What happens if we give someone another dose of drug while the previous dose is still trying to leave the body? What if those cheeky bacteria are cheering between doses because the last dose just hopped on a bus out of town and the next bus hasn’t arrived yet? Pharmacists are trained to predict when these things will happen. But how do they know?

Drugs need to reach a minimum concentration in the body for effects to start appearing. This concentration is referred to as the ‘Minimum Effective Concentration’ (MEC). Once the concentration of the drug falls below the MEC, the effects are over. Hence, drug dose is based on maintaining a specific concentration of the drug in your body to ensure the desired effect occurs. This all depends on the rate at which these drugs are eliminated from our bodies. So how is the rate of elimination determined?

Elimination Kinetics

There are two ways to describe how the body breaks down and uses different drugs, ‘zero-order kinetics’ and ‘first-order kinetics’.

In zero order kinetics, a constant amount of drug is eliminated over time. The elimination occurs at a predictable rate. Let’s think of this in terms of buying shoes. Imagine Myer has a sale and you have bought too many shoes. Your friend helps you get rid of the unwanted ones by agreeing to take one pair each week. Meanwhile, you are still buying more shoes. So now you have shoes coming into your wardrobe faster than you can get rid of them.

In zero order elimination, changing the concentration of the drug (continuing to buy more shoes) will not change the rate at which the drug is eliminated (how many shoes are in your wardrobe) as only a fixed amount of drug can be removed from the system (1 pair of shoes per week). This means that soon enough, your wardrobe will burst at the seams! Or, a drug overdose will occur.

In most toxic situations such as drug overdose or alcohol poisoning, the drug follows zero order elimination kinetics.
FIRST ORDER ELIMINATION KINETICS

Now that you have an idea about zero order kinetics, let’s look at first order kinetics. Most drugs will be eliminated from the body as a percentage rate based on how much the person has been given.\(^4\) The percentage rate is known as half-life.\(^5\) If a drug has a short half-life, it will be administered in more frequent doses. If it has a long half-life (is eliminated slowly from the body), it will be given less often.

It usually takes around 4-5 half-lives (with repeated dosing) to eliminate 95-97% of a drug from the body.\(^5\) Around this time, the first dose has been eliminated. This means that there will be no significant difference in the average drug concentration in the body from dose to dose. The drug has reached a steady state – a plateau level.\(^10\)

Elimination kinetics of a drug can change in overdose as if someone take too much of a drug that follows first order kinetics, it can still reach toxic levels in your body.\(^7\)

So, even though your friend is taking 20% of your shoes each week (the drug follows first order kinetics), your wardrobe may still someday burst if you continue buying shoes, but it will take a lot longer than if they were taking one pair a week (if the drug followed zero order kinetics). We’re almost there!

LOADING DOSE

In some cases, a loading dose is administered. This is an initial higher dose that is administered at the start of a course of treatment before reducing the dose to lower ‘maintenance’ doses.\(^6\) A loading dose is provided in cases where drugs are eliminated from the body very slowly otherwise it would take an extremely long time for the concentration of the drug in the body to reach the steady state.\(^6\)

Calculating Loading Dose (QL)\(^7\)

\[
QL = Vd \times Target \ Cp
\]

Target \(Cp\) = desired concentration of the drug in plasma

\(Vd\) = distribution of the drug in the body
References


Images

Drug Banner

Elimination Graphs

Shoes