للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

تجدون في guidance مادة الفارما على موقع النادي :

قبل ما نبلش المحاضرة... عشان أنا كتير منيحة الله يرضى عني😇😂
قررت أخليكم تكسبو أجر كبير بكل سهولة... شفتو محسني😌😂
طب شو هو الأجر وكيف يا لانا المتواضعة؟🤦🏻‍♀️😁
الأجر يا حلوين أنه تتبرعو برصيد الطباعة تبعكم اذا ما بتحتاجوه لطلاب بحاجته (قلتلكم اجر بسهولة)🤍💜
طيب شو لازم نعمل؟
أول شي لازم تفوتو ع بوابتكم ومن عند خدمات أخرى __ رصيد الطباعة
هلأ من هي الخطوة بس بدي تتأكدو انو رصيدكم موجود ولا خالص لو اعطاك (لا يوجد اي حركات طباعة حاليا) معناها الرصيد موجود وفيكم تتبرعو فيه
طيب تمام وكيف نتبرع؟
من بوبابتكم ومن عند خدمات أخرى __ الدخول لشبكة الانترنت (المختبرات واللاسلكية) بتاخدوا اسم المستخدم (والي هو رقمكم الجامعي) وبتنسخوا كلمة السر
واخر شي بتدخلو على QR code الي تحت👇 بتعبو فورم التبرع بالرصيد وبس.
سهلة القصة والله وفيها اجر كبير (اجر ع كل نقطة وحرف وكلمة انطبعت من رصيدك لشخص محتاج واجر بكل حرف اندرس من الورق الي انطبع برصيدك الي انت اصلا ما بتستخدمه).

Clinical significance of Enzyme Inhibition:

- ❖ Drugs inhibiting the microsomal enzyme systems → ↓ activity → تزيد تأثير الدواء

1. • ↓ their own metabolism →↑ drug level.
2. • ↓ metabolism of other drugs metabolized by these enzymes → drug interactions e.g.:
   - **Ciprofloxacin** (antibiotic) →↓ **warfarin** metabolism → bleeding effect زاد الـ
   - **Cimetidine** →↓ **carbamazepine** (علاج للصرع) metabolism → toxicity

- It occurs faster than enzyme induction.

