Water

Transport and regulation in the body

Kevin Moffat

Biologist Kevin Moffat explains the link between your blood, your brain and your kidneys and how together they control the hydration of your body

AQA: 3.1.7 Water; 3.2.3 Transport across cell membranes; 3.6.4.3 Control of blood water potential

Edexcel A: 1.2 The importance of water; 2.3 Osmosis; 8.8 Brain structure

Edexcel B: 1.7 Water; 4.2 Cell transport mechanisms; 9.9 Osmoregulation

OCR A:2.1.2(a) Properties of water; 2.1.5(e) Osmosis; 5.1.1 Principles of homeostasis; 5.1.2(c)(i) Structure and function of the mammalian kidney; 5.1.2(d) Control of water potential of blood; 5.1.5(h) The human brain

OCR B: 2.1.2 Water and its importance; 5.3.3 Kidney functions and malfunctions

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Key words

Water potential
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Kidney
Pituitary gland
Brain

By weight, the average human female is about 50% water and the average male 60%. For a 70 kg male that's around 42 dm^3 of water. Differences are due to disparities in body fat and muscle composition. But where is this water, how is it regulated and what happens when this regulation goes wrong?

Kate Mori was running her fourth marathon. Fit, experienced and a sports scientist, she was 'ahead of her thirst', well hydrated before she began. It was April 2007 and one of the hottest London marathons on record, with temperatures over 23°C. Amid frequent reminders from the race officials about dehydration, Kate made sure that she drank at every opportunity. However, as she passed the 18-mile mark, she felt ill. She knew she was in trouble. Determined to finish for her charity, and with support from other runners, she staggered to the finish line. Shortly afterwards she collapsed and was put on a saline drip in hospital. Her problem? Over-hydration, resulting in a potentially lethal low concentration of sodium in her blood and tissues.

This condition is termed **hyponatremia**. The combination of exercise, drinking too much and inappropriate release of **anti-diuretic hormone** (ADH) resulted in Kate suffering from exercise-associated hyponatremia (EAH). This is a well-documented condition and, although it is treatable with a saline drip to replace the sodium, it can be fatal. Victims of EAH include American footballers, on-duty soldiers and policemen, canoeists, ironmen, long distance swimmers and mountain bikers. Symptoms of hyponatremia have also been linked to cases of people involved in water drinking games or those with seemingly unquenchable thirst after taking drugs such as ecstasy. They all risk death.

The UK National Health Service advises adults to drink 2 dm^3 of water a day. If we don't drink fluids we will die of dehydration in a few days. We might be lucky and last a week. However, we may die far sooner if we drink too much water too quickly. The **median lethal dose** (LD50) of water for humans is just 6 dm^3 — dangerous if drunk over a period of a few hours. To understand this, we need to consider where our body stores water and how our physiology controls it.

Where is our water?

About two-thirds of the water in our body is inside cells. The rest is extracellular. The extracellular water is divided between the plasma in the blood vessels (intravascular) and the fluid surrounding the cells and organs (interstitial) (see Figure 1). Plasma volume is normally kept at around 3 dm^3 for men and 2.3 dm^3 for women. Plasma is the main fluid compartment that interacts directly with water inputs to the body — from food and drink — and water outputs including urine, sweat, breath and secretions from the gut. To understand how water in the body is controlled, we need to consider its movement between plasma, interstitial fluid and cells. Water moves by **osmosis**, owing to differences in **water potential**.

Why does water move?

Early in our biology education we learn about osmosis, particularly in the context of plant roots taking up water, or changes in the size of cells.

Terms explained

Anti-diuretic hormone (ADH) A short, nine amino acid polypeptide hormone.

Baroreceptors Receptors that sense pressure in arteries.

Blood brain barrier Cells that normally prevent the movement of substances between the blood and the brain.

Cytokines Molecules secreted by cells that stimulate other cells, frequently found in the immune system.

Homeostasis The maintenance of a physiological state.

Hyponatremia A concentration of sodium ions in body fluids that is below normal physiological concentration.

MDMA 3,4-Methylenedioxymethamphetamine, also known as ecstasy.

Median lethal dose (LD50) The dose of a substance that will kill 50% of a sample population.

Osmoreceptors Receptors that sense changes in the water potential of arterial blood.

Osmosis The movement of a solvent across a semipermeable membrane from a dilute to a concentrated solution.

TRPV (transient receptor potential vanilloid) channels Membrane ion channels that respond to mechanical movement, often as a result of osmotic changes to cells.

Water potential A quantitative measure of the tendency of water to move by osmosis.

