F214 Communication, homeostasis and energy

Unit 2: Excretion

Removing Substances from the Body

The process of excretion is the removal of metabolic waste from the body. These are the waste substances of metabolism, both catabolic and anabolic reactions. Substances which are excreted include those such as carbon dioxide, and nitrogenous wastes such as **urea**

Failure to remove carbon dioxide from the blood (transported usually as carbaminohaemoglobin) results in a temporary condition called **respiratory acidosis** which presents symptoms such as feeling faint, dizzy, weak, vomiting and the urge to increase breathing rate – or hyperventilation

The liver and the kidneys are two organs responsible for the removal of wastes from the body. The liver concerns the deamination of amino acids into ammonia and the conversion of ammonia into urea, which is removed from the body in urine, controlled by the kidneys

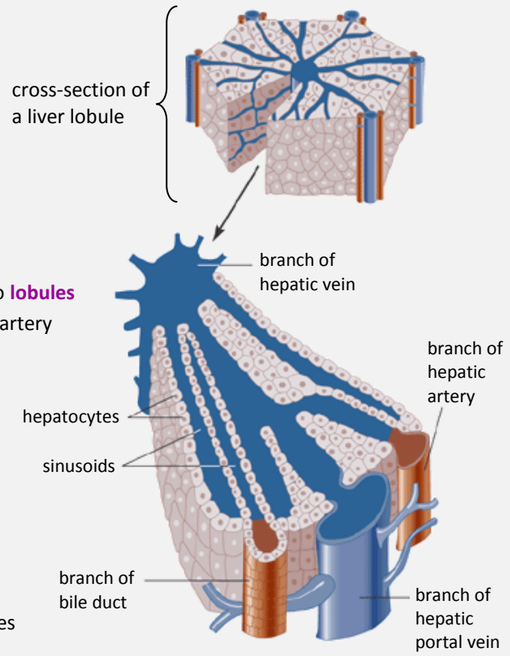
The Liver

The liver is an unusual organ in that it has two blood supply sources, receiving oxygenated blood from the heart (from the **hepatic artery**) and deoxygenated blood from the digestive system (through the **hepatic portal vein**). The **hepatic vein** takes blood from the liver to the vena cava to return to normal circulation. There is also the **bile duct** which runs from the gall bladder where bile is stored, to the liver. Bile is stored until needed during digestion. Liver cells are called **hepatocytes**

The liver is divided into lobes, which are further divided into **lobules** which are supplied with blood by extensions of the hepatic artery and hepatic portal vein called **inter-lobular vessels**

Branches of these vessels meet in chambers which run alongside the hepatocytes, called **sinusoids**. These hepatocytes are lined with microvilli so that there is a large area for exchange of substances between the cells and the fluid inside the sinusoids

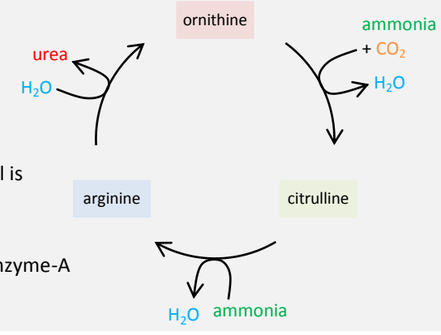
There are also **Kupffer cells** inside the sinusoid chambers which are responsible for the breakdown of erythrocytes, producing billirubin, the brown pigment which colours faeces



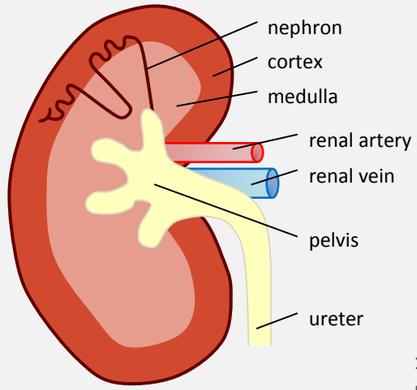
The Ornithine Cycle and Detoxification

When amino acids are to be excreted, firstly the amine group is removed to form **ammonia** (also producing **keto acid**). This is toxic and needs to be converted into a slightly less toxic and less soluble substance, and so the **ornithine cycle** modifies the molecule producing **urea**

The liver is also responsible for the **detoxification** of alcohol. Ethanol is dehydrogenated to produce **ethanal** (catalysed by ethanol dehydrogenase), and ethanal dehydrogenated to give **ethanoic acid** (catalysed by ethanal dehydrogenase), which can combine with coenzyme-A to give acetyl-CoA which can enter the link reaction and be respired