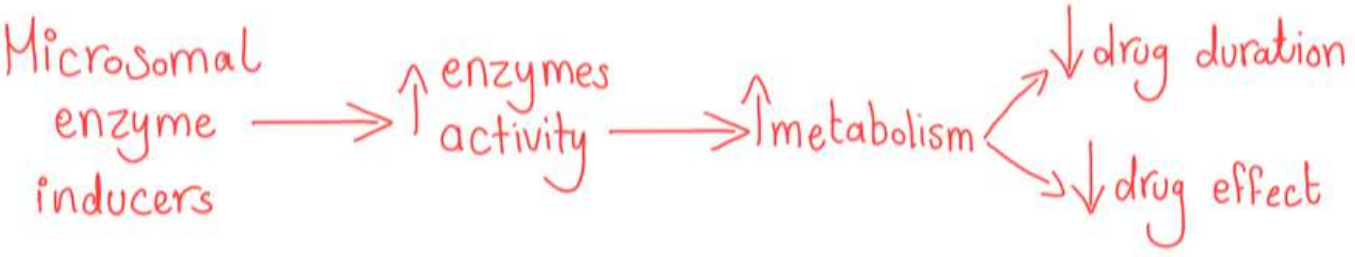
حفظ

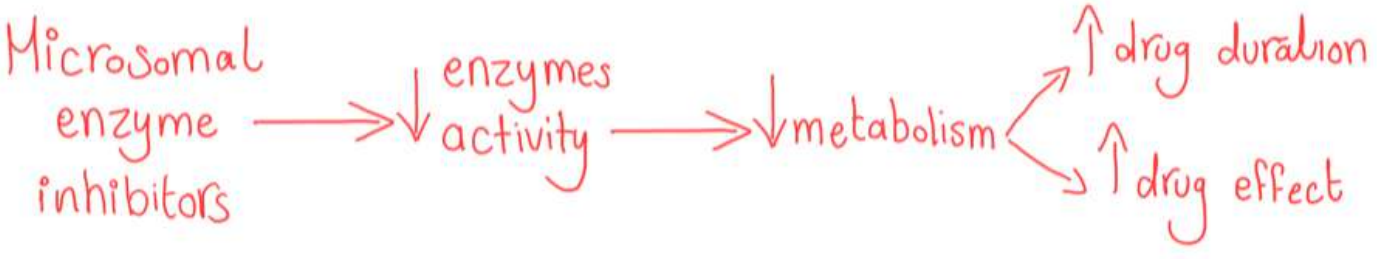
Examples of Enzyme Inhibitors

1 Cimetidine- 2 chloramphenicol - 3 ciprofloxacin- 4 erythromycin - 5 ketoconazol -

♀ **(F)** 6 estrogen, 7 progesterone, 8 contraceptive pills.

Summary





2. **Pathological factors which affect hepatic activity** e.g. liver failure starvation, cancer → ↓ activity of HME → need to adjust dose.

مضبوطة

Hepatic microsomal enzyme

3. **Pharmacogenetic variations in metabolizing enzymes** e.g. slow & fast acetylators (see pharmacogenetics).

لـ موضوع الجينات

4. **Hepatic blood flow**: drugs ↓ hepatic blood flow → ↓drug matabolism

5. **Age:** ↓ enzymatic activity in extremities of age [الكباركيس + الصغاركيس]

كبار السن... مع التقدم بالعمر رح تقل كل وظائف الجسم ويرضو ال liver فجرعته بتكون أقل من جرعة الadult
صغار السن... لسا بمرحلة النمو ف الliver مو متل الadult فجرعة الطفل بتكون أقل من جرعة الadult

- Premature babies have ↓ conjugate of chloramphenicol → fatal gray baby syndrome.

Hepatic microsomal enzymes

6. **Sex:** female sex hormones are HME inhibitors → receive lower doses than male, Especially anti-caner drugs

7. **Drug properties:** lipophilicity → hepatic metabolism of drugs. حيقل عمر وكفاءة الدواء

Hydrophobic drugs -> enter the liver -> increase the metabolism -> short duration of the drug
Hydrophilic drugs -> can not enter the drug -> more prolonged of the drug

8. **Drug dosage:** toxic dose can deplete substances needed for drug detoxification e.g. paracetamol toxic dose → depletion of GSH→ accumulation of toxic metabolite NAPQI

استنفاد

The gray baby syndrome is a type of circulatory collapse that can occur in premature and newborn infants and is associated with excessively high serum levels of chloramphenicol

EXCRETION OF DRUGS

1- The kidney:

- **It is the most important route** of excretion. It occurs through:

1. Glomerular filtration:

- For hydrophilic free (and lipophilic) (non-bound) drugs with M.W. (molecular weight) < 500 (i.e. < the glomerular pores). e.g. mannitol

Factors affecting glomerular filtration

1. Glomerular filtration rate (GFR) ⇝ ↑GFR → ↑Excretion
2. Plasma protein binding (PPB) → prevents filtration ⇝ ↑BPP → ↓Excretion
3. Molecular weight ⇝ ↓MW → Passage → ↑Excretion

From the book

Glomerular filtration: Drugs enter the kidney through renal artries, which divide to form a glomerular capillary plexus.

Free drug {not bound to albumin} flows through the capillary slits into the Bowman space as part of the glomerular filtrate. The glomerular filtration rate (GFR) is normally about 120 mL/min/1.73m2 but may diminish significantly in renal disease.