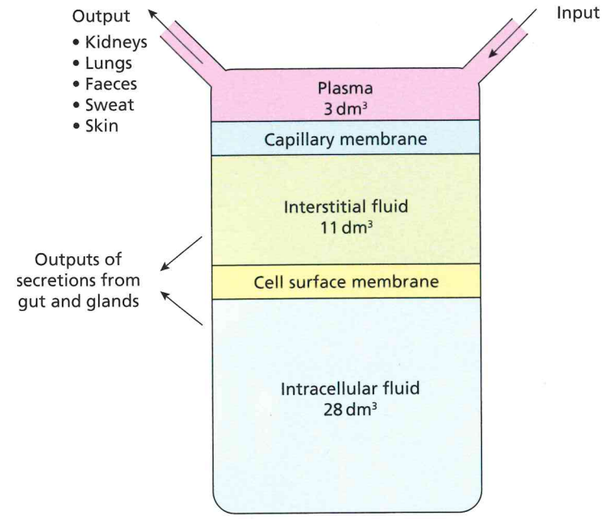

Figure 1 Fluid compartments. Our body fluids can be considered to be in three compartments separated by two partially permeable membranes. Blood plasma is responsible for the majority of exchange between the external environment and the fluid found inside our cells

Osmosis explains why water moves across a partially permeable membrane. The solvent (water) moves from the less concentrated solution to the more concentrated solution. Understanding water potential allows us to appreciate the forces underlying this movement (see Box 1).

In plant cells, the rigid cell walls contribute to the pressure component of water potential inside the cell. In animal cells, however, it is the concentrations of solutes that are the major determinants of water potential. A simple way to consider this is that the solute prevents water from moving freely by interacting with it, thus reducing the amount of free water and resulting in a lower water potential (see Box 1, Figure 1.1).

Sensing we are thirsty

When we sweat, urinate, defaecate and breathe, we lose water. The initial physiological response is the movement of water between compartments in the body owing to changes in water potential. Water loss increases solute concentration and hence decreases water potential in the plasma, resulting in the remaining water moving first from interstitial fluid and subsequently from cells (see Figure 1).

We normally maintain our water **homeostasis** by regulating thirst and urination. In severe situations, such as acute injury and blood loss, our arterioles undergo vasoconstriction in order to maintain blood pressure. This is mediated via **baroreceptors** located in the walls of blood vessels. An increase in concentration of solutes in blood plasma is sensed by **osmoreceptors**. Significant to thirst are osmoreceptors that are found in the brain, controlling the release of an important hormone, ADH.

Osmoreceptors are proteins called **TRPV channels** that are found in the cell surface membranes of neurones in brain regions where there is little or no **blood brain barrier**. Here they have close contact with blood vessels and

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Festival goers who take ecstasy risk developing EAH

therefore blood plasma (see Figure 2). These neurones shrink or expand as a result of changes in the water potential of blood, and they are exquisitely sensitive.

A decrease in water potential of the blood results in thirst and concentrates urine. This process is initiated by the mechanical movement of the TRPV channels as the neurone shrinks. The TRPV channels then directly alter the flow of ions across the neuronal membrane, generating action potentials that are sent to the brain's hypothalamus. The hypothalamus controls ADH secretion into the blood from the pituitary gland (see Figure 2). ADH then regulates water retention in our kidneys and, in the brain, gives rise to the sensation of thirst.

The kidneys

The major sites of fluid regulation are the kidneys' nephrons (see Figure 3). An ultrafiltrate is produced from the blood in the capillaries of the glomerulus. This then moves into the proximal convoluted tubules before entering the loop of Henle. The fluid moves through the distal convoluted tubule, enters the collecting ducts, and finally reaches the bladder for excretion from the body.

Human kidneys filter the blood around 20–25 times each day, producing about 1.5 dm^3 of urine, the majority of our daily water loss. The initial ultrafiltrate is similar to blood plasma, except for the proteins, which are not removed. In the proximal convoluted tubule, many ions, amino acids and vitamins are actively recovered. The descending loop of Henle is largely impermeable to ions, and water easily moves out by osmosis into the surrounding kidney medulla. The water potential in this part of the loop falls, becoming more negative.

Fluid movement through the ascending loop results in an increase in water potential, as this region is impermeable to water. Ions therefore move out, first by diffusion and then actively using energy from ATP. More water and ions are removed in the distal tubule, and the fluid entering the collecting duct has a high water potential.

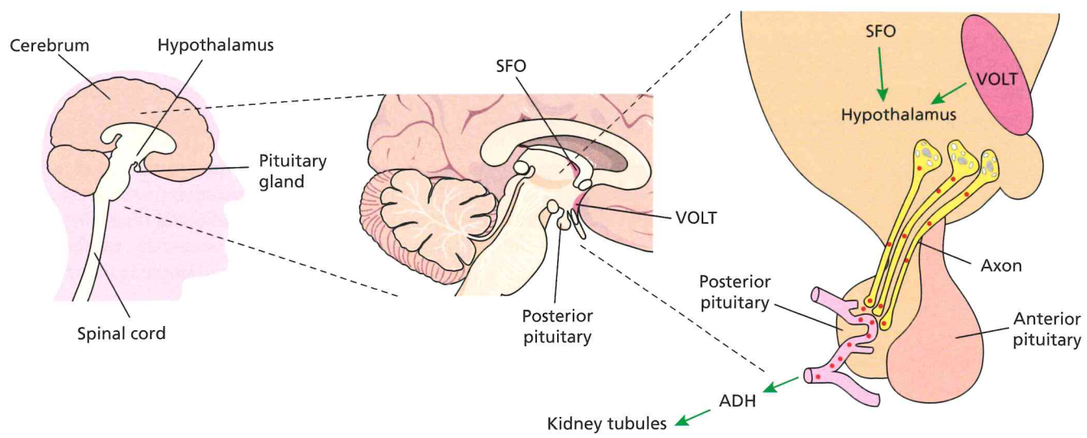

Figure 2 Osmoreception in the brain. Osmoreceptors are located in neurones in the vascular organ of lamina terminalis (VOLT) and the subfornical organ (SFO). These neurones send action potentials to hormone-producing neurosecretory cells in the hypothalamus, which regulate ADH secretion from the posterior pituitary gland