The Kidney and the Nephron

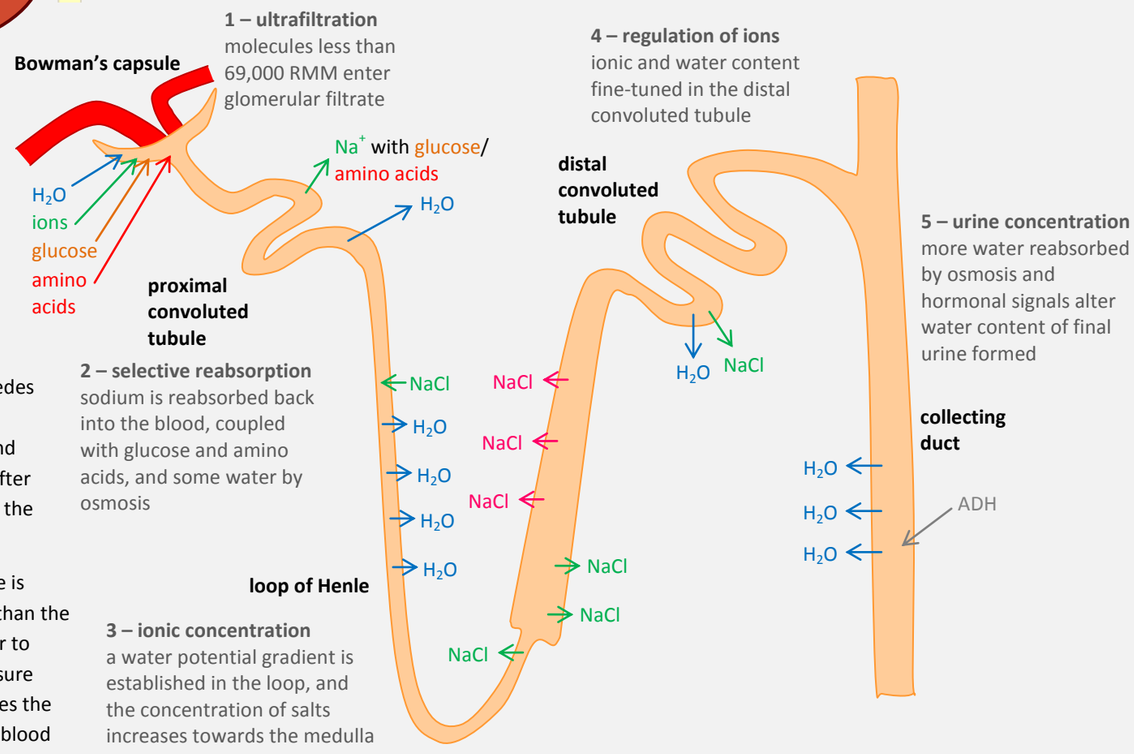


Humans usually have two kidneys. A kidney essentially has three sections: the outer **cortex**, the middle **medulla** and the inner **pelvis**. Each kidney contains roughly one million tiny tubules called **nephrons** which run through each section of the kidney

A nephron is made up of several sections in itself which each have different functions. At the start all substances within the blood plasma which pass through a renal capsule (which are below a certain size) are absorbed into the nephron. The substances which the body needs to take back into the blood (so not excrete) are done so later along the nephron, and those which need to be removed, mainly urea, remain in the nephron until they leave the tubule in the resultant **urine** and are removed from the body. The ureter connects the kidney to the bladder, where urine is stored, and then the urethra takes urine from the bladder to the outside world at regular intervals

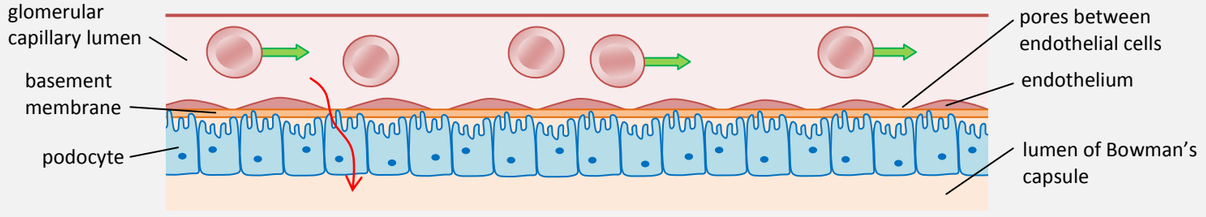
Blood enters the kidney through the renal artery, which splits into lots of networks of capillaries, housed inside capsules. A network of these capillaries is called a **glomerulus** and the arteriole which precedes them is called the **afferent arteriole**, and the arteriole which after the network is called the **efferent arteriole**

