Pharmacokinetic processes: distribution

Distribution

Distribution is the process by which drug passes from the bloodstream to body tissues and organs. It is how a drug moves from intravascular space, e.g. blood vessels, to extravascular space, e.g. body tissues, as it is carried around the body by the circulatory system (figure 1).

Therefore, factors that affect distribution include:

- solubility, including pK_a values and the effect of pH on solubility;
- partition/distribution coefficients.

How a drug gets into the bloodstream depends on the method of administration. A drug may get into the bloodstream directly, e.g. by intravenous injection, or by absorption, e.g. from the gastrointestinal tract if a drug has been taken orally.

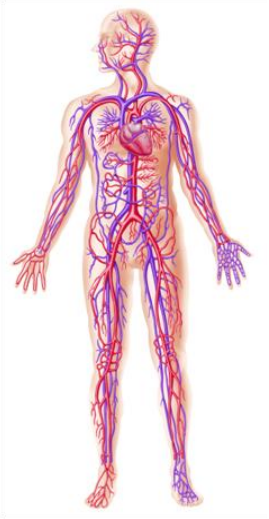

Figure 1 Once a drug is absorbed into the blood stream it is distributed throughout the body by the body's circulatory system.

The body may be described in terms of two regions.

- One region is tissues and organs that have a plentiful supply of blood, e.g. organs such as the heart, liver and lungs. This region is called the central volume of distribution.
- The other region is where blood supply is less. It is called the peripheral volume of distribution and is the total of tissue spaces not included in the central volume.

Together central volume of distribution and the peripheral volume of distribution make up the apparent volume of distribution.

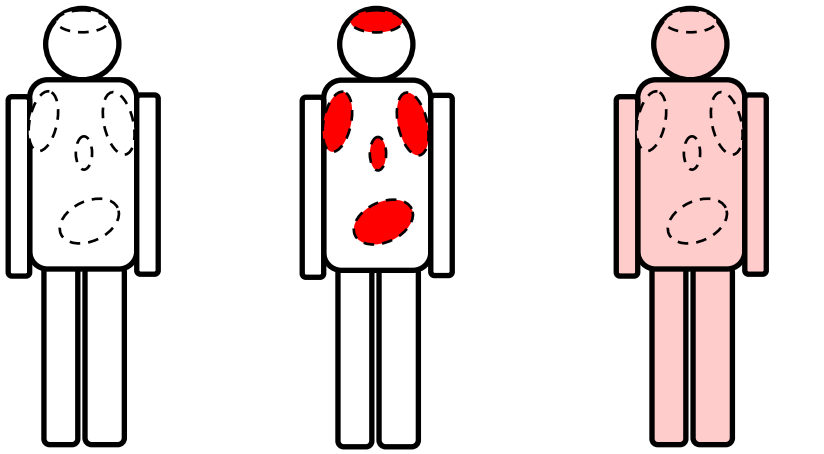

Figure 2 Distribution of a drug. Red areas in the middle drawing represent organs with a plentiful supply of blood.

Distribution to the central volume happens first, followed by distribution to the peripheral volume (see figure 2).

An understanding of mathematical models of distribution volumes are important for estimating the quantity of a drug in the body, the peak level of a drug and the time required for elimination from the body.

Dosage and volume of distribution

When administering a drug it is important to know the loading dose of that drug. This is the initial dose given before reducing to a lower maintenance dose. The starting point for working out a loading dose is to calculate the apparent volume of distribution (or, simply, the volume of distribution). Knowledge of the loading dose is also important for estimating blood concentration in the treatment of an overdose.

The concentration of a drug in blood plasma can be measured. The volume of distribution may be defined as the volume of blood plasma required to account for the total amount of drug in the patient's body, assuming it is present throughout the body at the same concentration as it is in the blood plasma. Dividing the volume by the patient's mass gives a result expressed in $dm^3\ kg^{-1}$. This value can be used to calculate loading doses for other patients.

Some calculations

Imagine an 'average' human body.

An 'average' human body contains about 5.5 dm^3 of blood. Blood is roughly 55% by volume liquid (blood plasma) and 45% by volume solid particles such as cells. So our average body contains about 3 dm^3 of blood plasma.

Next, our 'average' human weighs about 60 kg.

So the plasma volume is $3 \div 60 = 0.05\ dm^3\ kg^{-1}$

Note: $dm^3\ kg^{-1}$ is decimetres cubed per kilogram. Since 'decimetre cubed' is the same as 'litre', 0.05 $dm^3\ kg^{-1}$ is 0.05 litres per kilogram.

Now compare two drugs – Drug A and Drug B – taken by our average human (60 kg and 3 dm^3 of blood plasma).

	Drug A	**Drug B**
Mass of drug taken / mg	1000	350
Concentration of drug in blood plasma / mg dm^{-3}	2	20
Apparent volume of distribution / dm^3	$1000 \div 2 = 500$	$350 \div 20 = 17.5$
Apparent volume of distribution per kilogram / $dm^3\ kg^{-1}$	$500 \div 60 = 8.33$	$17.5 \div 60 = 0.29$

This tells us that:

- both drugs have an apparent volume of distribution greater than the plasma volume (0.05 $dm^3\ kg^{-1}$), but Drug A is almost thirty times greater than Drug B;
- both drugs have moved from intravascular space to extravascular space, but Drug A more so than Drug B;
- Drug A is more soluble in lipids than in water and binds strongly to tissue;
- Drug B is more soluble in water than in lipids and distributes into the extracellular fluid rather than binding to tissue.

Finding out

How can the relative water/lipid solubility be determined for a potential drug?