
Plasma half-life of drugs, steady state concentration, its clinical importance and factors affecting it.

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Plasma Half Life of Drug

Half-life is the time taken for the drug concentration to fall to half its original value

Drug Half-Life

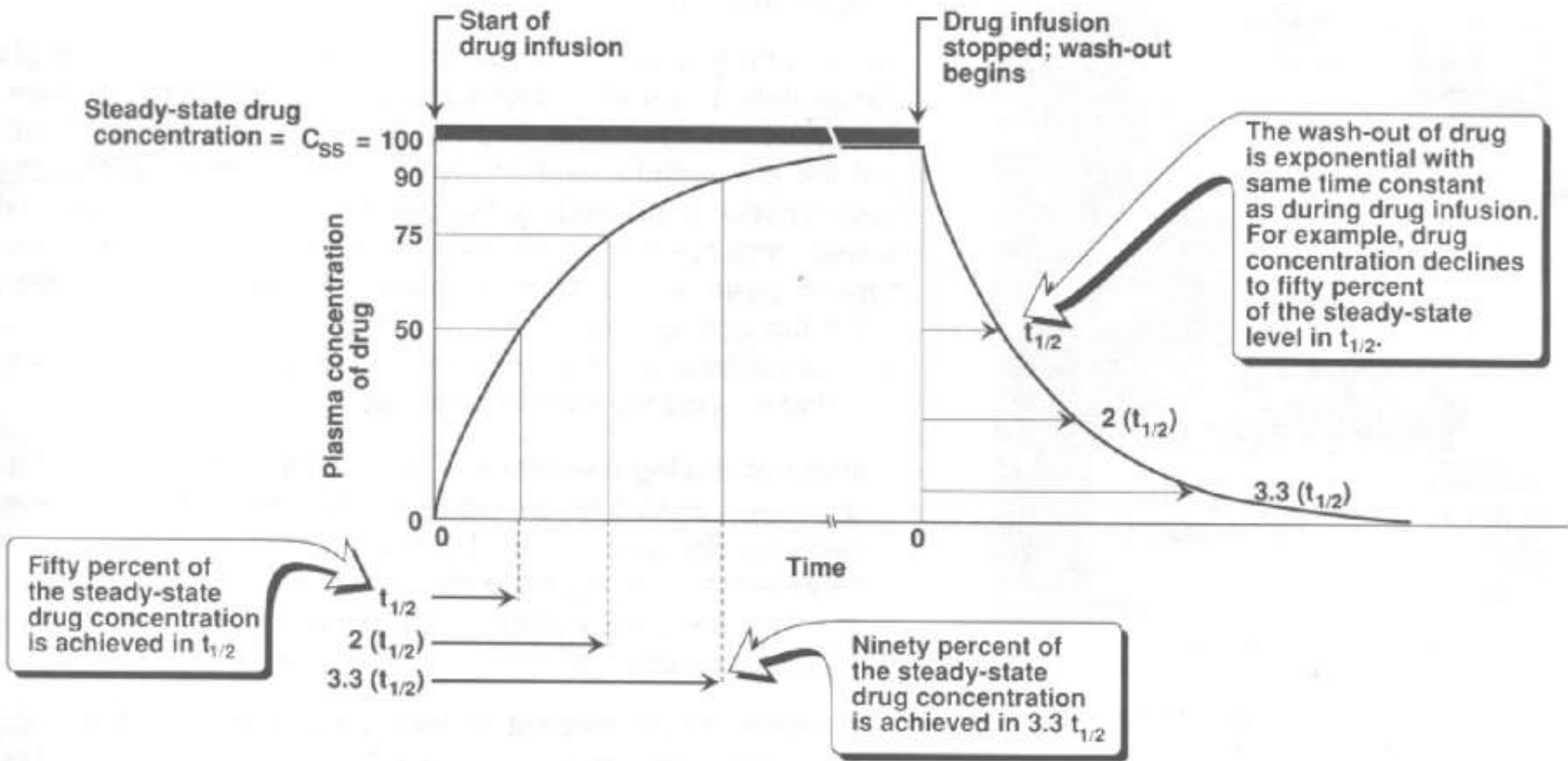


Figure 2.3
Rate of attainment of steady-state concentration of drug in plasma.

