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PLASMA HALF LIFE

I

- Define plasma half life
- Define and explain steady state concentration
- Explain the significance of plasma half life
- Enlist the factors effecting plasma half life
- Define 1st order kinetics and give examples
- Define zero order kinetics and give examples

Definition

It is the time period required for the amount of or the concentration of a drug to fall to 50 % of the earlier measurement

It is the time required to achieve half of the targeted concentration of drug in the plasma administered via any route

Types or Names of Half Life

Plasma half life

Biological half life

Distribution half life

Elimination half life

Biological half life

It is the general term which implies to the time period in which the initial concentration of the drug decreases by one half.

Not telling that by virtue of what this half life is achieved. It is not specific for any anatomical compartment

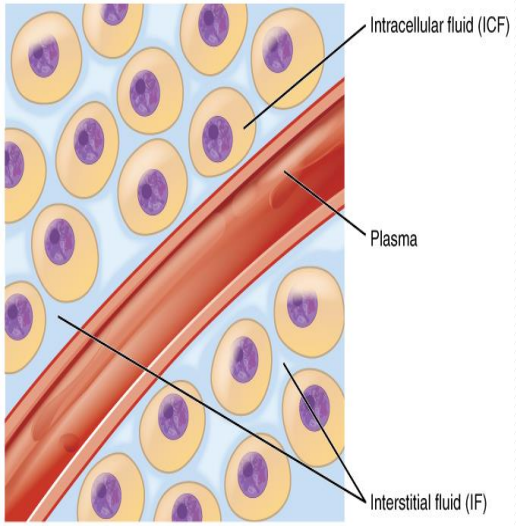
Plasma Half Life

$t_{1/2}$

It is the time required to decrease the drug concentration in the plasma to one half of its initial concentration.

To achieve half of the concentration the drug in the plasma after administration via any route.

Distribution Half Life



It is the time taken to decrease the drug concentration in the plasma to one half of its initial concentration by virtue of its distribution

Movement from one anatomical compartment to another

Elimination Half Life

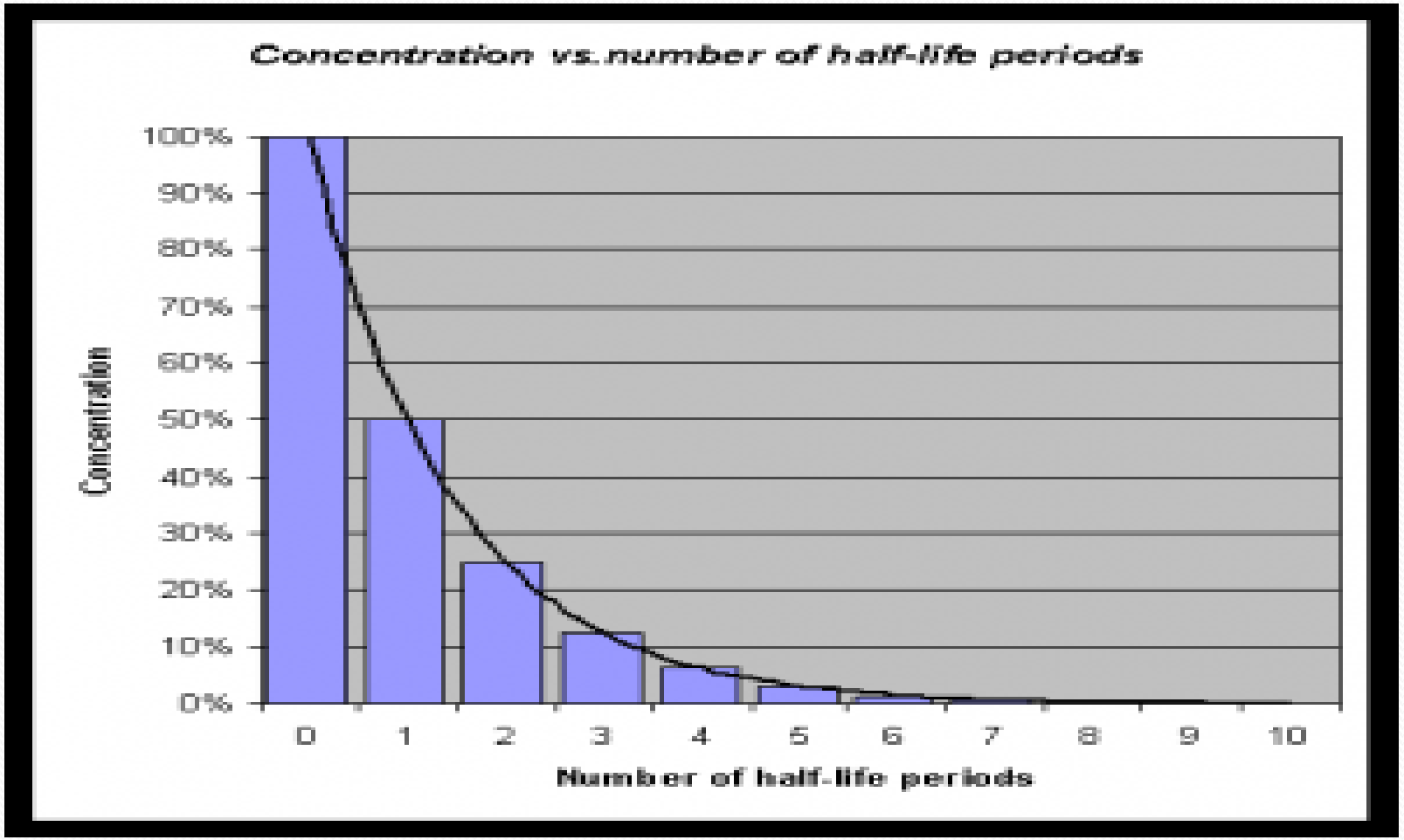
It is the time taken when one half of the drug appears in the urine or bile.