2. Active tubular secretion: through special transport system (carrier) → saturable & site for competition.

Duiretic

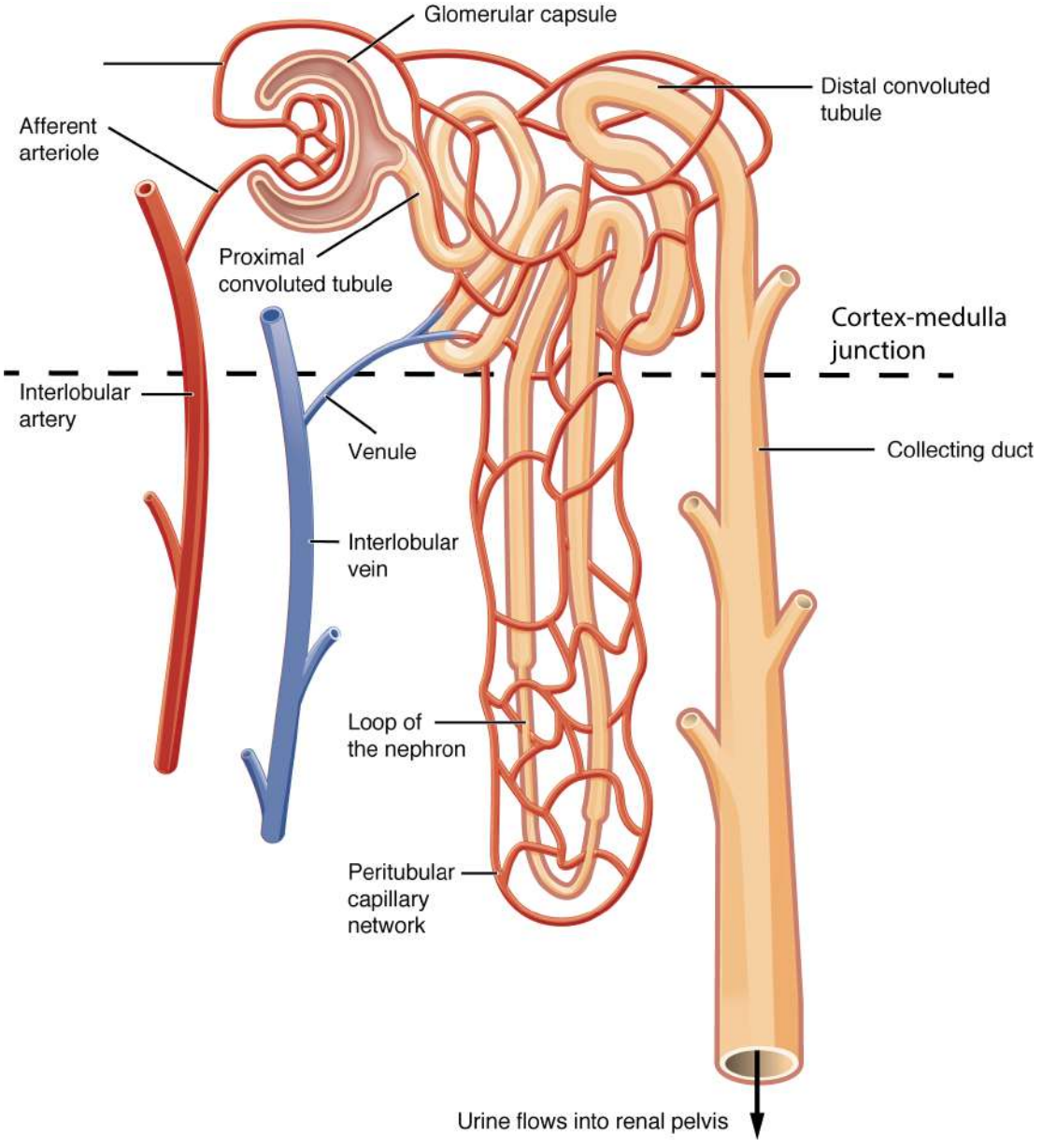
اسمه التجاري Lasix

- Acid carrier e.g. for penicillins, probenecid, frusemide, uric acid
  - Probenecid →↓ tubular secretion of penicillin→↑ duration of action of penicillin
  - frusemide →↓ tubular secretion of uric acid →hyperuricemia as an adverse effect.
    - There is too much uric acid in the blood
- basic carrier e.g. for digoxin, quinidine.

