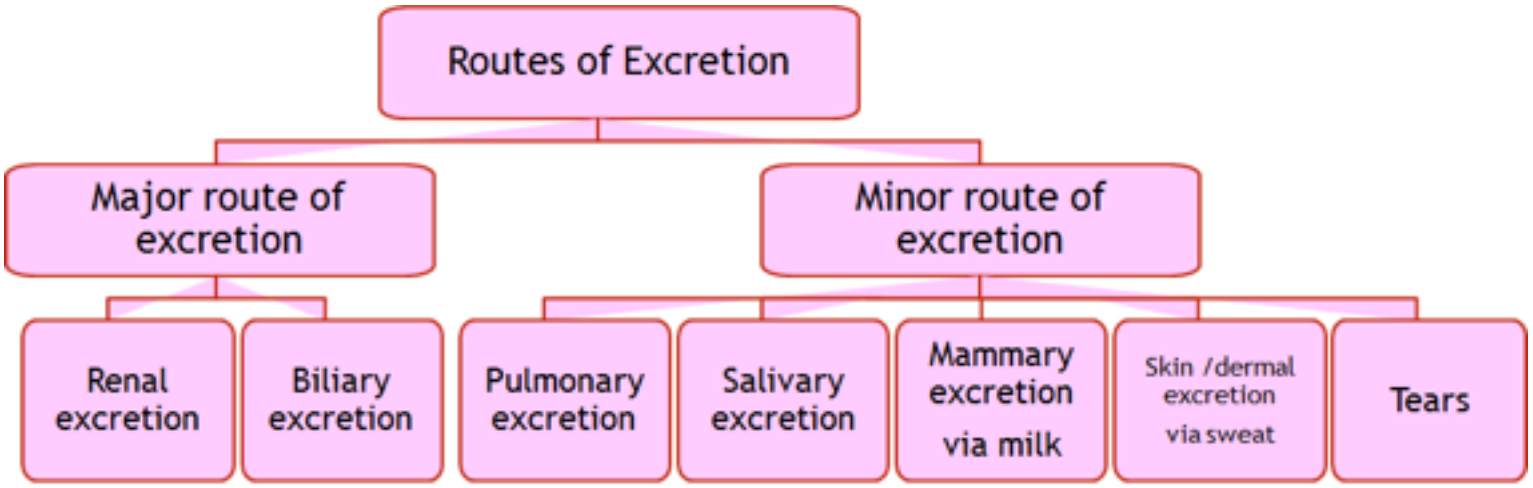
Objectives:

- Identify major and minor routes of excretion including renal elimination and biliary excretion
- Describe enterohepatic circulation and its consequences on duration of drugs.
- Describe some pharmacokinetics terms including clearance of drugs.
- Biological half-life (t ½), multiple dosing, steady state levels, maintenance dose and Loading dose.

Titles Very important Terms Extra informations

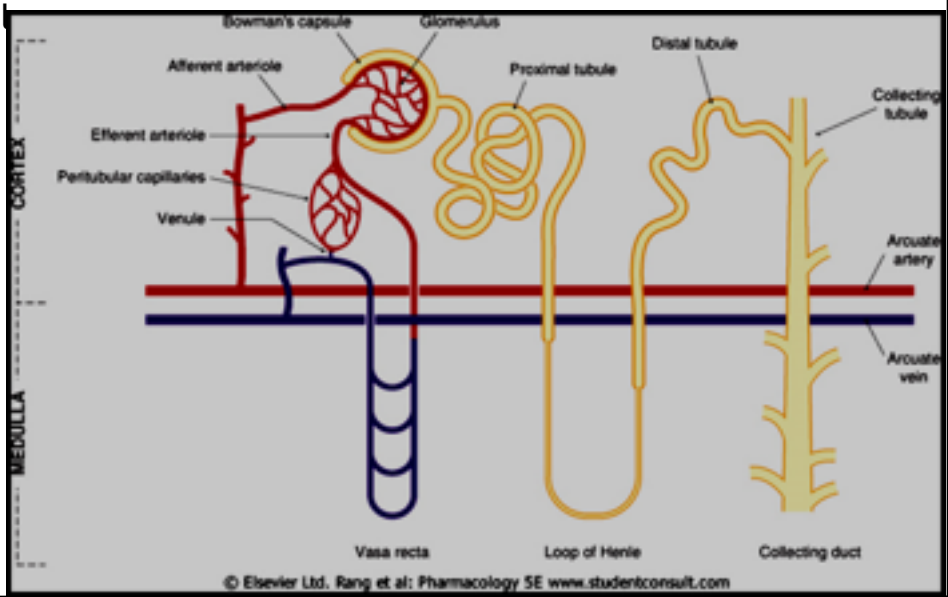
Success Doesn't Come To You, You Go To It!