The efferent arteriole is significantly smaller than the afferent one, in order to establish a high pressure potential, which forces the substances from the blood into the nephron



Ultrafiltration

The significantly larger pressure in the glomerular capillaries than the efferent arteriole forces substances with a relative molecular mass (RMM) of less than 69,000 through the **basement membrane** and into the nephric filtrate. This process is called **ultrafiltration**



Substances which enter the filtrate first pass through pores in the endothelial membrane lining the capillaries. Underneath the endothelium is the basement membrane, made of collagen and other fibres, and the substances pass through gaps which allow sizes of 69,000 RMM and lower through. They then flow between cells called **podocytes** which line the inner membrane in order to enter the **Bowman's capsule** (renal capsule)

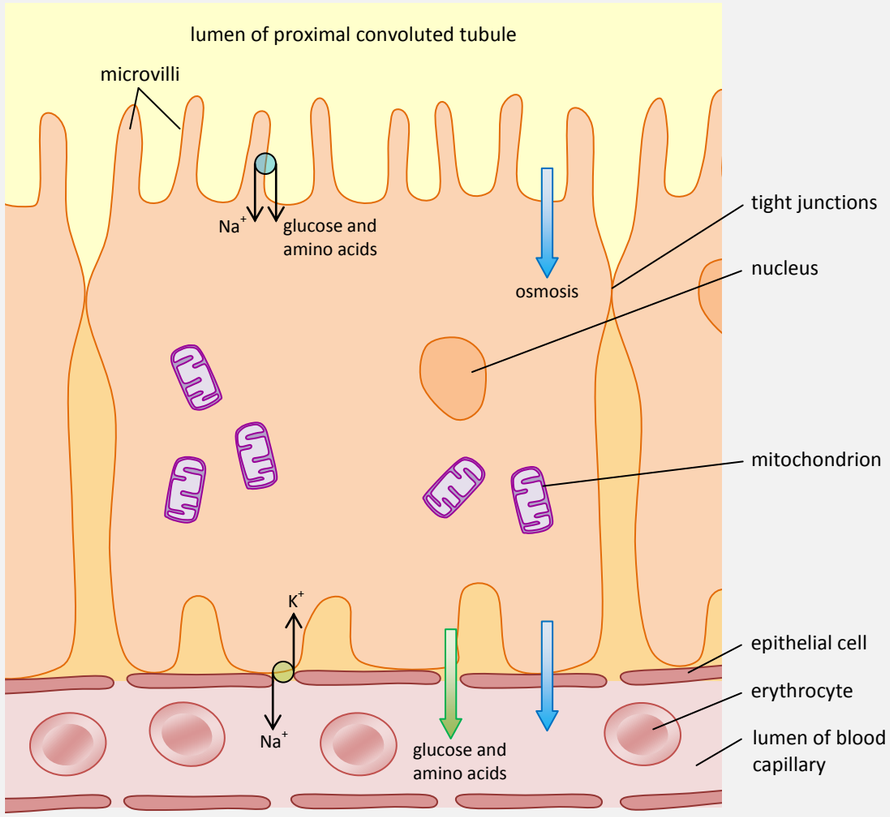
Selective Reabsorption

The substances which enter the glomerular filtrate include water, ions, glucose, amino acids and urea. Certain small proteins may squeeze through the basement membrane and into the filtrate, but most are larger than 69,000 RMM and so do not

In the **proximal convoluted tubule**, approximately 85% of the filtrate contents are absorbed back into adjacent blood vessels in a process called **selective reabsorption**

Sodium-potassium pumps on the membrane closest to the blood vessel are actively transporting sodium ions out of the cell lining the convoluted tubule wall (and potassium ions in). This means the concentration of Na^+ inside the cell drops, and so Na^+ diffuses into the cell from the tubule through channel proteins which co-transport amino acids and glucose alongside the Na^+

