2.2: Measurement of Compartment Volumes

2.2.1: The Dilution Principle

Compartment volumes are measured by determining the volume of distribution of a tracer substance. A known amount of a tracer is added to a compartment. The tracer concentration in that compartment is measured after allowing sufficient time for uniform distribution throughout the compartment. The compartment volume is calculated as:

\[
\text{Volume} = \frac{\text{Amount of tracer}}{\text{Concentration of tracer}}
\]

Ideally, the tracer should have certain properties (see box)

**Properties of an Ideal Tracer**

The tracer should:

- be nontoxic
- be rapidly and evenly distribute throughout the nominated compartment not enter any other compartment.
- not be metabolised
- not be excreted (or excretion is able to be corrected for) during the equilibration period
- be easy to measure
- not interfere with body fluid distribution
If the tracer is excreted in the urine, then the loss can be determined and corrections made in the calculation. If the tracer is metabolised, a series of measurements can be made and assuming exponential decline (first order kinetics), the volume of distribution can be determined by extrapolation back to zero time.

### 2.2.2: Total Body Water

This is estimated by measuring the volume of distribution of isotopes of water. Tritium oxide (THO) is used because it is a weak beta emitter making it easy to measure in a liquid scintillation counter. Rapid mixing of tritiated water throughout all compartments occurs during a 3 to 4 hour equilibration period. Results are accurate and reproducible to within 2 percent.

### 2.2.3: Extracellular Fluid

Tracers used fall into 2 groups:

- Ionics (eg 82Br, $^{35}$SO$_4$, chloride isotopes)
- Crystalloids (eg Inulin, mannitol)

The ionic tracers are small and distribute throughout the ECF but there is some entry into cells. ECF will be overestimated with these tracers

The crystalloids are larger and less diffusible throughout the ECF. They do not enter cells but the lack of full ECF distribution results in a low estimate of ECF.

What is measured is not the true ECF so it is conventional to refer to the compartment measured not as ECF but as a space defined by the tracer used and the equilibration time (eg 20 hour bromide space).

Measurements indicate that the ECF can be modelled as consisting of:

- a rapidly equilibrating pool ("functional ECF") which makes up about 27 to 30% of total body water (This rapid pool represents plasma and most of the ISF)
- a slowly equilibrating pool (24 hours) which makes up 15% of total body water. (This slow pool mostly represents the water of dense connective tissue and bone and some of the transcellular fluid)

### 2.2.4: Plasma Volume

Measurement of plasma volume requires a tracer which is mostly limited to this compartment and this is achieved by using a tracer which binds to albumin.

The tracers used are the azo dye known as **Evan's blue** (or T1824) which binds avidly to albumin, or **radio-iodine labelled serum albumin (RISA)**. Distribution is rapid but no equilibrium is reached because of continuous disappearance of albumin from the vascular space. This problem is overcome by using serial measurements and plotting the disappearance curve of the label. This is a first order process (ie exponential decline) which gives a straight...
line when plotted on a logarithmic scale. Extrapolation back to zero time allows estimation of the virtual concentration at this time. The volume is determined via the dilution principle using this concentration at zero time. As the concentration of the tracer is determined in a plasma sample, the measured volume of distribution is the plasma volume.

### 2.2.5: Blood Volume

The tracer is the patient's own red cells which are tagged with radio-chromium (Cr\(^{51}\)-red cells). Typically a 10 ml sample of the subject's blood is incubated with a sodium chromate solution, the label is taken up by the red cells and any excess in the solution is removed by dilution and centrifuging with removal of fluid. The labelled red cells are centrifuged, resuspended in saline and infused into the patient. The volume of distribution (VD) is determined after about 30 minutes. As the radioactive label distributes throughout the whole intravascular compartment, the measured VD is the blood volume (rather than the red cell volume). The distribution of the label is not uniform because the haematocrit is different in different parts of the circulation. It is usual therefore to measure the amount of the label in a red cell sample and therefore to directly measure the red cell volume.

Plasma volume or red cell volume can be determined indirectly if the blood volume and haematocrit (Hct) are known.

**Formulae for Blood Volume**

\[
\begin{align*}
\text{Blood Volume} &= \text{Plasma volume} \times \frac{100}{100 - \text{Hct}} \\
\text{Blood Volume} &= \text{Red cell volume} \times \frac{100}{\text{Hct}}
\end{align*}
\]

(where Hct = Haematocrit)

As mentioned previously, there are several problems in estimating an average or 'whole body' haematocrit:

- Haematocrit measured in the laboratory overestimates true haemotocrit because about 4 to 8% of the plasma remains trapped with the red cells in the tube
- Blood from capillaries has a lower haematocrit then in larger vessels because of axial streaming of red cells. (Haematocrit in muscle capillaries is typically only 0.20 !)
- Large vein haematocrit is higher then in arteries because the various reactions in the red cell due to carbon dioxide transport lead to an increase in the number of particles intracellularly and an osmotic increase in water content

Accounting for these effects, the whole body haematocrit can be estimated as about 91% of large vein haematocrit and this value should be substituted in the equations.

### 2.2.6: Other Major Compartments

**Interstitial Fluid**

There is no tracer which are distributed only throughout this compartment. ISF is determined indirectly as the difference between concurrently measured ECF & plasma volumes. Measurement error is the sum of the errors of the two
individual measurements and can be significant.

**Intracellular Fluid**

There is no tracer available so ICF is measured indirectly as the difference between concurrently measured total body water and ECF. The volume of ICF decrease with increasing age and this accounts for most of the age-related decline in total body water.

**Transcellular Fluids**

There is no tracer for the measurement as a whole of the myriad components of transcellular water. Methods exist for the estimation of the various components individually.