Excretion



Structure of Kidney

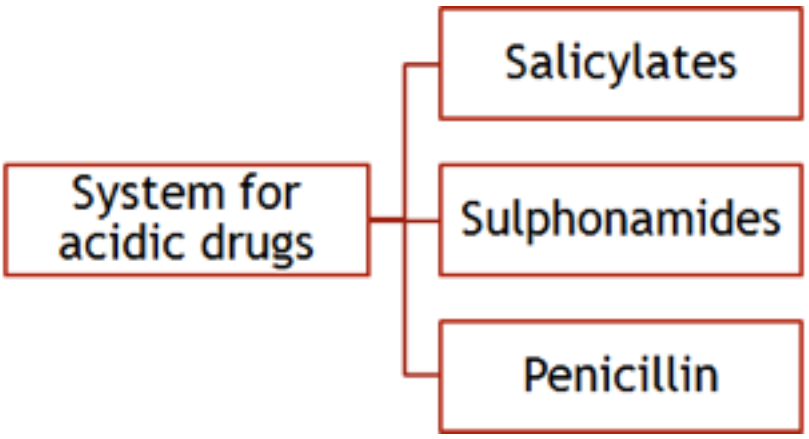
- The structure unit of the kidney is nephron
- It consists of:
  - Glomerulus
  - Proximal convoluted tubul
  - Loop of Henle
  - Distal convoluted tubules
  - Collecting ducts



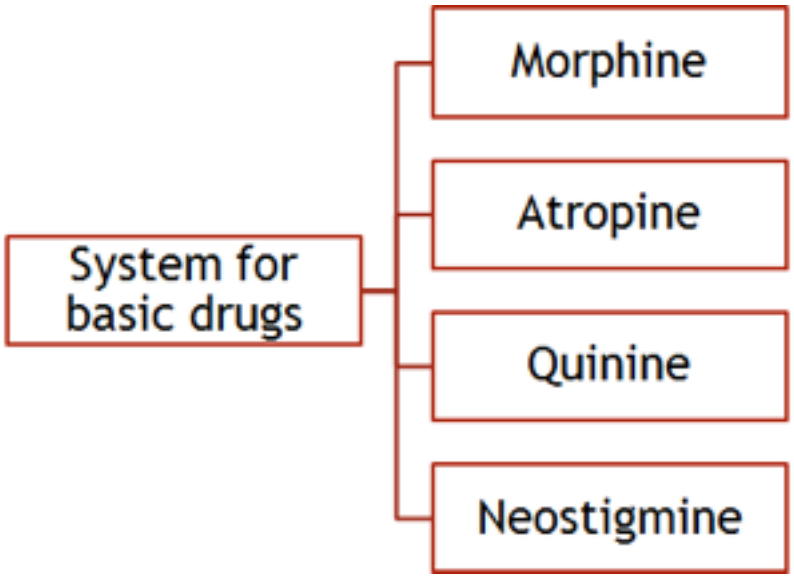
The principle processes that determine the urinary excretion of drugs are

Glomerular Filtration	Passive tubular reabsorption	Active Transport Secretion

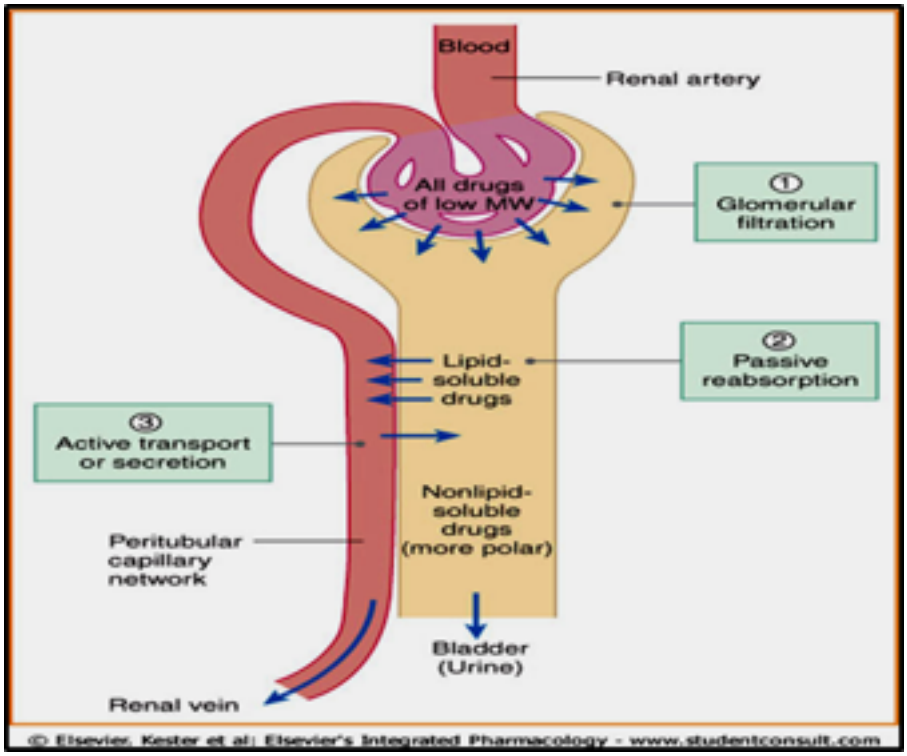
• Depends upon renal blood flow (600 ml/min)
• GFR 20% of renal blood flow = 125 ml/min.
• Glomerular filtration occurs to:
  ○ Low molecular weight drugs.
  ○ Only free drugs (unbound to plasma proteins) are filtered.
	• In distal convoluted tubules & collecting ducts.
	• Passive diffusion of unionized , lipophilic drugs.
	• Lipophilic drugs can be reabsorbed back into blood circulation and excretion in urine will be low.
	• Ionized drugs are poorly reabsorbed& so urinary excretion will be high.
		• Occurs mainly in proximal tubules ; increases drug concentration in lumen.
		• Organic anionic and cationic transporters mediate active secretion of anionic and cationic drugs.
		• Can transport drugs against conc. gradients.
		• e.g. Penicillin.