Box 1 Water potential

Water moves from a region of high water potential to a region of lower water potential (see Figure 1.1). Water potential is determined by two things — pressure and solute concentration. Water potential is represented by the Greek letter ψ (psi) with units of kilopascals (kPa). Water potential is effectively a measure of free water molecules in a solution. Pure water has the highest ψ of 0 kPa. The more solutes, the less free water. This is because solute interacts with water molecules so that they are not free to move. And the lower the water potential the more negative the kPa value. For example, a 0.15 M solution of sucrose has a ψ of –370 kPa.

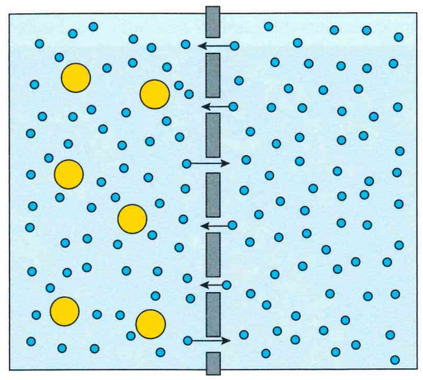

Figure 1.1 Osmosis and water potential. Yellow circles represent the solute (e.g. ions) and blue circles represent the solvent, water. The two sides are separated by a partially permeable membrane. With the solute only on the left, the higher concentration of free water is on the right, giving the right-hand side a higher water potential. The net flow of water is therefore to the left by osmosis

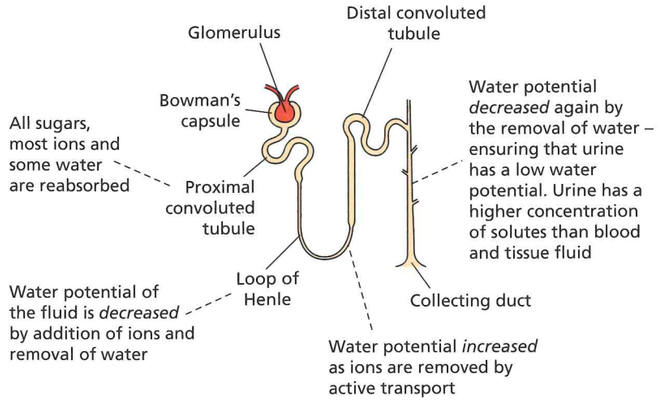

Figure 3 Water potential changes in a nephron of the kidney during production of urine

As it passes down the collecting duct, the high concentration of ions in the surrounding medulla results in a flow of water out of the duct. This results in urine that has a lower water potential — more concentrated solutes — than blood.

Importantly, the amount of water removed from the collecting duct is regulated by controlling its permeability to water. Dehydration lowers water potential in the blood, driving the thirst response via TRPV channels. The ADH subsequently released from the pituitary gland binds to receptors on the epithelial walls of the collecting ducts, stimulating an increase in the number of water channels — called aquaporins — in their cell surface membranes. This allows more water to leave the collecting duct by osmosis, resulting in further concentration of urine.

What can go wrong?

There are multiple causes of EAH: loss of sodium ions in sweat, internal production of water from metabolism, as well as a large intake of fluid through drinking. An Italian research team found that during glycogen metabolism and muscle injury — both common in intense exercise — a **cytokine** called IL-6 is released from muscle. This cytokine stimulates ADH release independently of osmoreceptors. Thus, during extreme exercise, even when well hydrated, ADH may continue to stimulate thirst and reduce urination, increasing water retention and therefore sodium dilution.

The causes of hyponatremia for users of ecstasy (**MDMA**) are different. Rather than IL-6, there is now evidence that a metabolite of MDMA can directly stimulate ADH secretion from the pituitary gland. The effect is the same as for EAH — to lower the concentration of sodium ions in body tissues. At best this is treatable with saline drips. At worst it results in death.

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Further reading

Read Kate Mori's story as reported in the *Telegraph*, 26 March 2012: **https://tinyurl.com/z36gs3j**

Watch a 4-minute documentary on the death of Jennifer Strange, after trying to win a Wii in a water drinking competition on a US radio station: **www.youtube.com/watch?v=ioKDf-JvKDo**

Key points

- Controlling hydration levels is important for health.
- Water moves between body compartments by osmosis owing to differences in water potential.
- The brain and pituitary hormones are critical for maintaining homeostasis.
- Water potential of blood plasma is controlled by the kidney.