Formula of plasma half life

Plasma Half Life is Expressed as

$$t_{1/2}=0.693 \times Vd / Cl$$

0.693=constant


Concentration vs.number of half-life periods
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Concentration
0
1
2
3
4
5
6
7
8
9
10
Number of half-life periods

Steady state concentration

When rate of elimination of drug becomes exactly equal to the rate of administration this is called steady state concentration.
It is depicted by a plateau on the concentration time curve.

It takes $4 - 5t_{1/2}$ to achieve steady state concentration.

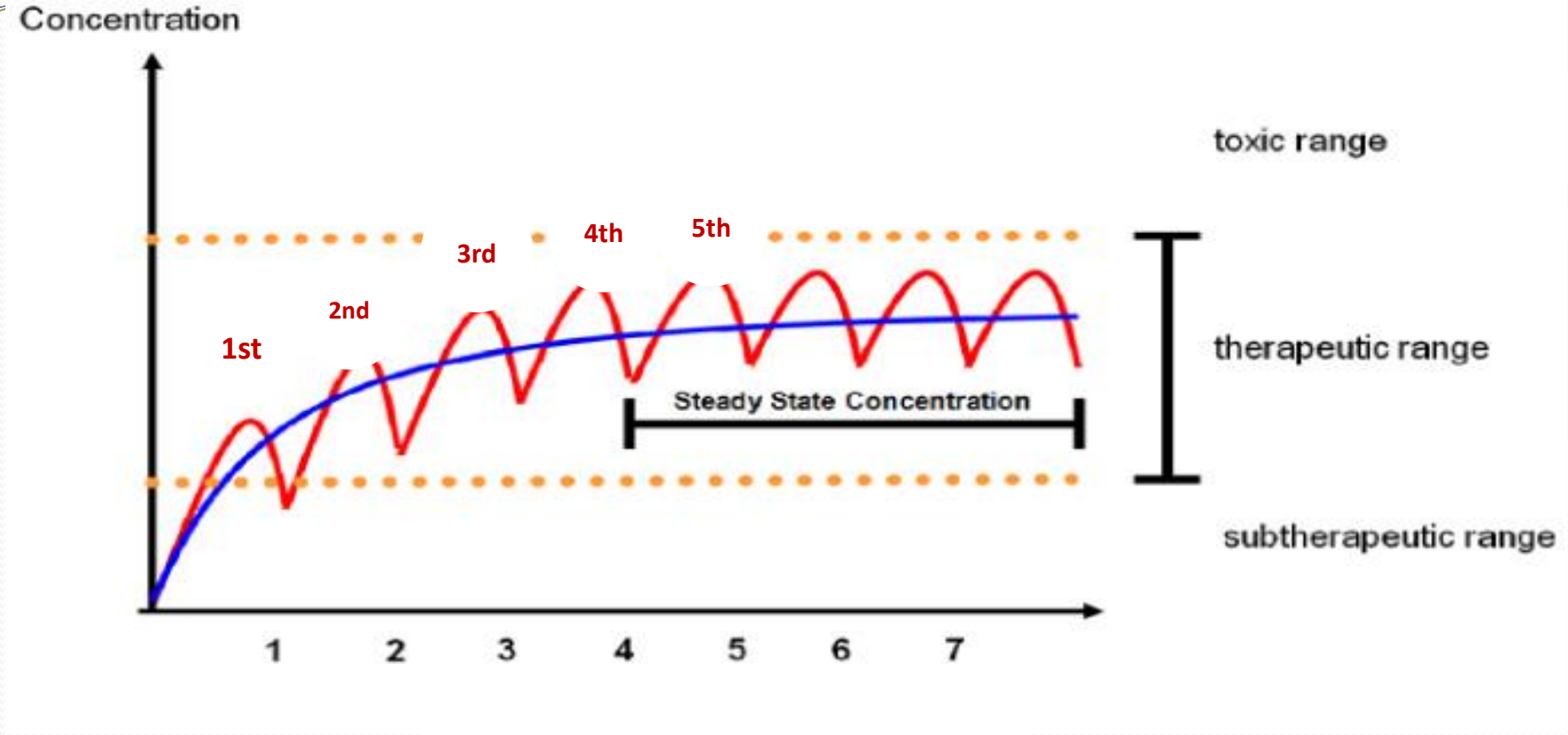
After 1st dose= full 1 dose = 0.5 dose= 50 % C_{SS}