Transport of acidic drugs is blocked by probenecid



-ine in a drug usually means the drug is basic.

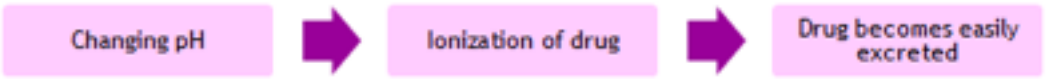


Urinary pH Trapping (Ion Trapping)

- Changing pH of urine by chemicals can inhibit or enhance the drug reabsorption from renal tubules back into blood circulation.
- Ion trapping is used to enhance renal clearance of drugs during toxicity.
- Urine is normally slightly acidic and favors excretion of basic drugs.

❖ Acidification of urine using ammonium chloride (NH_4Cl) increases excretion of basic drugs such as amphetamine.

❖ Alkalinization of urine using sodium bicarbonate ($NaHCO_3$) increases excretion of acidic drugs such as aspirin.



Drugs excreted mainly by the kidney include:

- Aminoglycosides antibiotics (as gentamycin)
- Penicillin.
- Lithium

These drugs should be prescribed carefully in

- patients with renal disease.
- Elderly people

biliary excretion

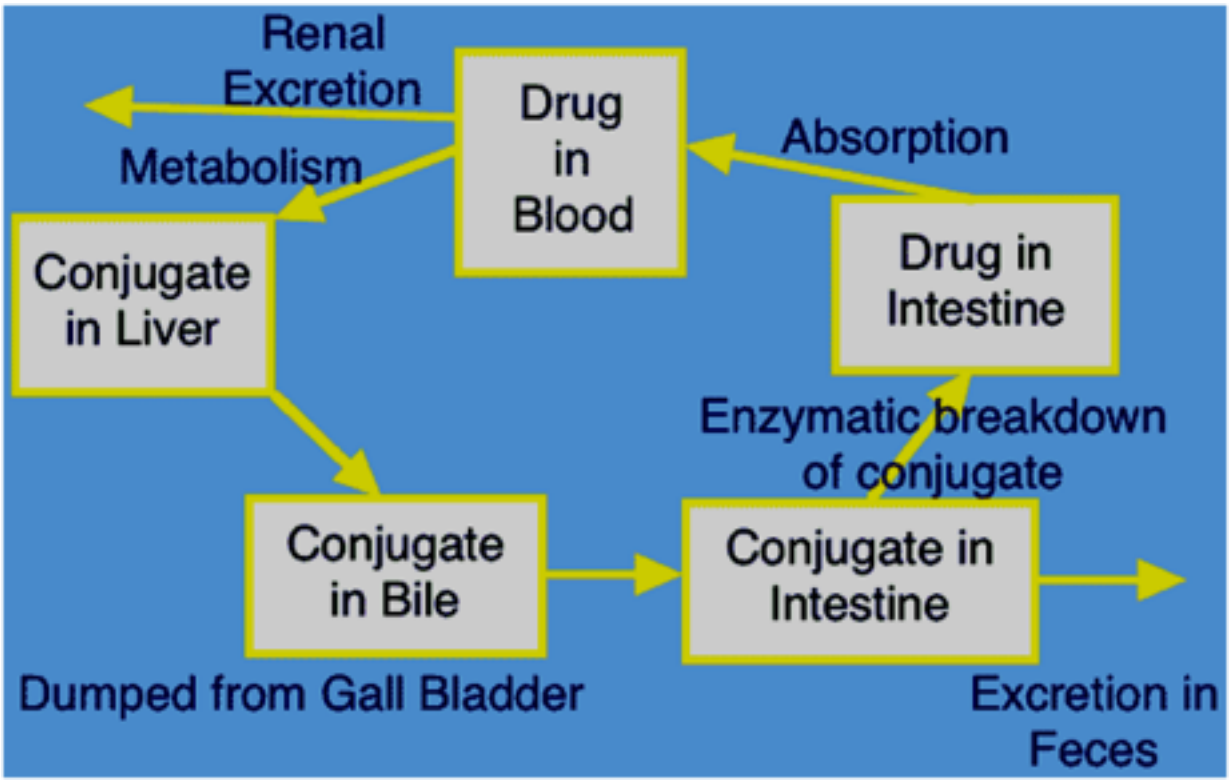
- Occurs to few drugs that are excreted into feces.