This increases the concentration of glucose and amino acids inside the cell, and so the resultant concentration gradient forces them to diffuse out of the cell and into the blood capillary, back into the blood. The movements of molecules through the cell creates osmotic gradients, so water follows by osmosis from the tubule into the cell and capillary



These cells lining the proximal convoluted tubule walls are very specialised. They have **tight junctions** between each cell to prevent substances from simply passing through them (such as urea, which is not wanted back in the blood). They also have a large number of **microvilli** on the tubule side to increase the surface area for facilitated diffusion of sodium with glucose and amino acids. The microvilli are arranged into a **brush border** with many of these co-transporter proteins

Creating a Water Potential Gradient

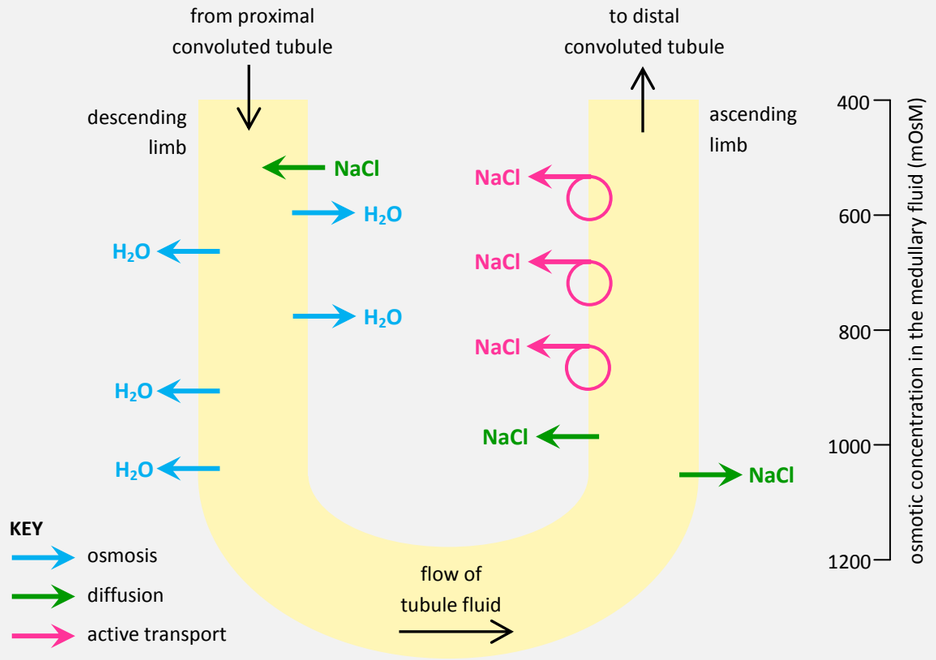
Approximately 60% of water in the nephric filtrate is reabsorbed during selective reabsorption. More water is reabsorbed at the **loop of Henle** during water reabsorption

There are two pieces of the loop: the **descending limb** and the **ascending limb**. The arrangement of the loop allows salts (sodium chloride) to flow out of the ascending limb and into the descending limb. The deeper down into the medulla (the further down the limbs) the lower the water potential – due to the loss of water from the descending limb by osmosis and the diffusion of salts from the surrounding fluid into the tubule

The water potential increases more and more as the tubular fluid flows back up through the ascending limb, because sodium and chloride diffuse and are actively transported out of the limb and as water cannot leave the limb as its walls are impermeable to water. The loss of salts but no loss of water means the water potential increases inside the ascending limb

This arrangement is known as the **hairpin countercurrent multiplier** mechanism due to the opposite flow in each limb and the fact that the longer the loop, the more concentrated the medullary tissue fluid becomes