After 2nd dose= 0.5 + 1 doses = 1.5 doses
Then ½ was eliminated=0.75dose left=75% C_{SS}

After 3rd dose= 0.75+1 = 1.75 dose=
Then ½ was eliminated=0.875doses=88% C_{SS}

After 4th dose= 0.875+1 dose =1,85 dose
Then ½ was eliminated=0.937=94% C_{SS}

After 5th dose= 0.937+1 dose =1.937 dose
Then ½ was eliminated=0.968=97% C_{SS}



It takes 4-5 half lives to achieve steady state concentration

Infusion at a constant rate

- When a drug is infused at a constant rate, the rate of elimination becomes equal to the rate of administration and a steady state is achieved called the **STEADY STATE CONCENTRATION**.
- This is depicted by a PLATEAU on the conc time curve.

Intermitent administration

- If the administration is continued intermittently , the plasma conc will depicted by **PEAKS and TROUGHS** .
- The heights of the peaks will be equal and the depth of the troughs will be equal to each other.
- As the mean conc remains constant , the conc in this pattern is also called **THE STEADY STATE CONCENTRATION.**

On starting the administration of the drug

- On starting the administration of the drug , the concentration goes on increasing till a steady state concentration , depicted by a PLATEAU is reached in which administration rate becomes equal to that of elimination .

On altering the rate of administration

- On altering the rate of administration ,the steady state conc is changed to a new steady state concentration.

Contd

Changes in the plasma conc. on starting , altering or stopping the drug administration can be predicted by plasma **half life**.

ON WITHDRAWL OF THE DRUG

[t ½] = To 5o%

[2 t ½] = To 25%

[3 t ½] = To 12.5%

[4 t ½] = To 6.25%

[5t ½] = To 3.12%

Half life of some representative drugs

- Aspirin ----------4hrs
- Penicillin G-----30 min
- Doxycycline --- 20 hrs
- Digoxin---------40 hrs
- Digitoxin--------7 days
- Phenbarbitone -90hrs

Significance of the half life

To determine the duration of action of the drug.

To determine the frequency of drug administration.

To evaluate the dose [by the Vd , protien binding and the elimination]

To determine the time required to reach the steady concentrtation

To calculate the loading dose

[t ½ x tc x CL/o.693]

To know about the maintenance dose

[Vd x Css ½ x o.693

To find the defect in the distribution, metabolism or clearance[to asses the disease]

factors effecting Plasma Half Life

Concurrent administration of another drug that displaces the first drug from albumin decreases its t ½.

Decrease in the rate of metabolism when an enzyme inhibitor is given. {increase in the t1/2.}

low extraction ratio increases the half life as in the liver and kidney disease

Decreased renal blood flow as in cardiogenic shock, cardiac failure or hypovolemia [hemorrhage] increases its t ½

1^{st} order kinetics

When the rate of elimination of drug is directly proportional to the concentration of drug in plasma.

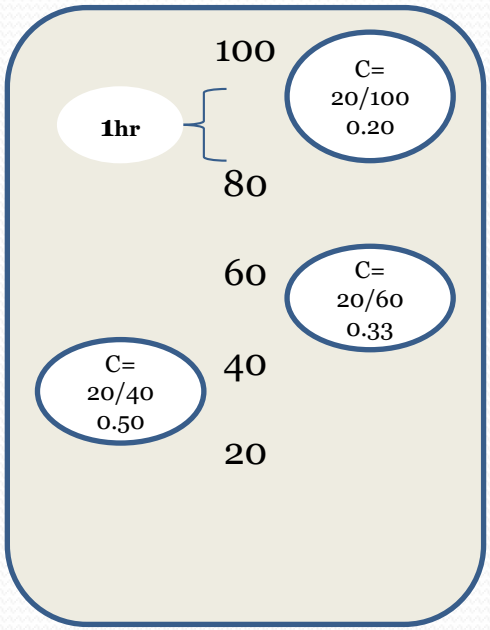
In 1^{st} order kinetics a constant fraction is eliminated per unit time.

$t_{1/2}$= constant
Rate of elimination∞ Plasma concentration
Clearence=rate of elimination/total plasma concentration= constant

Zero order kinetics

$t_{1/2} \propto P\ C$
R=constant
$CL \propto 1/PC$

A constant amount of drug is eliminated /time.



Why some drugs follow 1st order kinetics and some follow zero order kinetics

In 1st order kinetics the metabolizing enzymes are sufficient

In zero order kinetics the metabolizing enzymes gets saturated.

Almost all the drugs follow first order kinetics

Warfarin
Alcohol
Theophyline
Tolbutamide
Phenytoin


Thank You