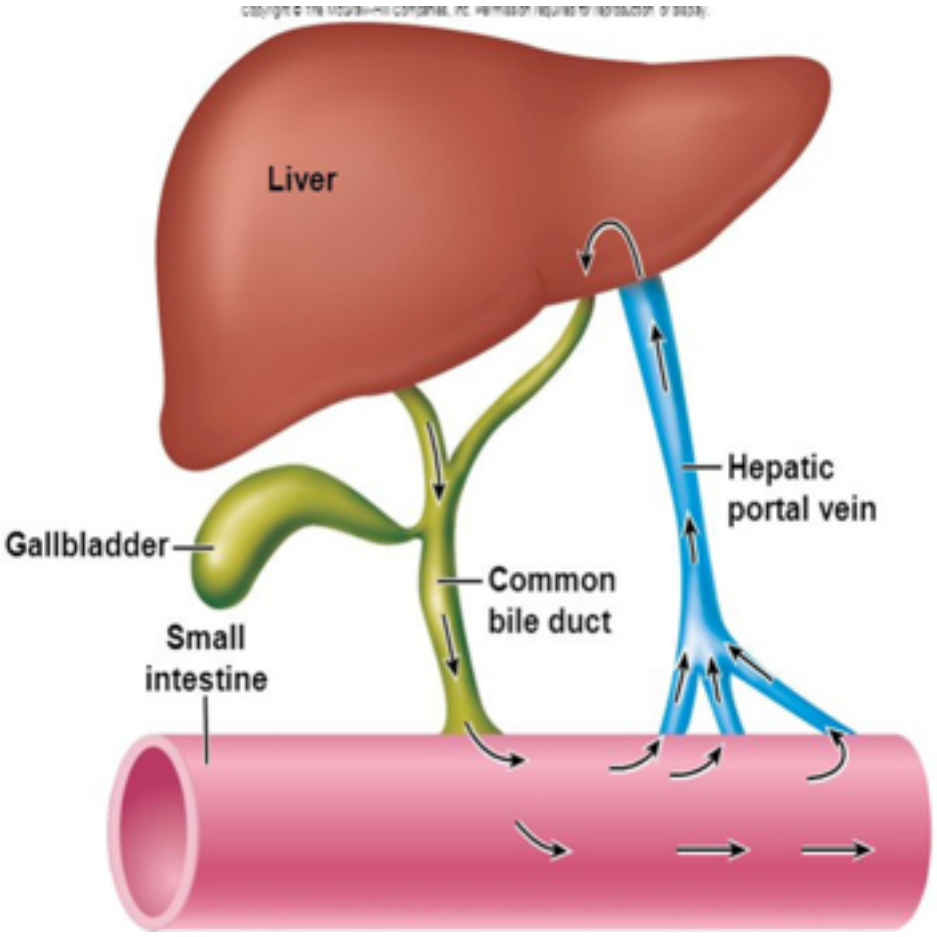
- Such drugs are secreted from the liver into bile by active transporters, then into duodenum.
Some drugs undergo enterohepatic (inestine+hepatocyte) circulation back into systemic blood circulation