Loop of Henle



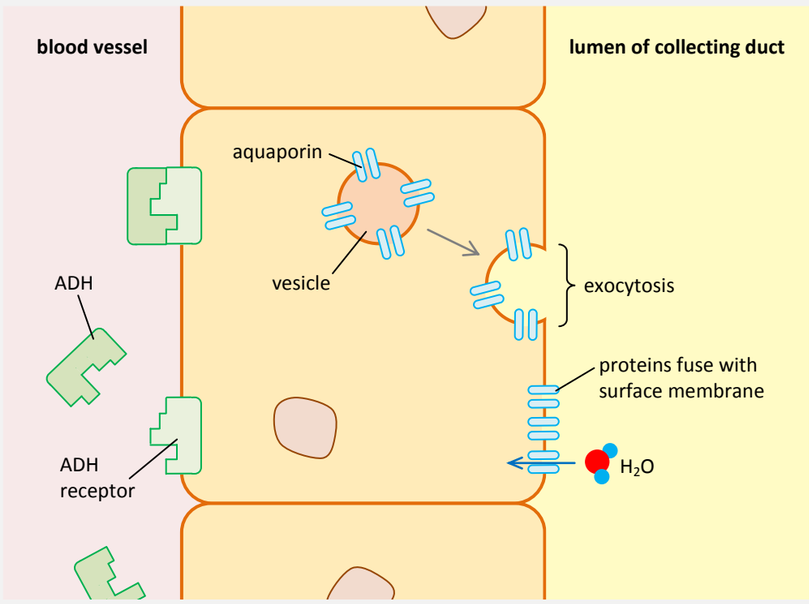
Water is lost from the descending limb by osmosis. This limb does not actively extrude NaCl like the ascending limb. At the base of the ascending limb, due to the high concentration of NaCl inside the tubule, the salts diffuse out of the limb and into the tissue fluid. However, further up the limb the salts are actively transported out into the fluid due to the decrease in NaCl concentration inside the limb. The longer the loop, the more this arrangement allows for gradients to be set up so more water can be reabsorbed to the blood

Osmoregulation

The final amount of water reabsorbed back into the blood is controlled by the hormone **ADH** (antidiuretic hormone) which is released from the **posterior pituitary gland** when **osmoreceptors** in the **hypothalamus** detect a low water potential in the bloodstream

When the water potential of the blood is particularly low, so more water needs to be reabsorbed, the osmoreceptors shrink due to water moving out of them via osmosis. This stimulates the **neurosecretory** cells to release ADH

When the cells lining the walls of the **collecting duct** detect the hormone it binds to its complementary receptor. This stimulates a chain of reactions ultimately causing vesicles inside the cell containing **aquaporins** (channel proteins permeable to water) to move to the cell surface and undergo exocytosis. This causes the aquaporins to be inserted in the plasma membrane closest to the lumen of the collecting duct, so that more water is reabsorbed from the urine into the cell, to then re-enter the blood via osmosis



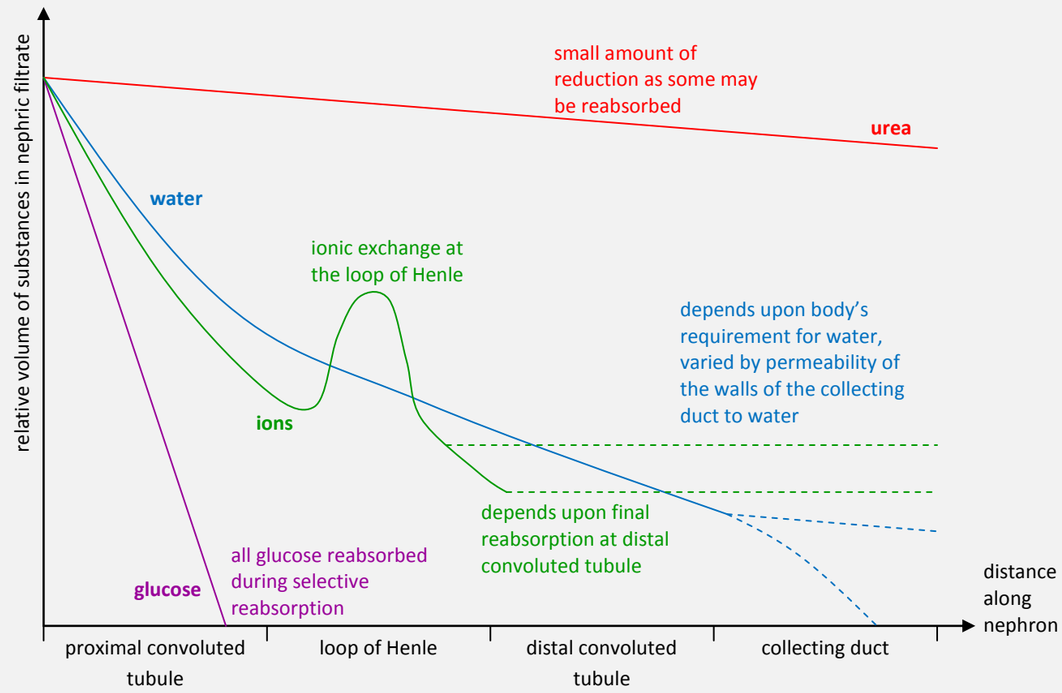
When the water potential of the blood is higher, the osmoreceptors in the hypothalamus are not triggered and so ADH is no longer released. This means that the water which is in the urine does not need to be reabsorbed. The stoppage of ADH release means that aquaporins are no longer being inserted into the membranes, so water is not reabsorbed. In fact, the cells lining the collecting duct turn in on themselves to remove the aquaporins from the membrane and they are then reinserted into vesicles inside the cell again