If drug has short duration of action, design drug with larger half life

If drug too toxic, design drug with smaller half life

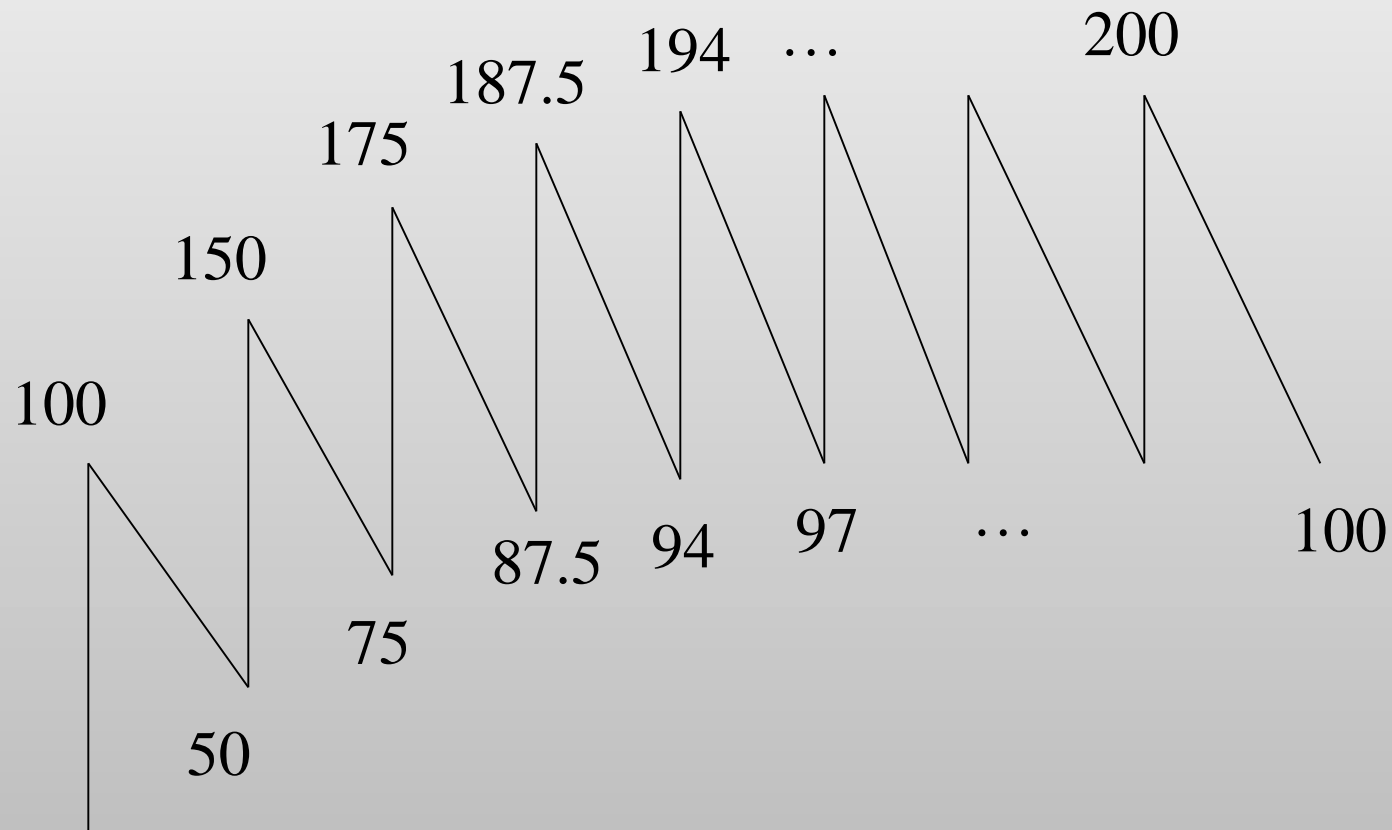
Steady-State Concentration

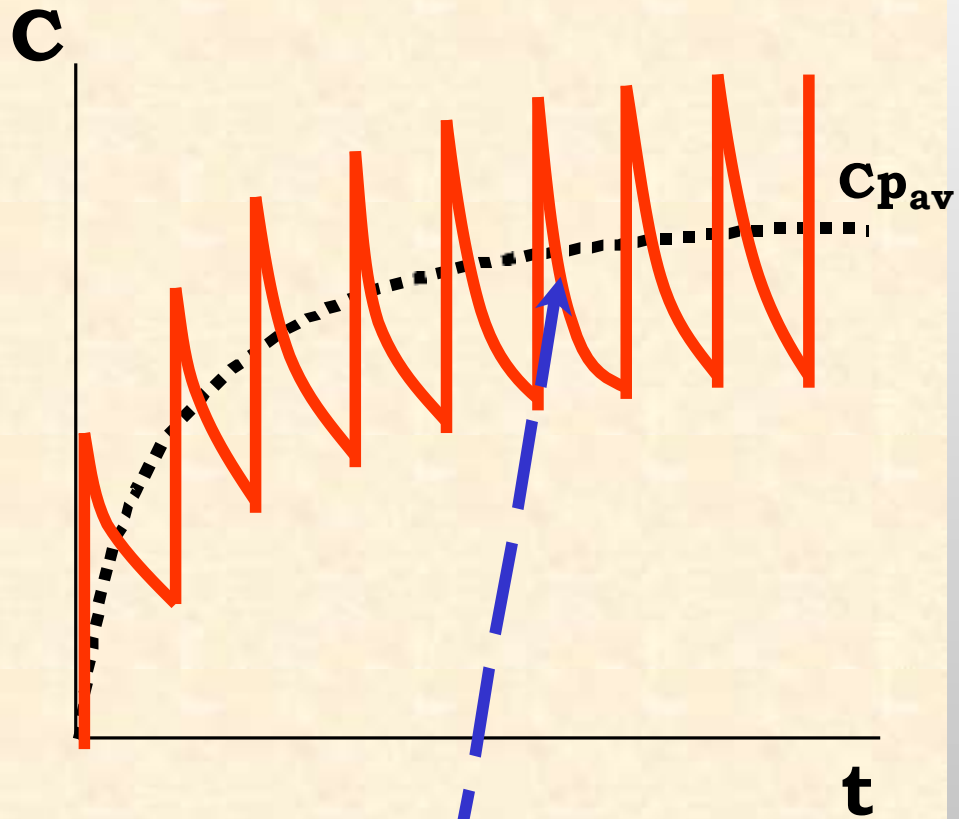
Steady-state occurs after a drug has been given for approximately five elimination half-lives.

At steady-state the rate of drug administration equals the rate of elimination and plasma concentration - time curves found after each dose should be approximately superimposable.

Accumulation to Steady State

100 mg given every half-life





Four half lives to reach steady state

What is Steady State (SS) ?
Why is it important ?

Rate in = Rate Out

Reached in 4 – 5 half-lives (linear kinetics)

Important when interpreting drug concentrations
in time-dependent manner or assessing clinical
response

Therapeutic Drug Monitoring

Therapeutic Index

Therapeutic index = toxic dose/effective dose

This is a measure of a drug's safety

- A large number = a wide margin of safety
- A small number = a small margin of safety

Drug Concentrations may be Useful when there is:

An established relationship between concentration and response or toxicity

A sensitive and specific assay

An assay that is relatively easy to perform

A narrow therapeutic range

A need to enhance response/prevent toxicity

Why Measure Drug Concentrations?

Lack of therapeutic response

Toxic effects evident

Potential for non-compliance

Variability in relationship of dose and concentration

Therapeutic/toxic actions not easily quantified by clinical endpoints

Therapeutic Window

Useful range of concentration over which a drug is therapeutically beneficial. Therapeutic window may vary from patient to patient

Drugs with narrow therapeutic windows require smaller and more frequent doses or a different method of administration

Drugs with slow elimination rates may rapidly accumulate to toxic levels....can choose to give one large initial dose, following only with small doses