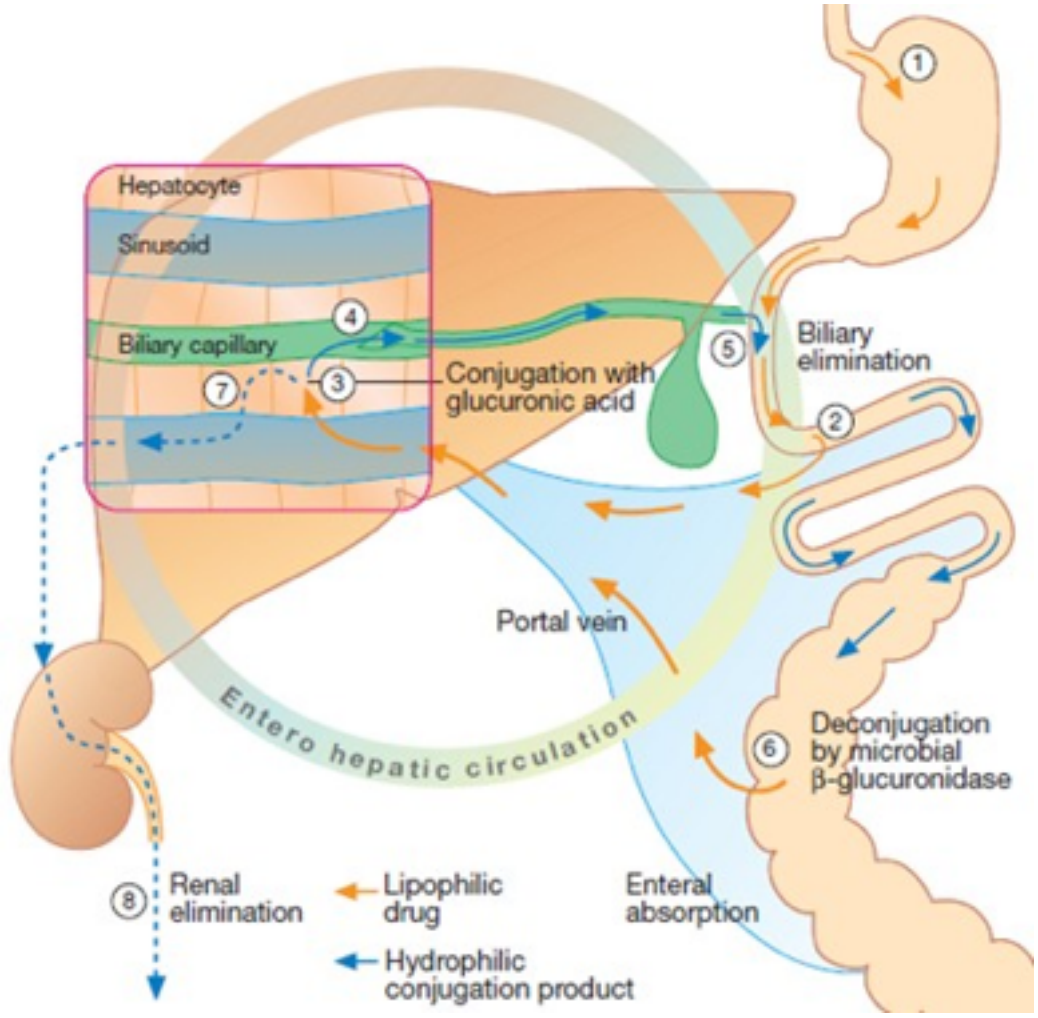
- Drugs excreted in the bile in the form of glucouronides will be hydrolyzed in intestine by bacterial flora liberating free drugs that can be reabsorbed back into blood if the drugs are lipid soluble.

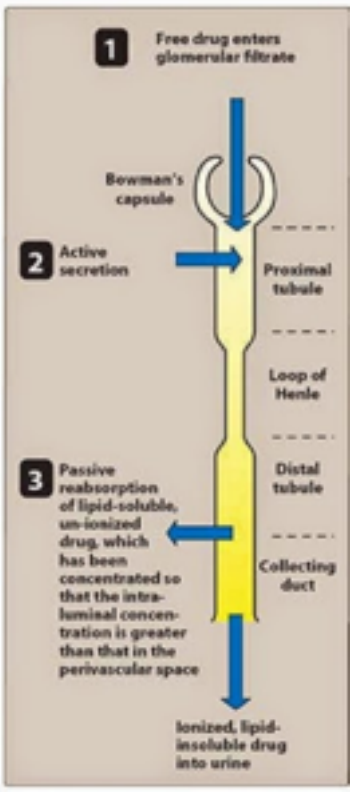
- This prolongs the duration of action of drugs e.g. digoxin, morphine, thyroxine.