شرحناعن هاي النقطة قبل

هلا ال carrier بينقل مربكات كتير مو مركب واحد... فال carier الي بينقل ال uric acid هو نفس ال carrier الي بينقل ال frusemide (هاد ما بيشتغل وهو موجود بالدم لازم يدخل ال kidney عن طريق carrier وهاي هي عملية secretion) ف ال carrier لانه بينقل ال frusemide وبرضو ال uric acid رح يصير بينهم competition فال crrier رح يترك ال uric acid ويكمل بشغل ال frusemide عشان هيك ال uric acid بيتراكم بالدم وبيعملي hyperuricemia

هي صورة توضيحية عشان تقدرو عليها تتخيلو الي بصير بكل مكان😅



From the book (نصيحة اقرأوه)

Drugs that were not transferred into the glomerular filtrate leave the glomeruli through efferent arterioles, which divide to form a capillary plexus surrounding the nephric lumen in the proximal tubule.

Secretion primarily occurs in the proximal tubules by two energy-requiring active transport systems:

one for anions (for example, deprotonated forms of weak acids}

one for cations (for example, protonated forms of weak bases}.

Each of these transport systems shows low specificity and can transport many compounds.

Thus, competition between drugs for these carriers can occur within each transport system.

[Note: Premature infants and neonates have an incompletely developed tubular secretory mechanism and, thus, may retain certain drugs in the blood.]

3. Active tubular reabsorption: secretion عكس ال

- Unionized form of drug (lipophilic) → tubular reabsorption

❖ **Changes in urinary pH:** affect excretion of drugs

ABC

- Alkalinization of urine (**Na or K** Acetate, **B**icarbonate, **C**itrate) → ↑ renal excretion of weak acid drugs e.g. Aspirin, Barbiturates
- Acidification of urine (NH_4Cl or Ascorbic acid "vit.**C**") → ↑ renal excretion of weak base drugs e.g. amphetamine. ephedrine

From the book :

Distal tubular reabsorption: As a drug moves toward the distal convoluted tubule, its concentration increases and exceeds that of the perivascular space.

The drug, if uncharged, may diffuse out of the nephric lumen, back into the systemic circulation.

Manipulating the urine pH to increase the fraction of ionized drug in the lumen may be done to minimize the amount of back diffusion and increase the clearance of an undesirable drug.

Generally, weak acids can be eliminated by alkalinization of the urine, whereas elimination of weak bases may be increased by acidification of the urine. This process is called “ion trapping”.

For example, a patient presenting with phenobarbital (weak acid) overdose can be given bicarbonate, which alkalinizes the urine and keeps the drug ionized, thereby decreasing its reabsorption.

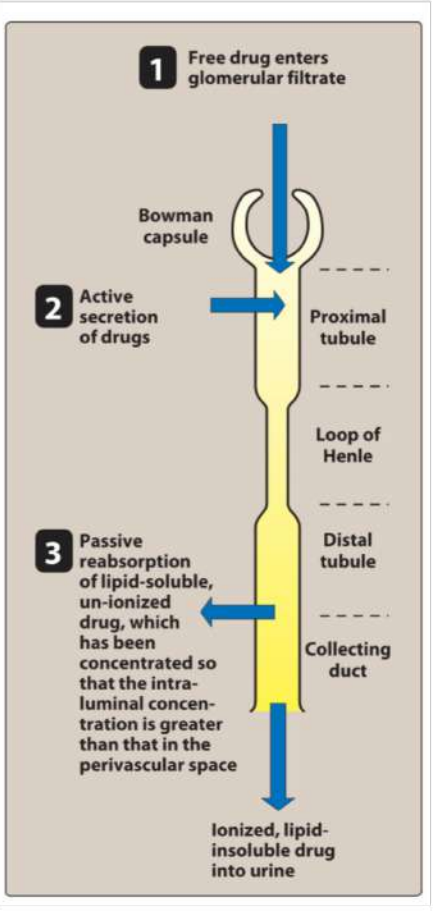
Net excretion = GF + TS - TR

If the net excretion is 120 = excretion through GF

If the net excretion is more than 120 = Secretion mechanism

If the net excretion is less than 120 = Reabsorption dependance

مهم جدًا ، وبيجي عليه سؤال



2- GIT:

* **Saliva**: e.g. Morphine ①, Iodine ②, Metronidazole ③ → metallic taste [مر] طعم معدني

* **Stomach:** e.g. Morphine → gastric wash (غسيل المعدة) is done in aute morphine toxicity despite it is administrated by IV route. (**)

