PHARMACOKINETICS 4

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Pharmacokinetics

what the body does to the drug?

- Absorption
- Distribution
- Metabolism
- Excretion.

EXCRETION OF DRUGS

- **Kidney:** most important organ for excretion
- Excretion occurs through:

1. **Glomerular filtration** (free particle, water soluble, small)
2. **Proximal convoluted tubules (PCT)** (larger size, weak acid or weak base, lipophilicity, active secretion)
3. **Distal convoluted tubules (DCT)**

1-Glomerular filtration

Bowman capsule

- All free drug molecules whose size is **less** than the glomerular pores are filtered into Bowman's capsule.

2-Proximal convoluted tubules (PCT)

Active secretion occurs either through

require carrier

acid drug → weak acid carrier → urine

basic → basic

aspirin

- acid carrier e.g. for penicillin, probenicid, salicylic acid.
- basic carrier for amphetamine and quinine.

3-Distal convoluted tubules (DCT)

- Lipophilic drugs may be reabsorbed back to systemic circulation.

[الذي يغير ال pH ....]

- *Alkalinization of urine* keeps acidic drugs ionized and increases their excretion.
- *Acidification of urine* keeps basic drugs ionized and increases their excretion.

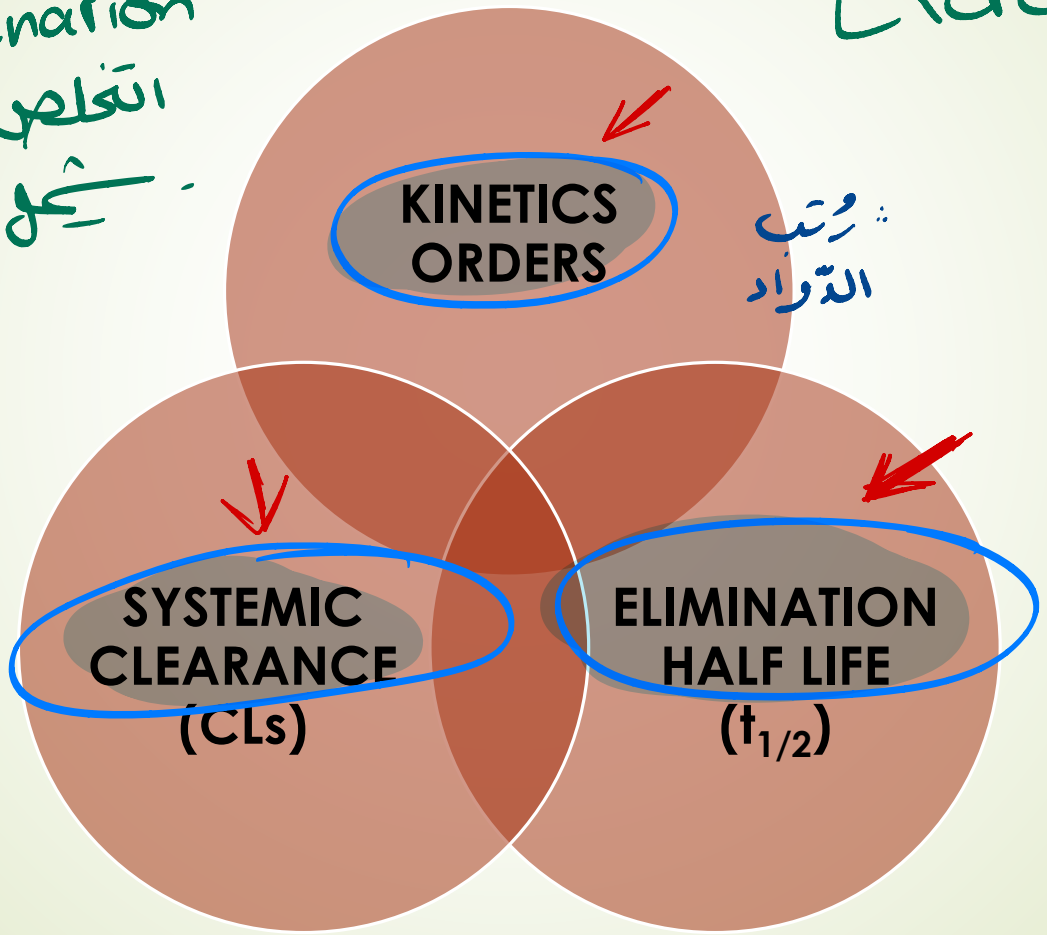
Other sites of excretion:

- **Bile:** e.g. Doxycycline, Azithromycin.
- **Lungs** e.g. Volatile anesthetics.
- **Saliva** e.g. Iodides.
- **Sweat** e.g. Rifampicin.
- **Milk**: this is important in lactating mothers.