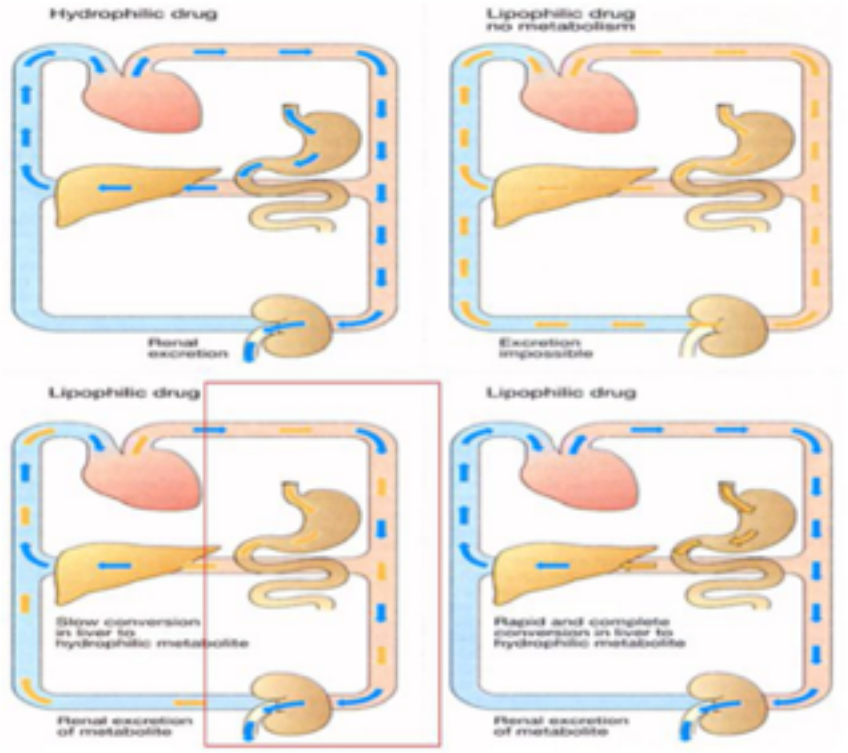
توضيح : الدواء في الكبد يرتبط بـ glucouronic acid في الطور الثاني في عملية الابسوربشن فبكذا يصير water soluble وقابل للخروج فلما يروح للـ intestine البكتيريا النورمال فلورا هناك تفكه من الاسيد المرتبط فيه فيرجع ليبيد سولبل مرة ثانية فيقدر الجسم يمتصه مرة ثانية فتزيد مدة بقاء الدواء


Renal Excretion
Drug in Blood
Absorption
Metabolism
Drug in Intestine
Conjugate in Liver
Enzymatic breakdown of conjugate
Conjugate in Bile
Conjugate in Intestine
Dumped from Gall Bladder
Excretion in Feces


Liver
Hepatic portal vein
Gallbladder
Common bile duct
Small intestine







Clearance

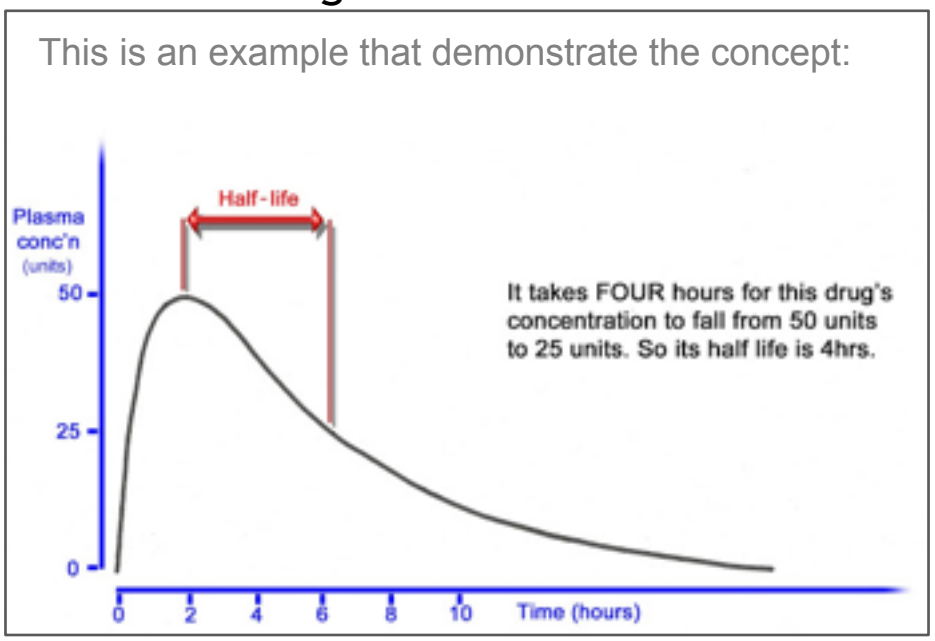
- Definition : Its the volume of plasma the gets filtered of drugs per unit time.
- Clearance is the propotionality factor used to determine rate of elimination.

https://www.youtube.com/watch?v=csywV3MYHDg(اول خمس دقايق شرح كامل)

Plasma half-life (t ½)