هلا غسيل المعدة بنعمله بس يكون الدوا متاخد oral عشان اقلل ال absorption فيمنع ال toxicity

هلا ال morphine حتى لو اتاخد عن طريق IV برضو نعمل غسيل معدة لانه ممكن الجرعة العالية ممكن تنزل ع المعدة وتوصل الامعاء ويصرلها reabsorption وهيك بتزيد السمية عشان هيك بنعمل غسل معدة حتى لو IV

* **Bile:** in active or conjugated form → intestine → EITHER
  - Excreted in large intestine → stool
  - Reabsorbed → enterohepatic circulation e.g. Morphine, Rifampicin (Free drugs)
  - Some antibacterials are excreted in bile in an active form → useful in: 1 treatment of cholecystitis (↱ is when a gallbladder is in flimated.) & typhoid fever e.g. Ampicillin
    2 patients with renal impairment (No need for dose adjustment)

* **Stool:** conjugated metabolites & poorly absorbed orally

3- Lungs: e.g. volatile liquids (inhalant general anesthesia), gases (CO_2)

4- Sweat: e.g. Rifampicine → red discoloration of sweat

5- Breast Milk: - Many drugs are excreted in breast milk → can affect baby

- lipid soluble ① and basic ② drugs are trapped in breast milk

نصيحة قبل ما تبدأوا : هاد الموضوع مهم و حيجي عليها اسئلة كثير بالامتحان اتأكدوا من هاد الشي ، احضروا عبدالمتعال فودة ، فيديو رقم 8 و بعدها اقرأوا التفريغ

PARAMETERS OF ELIMINATION = Metabolism + Excretion

1. Systemic clearance (Cls)

Definition

- It the volume of a fluid cleared from the drug per unit time.

$$Cls = K_{el} \times V_d$$

ثابت ال elimination

- K_{el} → Elimination rate constant = $\frac{0.693}{t_{1/2}}$ = 0.7

$$Cls = \frac{.7 * Vd}{t1/2}$$

مش مطلوب

[(0.693) is the natural logarithm of 2 (i.e. In 2) and gets into the equation because ($t_{1/2}$) involves a halving of concentration → $-Kel = \frac{\ln(C_2/C_1)}{t_{1/2}} = \frac{\ln(1/2)}{t_{1/2}} \rightarrow Kel = \frac{\ln(2)}{t_{1/2}}$]

- So, systemic clearance $Cl = \frac{0.693}{t_{1/2}} \times V_d$

- The systemic clearance is equal to the sum of individual organs clearances

  i.e. the clearnce by the liver, kidney, lung, ….etc.

Cls = renal clearance (Clr) + non-renal clearance (Clnr)

Factors affecting drug clearance

1. Blood flow to the clearing organ (directly proportional). علاقة طردية
2. Binding of the drug to plasma proteins (inversely proportional). علاقة عكسية
3. Activity of processes responsible for drug removal as hepatic enzymes, glomerular filtration rate and secretory processes (directly proportional). علاقة طردية

Significance of clearance الأهمية

1. Calculation of the maintenance dose (**MD**)
2. Adjustment of the **dosing regimen** for drugs eliminated by glomerular filtration e.g. dosing of gentamicin

***loading dose is an initial higher dose of a drug that may be given at the beginning of a course of treatment. الجرعة الكبيرة الأولية**

***maintenance dose is the maintenance rate [mg/h] of drug administration equal to the rate of elimination at steady state. الجرعات الصغيرة الي بعطيها بعد الجرعة الكبيرة**

***dosing regimen is the frequency (dosing interval) and dose at which a drug is to be administered**

من خلال الclearance الدكاترة بعرفوا كم نسبة الدواء الي لازم تعطى للمريض و خصوصا لو كان عنده failure بأحد الاعضاء الي بتعمل excertion

مثلا ادوية السرطان، بتعتمد بالexcertion على الكلية ، لو كان المريض عنده kidney failure لازم الدكاترة يحسبوا ال clearance لحتى ما يعطوه جرعة زيادة

مثلا لو كان ال50%= clearance معناته جرعة الدوا الجاي ما بعطيها كلها بس بعطي 50% منها