PARAMETERS OF ELIMINATION

Elimination
التخلص
metabolism
excretion

Excretion إخراج



KINETICS ORDERS

First order kinetics

الطبيعي

طبيعي

Zero order kinetics

غير طبيعي

"PEA"

First order kinetics (most drugs):

التناسب مع التركيز: كلما زاد تركيز الدواء في الدم، زادت كمية الدواء المزالة في كل وحدة زمنية. على سبيل المثال، إذا كان لديك 100 ملغ من الدواء، وكان معدل الإزالة 10% في الساعة، ستفقد 10 ملغ في الساعة. إذا ارتفع التركيز إلى 200 ملغ، ستفقد 20 ملغ في الساعة.

- Rate of elimination is directly proportionate to the blood concentration of drugs (**constant percentage** of the drug is eliminated per unit of time) *

whatever the amount

- **Constant "$t_{1/2}$"***
- Repeated dosing increases drug concentration and accordingly the rate of elimination increases till the rate of administration equals the rate of elimination.

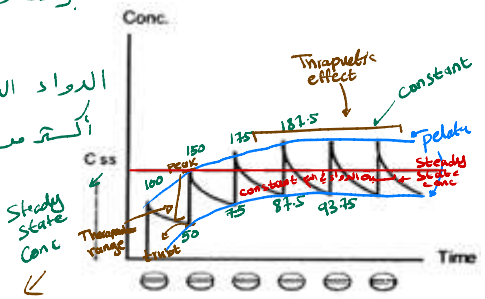
* increase dose → increase elimination rate

- Css can be reached after 4-5 $t_{1/2}$
- Css is directly proportionate to the dose.

Symptoms "أعراض المرض"

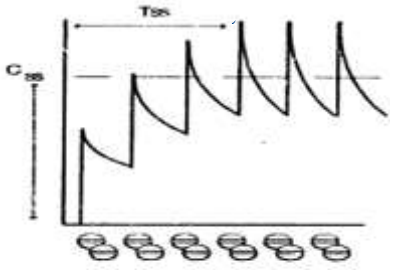
جرعة واحدة ← علاج

الدواء الذي يعالج المرض يحتاج أكثر من جرعة



- constant plasma conc. for Drug in Blood
- Steady state الدواء يعطي Therapeutic effect

if the t1/2 was 8 → Therapeutic effect is after (40-48) hour



↑ dose → ↑ Css

Zero order kinetics

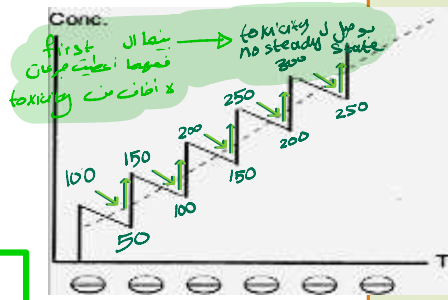
(phenytion and salicylate)

PEA

(Aspirin)

Ethanol (Alcohol)

- Rate of drug elimination is constant i.e. ***constant amount*** of drug is eliminated per unit of time.
- "$t_{1/2}$" (half life) is not constant.
- No Css is reached by repeated dosing.
- Any change of the dose may cause toxicity.
- Some drugs follow 1st order kinetics in small dose and zero order kinetic at large doses i.e. the elimination mechanism is said to be saturated (saturation kinetics).



ELIMINATION HALF LIFE ($T_{1/2}$)

- It is the time required to reduce the plasma concentration of the drug to half the initial concentration (the time required for drug concentration to be changed by 50%).
- $T_{1/2} = 0.7\ V_d/CLs$

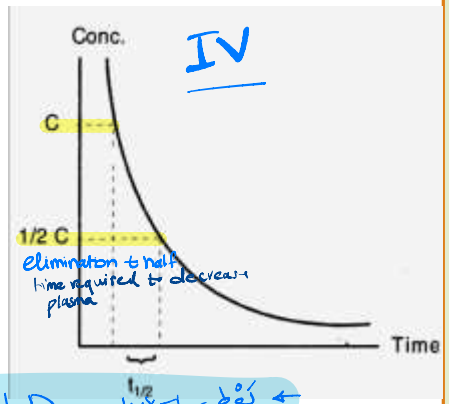
لو كان t½ قليل 10min
↵ أفضل طريقة لإعطاء الدواء هي التقطير* [IV infusion]*

Importance of elimination $T_{1/2}$:

جرعة الدواء

- It determines the dosage interval (T).
- It indicates time required to attain الهدف

  Css (about 4-5 $t_{1/2}$):



- If "$t_{1/2}$" is very short (minutes), the drug should be given by IV infusion [dopamine].

Long t½ → LD يُعطى الأول followed by M.Dose

جرعة LD لا أحد يعطاها أبقاء نصف أول مرة

t-half is 7days

- If "$t_{1/2}$" is long [digoxin], the drug should be administered in loading dose followed by maintenance dose

Css حتى أوصل الدواء الى Therapeutic effect العلاجي الى target plasma effect → Loading dose ← الحل

الجرعة "الصغيرة" التي ازمت بدا

after (4-5) t½ of single dose → almost complete elimination

Factors affecting elimination "$t_{1/2}$":

- State of eliminating organs i.e. liver & kidney function.
- Delivery of drugs to the eliminating organs: affected by plasma protein binding and Vd of the drug.