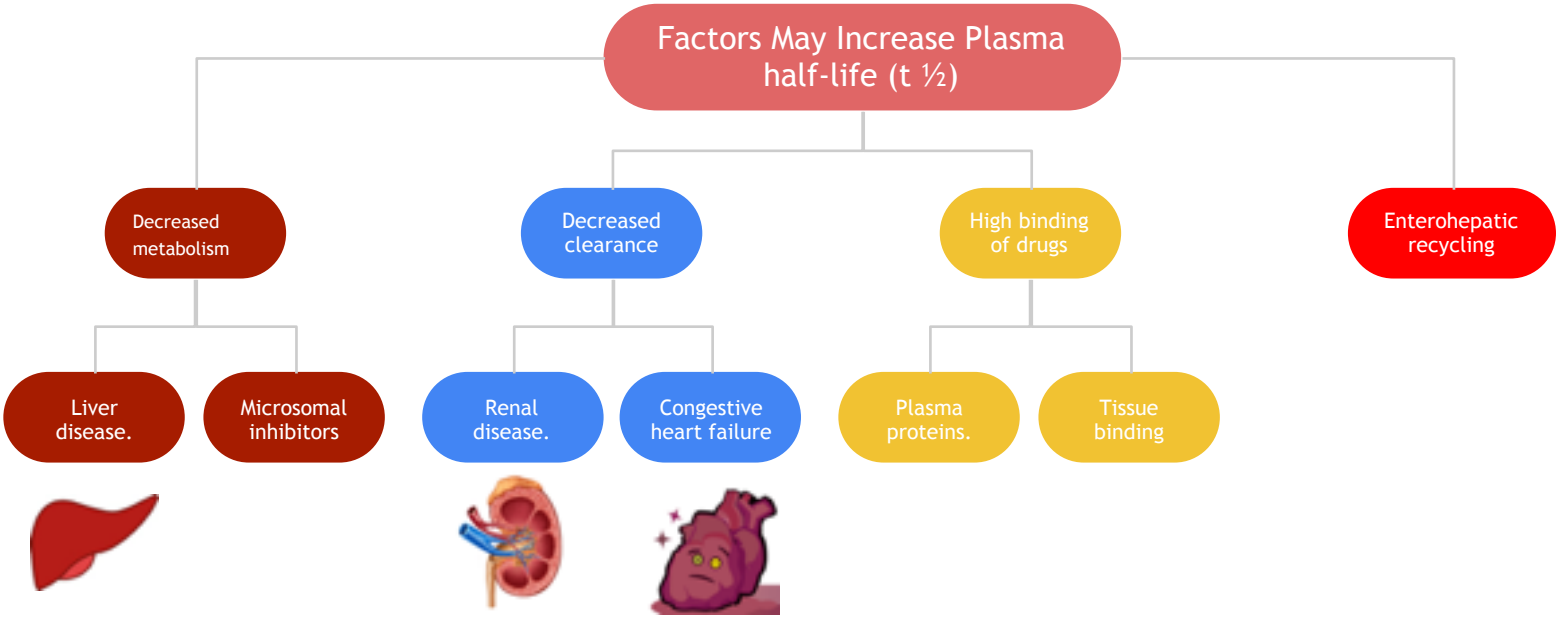
- It Is the time required for the plasma concentration of a drug to fall to half of its initial concentration.
- It Is a measure of duration of action.
- It Determine the dosing interval

This is an example that demonstrate the concept:



Drugs of long plasma half life
-Digoxin, Thyroxine

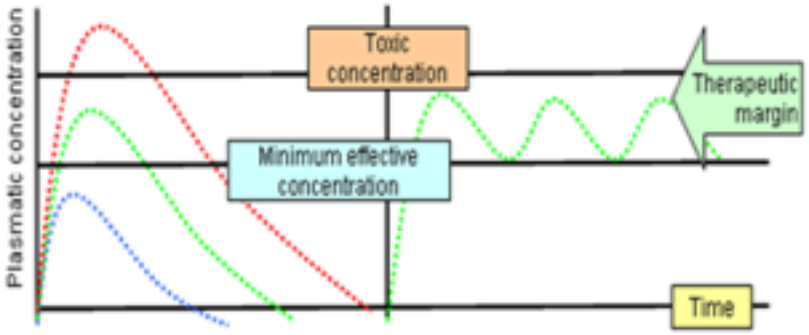
Drugs of short plasma half life
-Penicillin, tubocurarine.



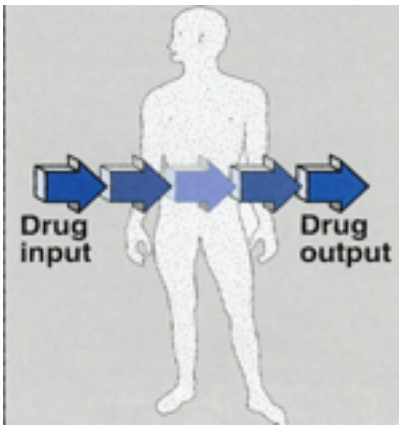
Steady State

-A state at which the therapeutic plasma concentration of the drug (mg/ml) remains constant with the therapeutic window (the range between effective and toxic levels of drugs).

يعني ما يوصل تركيزه بالجسم لمستوى
السمومية ولا ينزل عن مستوى فعالية الدواء

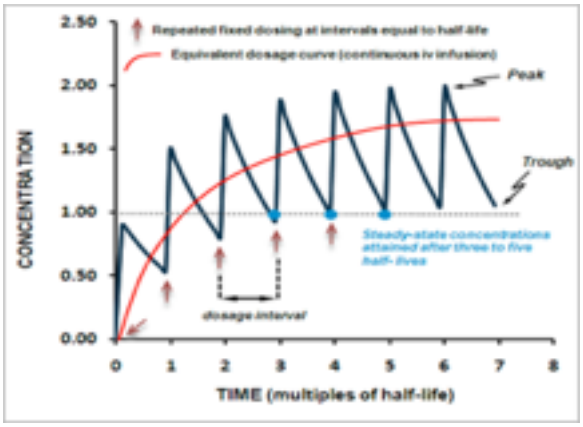


-At steady state:
rate of drug administration = elimination rate



Q/How many half-lives would be necessary to reach steady state ?