Vd↑ $t_{1/2}$ ↑

Vd↓ $t_{1/2}$ ↓

SYSTEMIC CLEARANCE (CLs)

- *It is the volume of fluid cleared from the drug per unit of time.*
- *Systemic CLs = Renal clearance (CL_r) + non-renal clearance (CLnr)*

Significance of clearance:

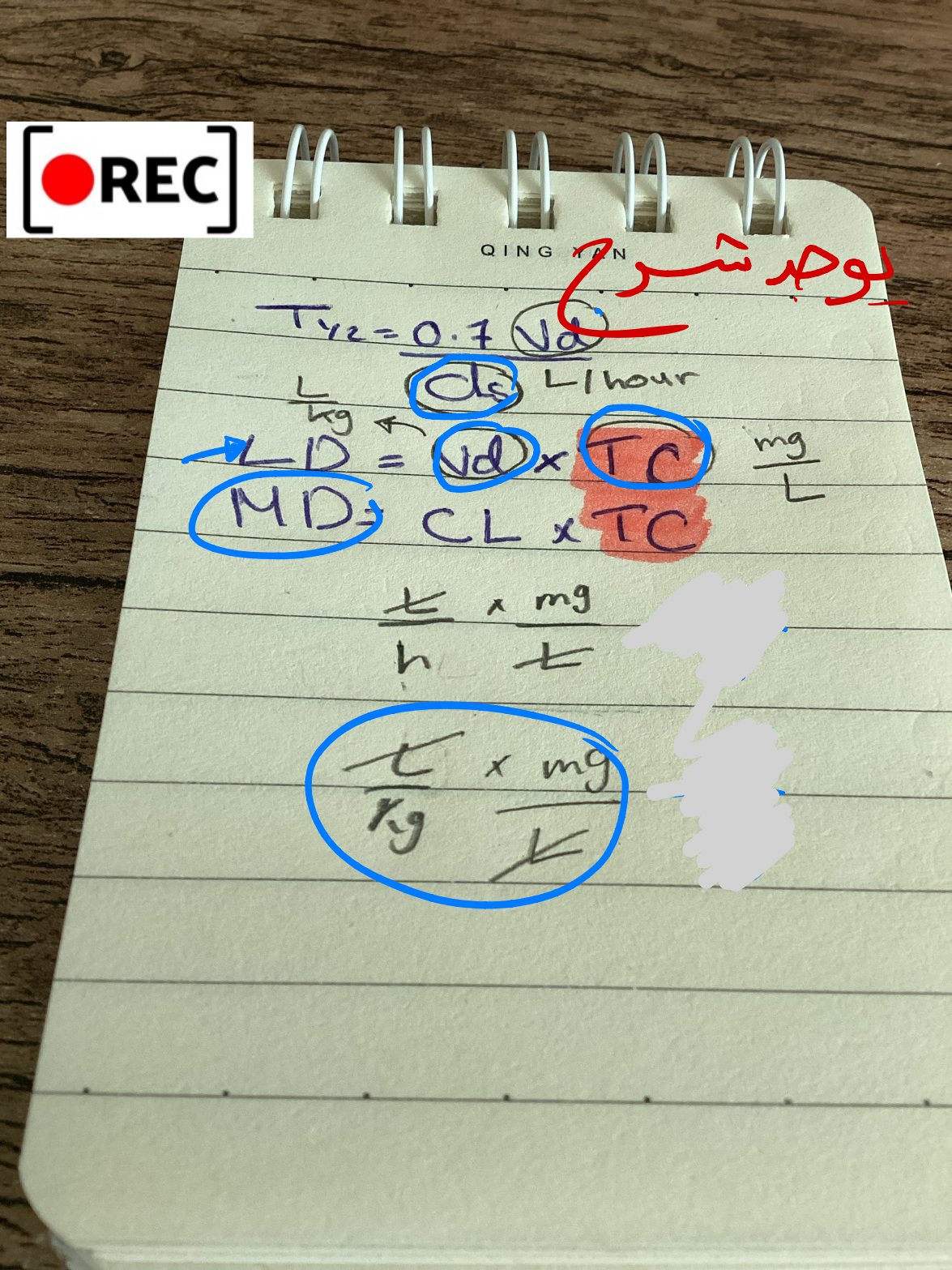
- Calculation of the maintenance dose

- **Loading dose:** The dose required to achieve a desired plasma concentration (desired Css) rapidly, followed by routine maintenance dose.

Loading dose = Vd ×TC

- **Maintenance dose:** The dose given to maintain the desired Css.

Maintenance dose = CLs ×TC (Target concentration).


REC
QING YAN
بوحد شرح
$T_{1/2} = \frac{0.7 \times Vd}{Cl_s}$ L/hour
$\frac{L}{kg}$
$LD = Vd \times TC$ $\frac{mg}{L}$
$MD = CL \times TC$
$\frac{L}{h} \times \frac{mg}{L}$
$\frac{L}{kg} \times \frac{mg}{L}$

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Thank you!