A/Steady state concentration is attained after 5-3 half lives
E.g. Morphine

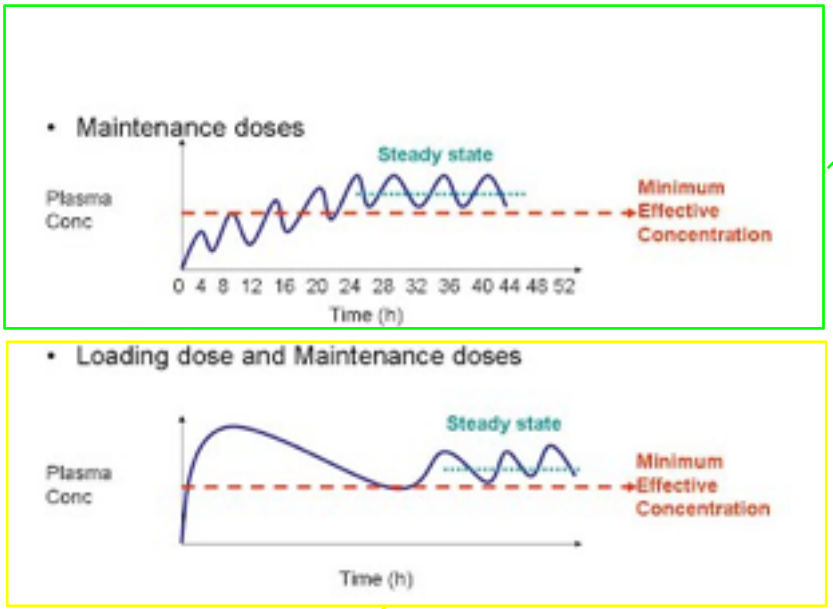


Loading Dose

is the large initial dose that is given to achieve rapid therapeutic plasma level.
After administration of the drug, the plasma concentration decreases due to distribution of drug to other tissues.
These doses balances the drug distribution.
This is important for drugs with long half lives.

Maintenance Doses

are the doses required to maintain the therapeutic level of the drug constant or the steady state of the drug.
These doses balance the amount of drug lost during metabolism and clearance.
The patient needs to take regular doses of a drug such as amoxicillin (500 mg) / 8 hours to maintain the therapeutic level.



Clinical Application of Loading Dose

A loading dose may be desirable if the time required to attain steady state of drug (4 elimination t1/2 values) is long and rapid relief is required in the condition being treated.
E.g. t1/2 of lidocaine (antiarrhythmic drug) is usually 1 2-hours. Arrhythmias after myocardial infarction are life-threatening, and one cannot wait 4 8-hours to achieve a therapeutic concentration.
Use of a loading dose of lidocaine in the coronary care unit is standard.

MCQs

(1The major route of excretion is:

a- Salivary excretion.
b- Dermal excretion .
c- Biliary excretion .
d- Tears .

(2An example of an acidic drug is:

a- Mormorphine
b- Penicillin
c- Quinine
d- Atropine

(3Glomerular filtration of a drug is affected by its:

a- Lipid solubility
b- Plasma protein binding
d- Degree of ionization
d- Rate of tubular secretion

(4When the same dose of a drug is repeated at half life intervals, the steady-state (plateau) plasma drug concentration is reached after:

a- 3 5-half lives
b- 4–6 half lives
c- 6–7 half lives
d- 8–10 half lives

(5Digoxin (long t1/2) should be prescribed in:

a- few doses a day
b- many doses a day
c- no doses at all
d- both A+C

(6Which of the following increases when the lipid-soluble drugs undergo the enterohepatic circulation?

a- the drug's pH
b- the duration of action
c- the rate of excretion
d- the rate of metabolism

Answers

1-C 2-B 3-B 4-A 5-A 6-B

Pharmacology
Team 437

MED437
KING SAUD UNIVERSITY

Useful videos:

Pharmacokinetics 5 - Excretion

Team members:

Boys:

Abdullah abdurahman al-asseri
Bader Altamimi
Fayez Ghiyath Aldarsouni
Maan Abdulrahman Shukr
Mohammed alnajeim
Omar Alsuhaibani
Sultan Omar Almalki
Yazeed abdullah alkhayyal
Majid alshali
Mohammad alasqah
Adel Alorainy

Team Leaders:

YAZEED ALI ALHARBI