The Nephric Filtrate

The table below shows the substances along each section of the nephric filtrate and their quantities

	Renal capsule (glomerular filtrate)	**Proximal convoluted tubule**	**Loop of Henle**	**Distal convoluted tubule**	**Collecting duct**	**Urine**
glucose	✓	reabsorbed	**not present in filtrate**			
amino acids	✓	reabsorbed	**not present in filtrate**			
proteins	✗ (only small proteins)	**not present in filtrate**				
water	✓	60% reabsorbed	much reabsorption	more reabsorbed	possible further reabsorption	✓ (small amounts)
urea	✓	✓	✓	✓	✓	✓
ions	✓	partially reabsorbed	mostly reabsorbed	final reabsorption	**not present in filtrate**	

The graph below shows the various concentrations of substances along the nephron



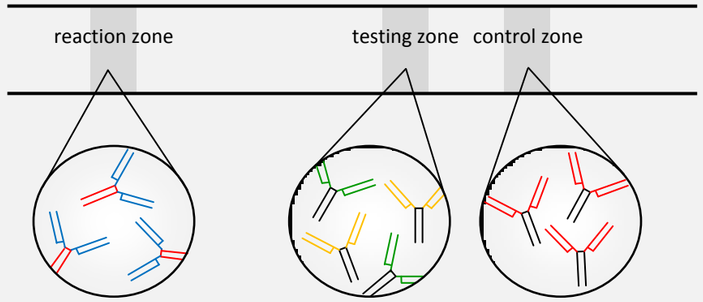
Drugs Testing

Urinary tests can be conducted to test for drugs, in particular anabolic steroids. These increase protein-synthesis which builds up cell tissue, particularly in muscles. This is why they are taken often by athletes and sportsmen. The drugs when taken have a half-life usually of around a day, but remain in the blood for days after taking them

Anabolic steroids can be tested for using **gas chromatography** or **mass spectroscopy**. Gas chromatography is a process which vaporises a sample in the presence of a gaseous solvent and passes it down a long tube lined by an absorption agent. Each substance dissolves differently in the gas and stays there for a unique **retention time** (a time the substance remains in place, specific to each individual chemical substance). Eventually, the substance comes out of the gas and is absorbed onto the lining. This is then analysed to create a **chromatogram**, which displays the results. Standard samples of drugs, as well as the urine samples, are run so that drugs can be identified and quantified in the chromatograms

Pregnancy Testing

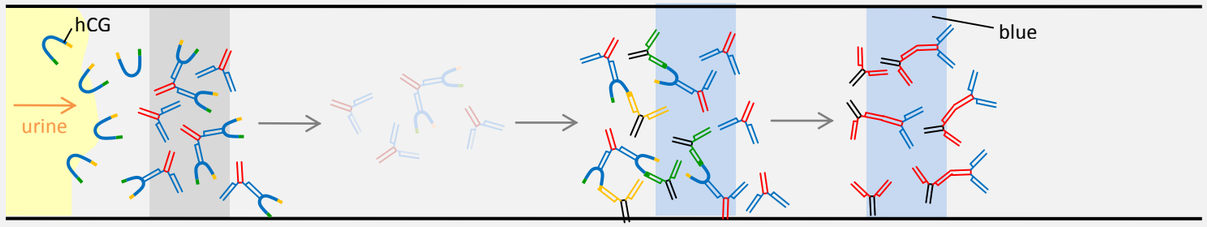
The hormone **human chorionic gonadotrophin** (hCG) is produced by pregnant women and so can be used to test for pregnancy. A pregnancy test strip consists of three different zones



The reaction zone contains **monoclonal antibodies** which recognise one specific feature of hCG only and will bind only to that molecular feature. They also have **blue beads** attached so that they can be seen on the testing strip

The testing zone contains **polyclonal antibodies** which are immobilised and can bind to many parts of the hCG molecule. This allows them to bind to hCG even when the monoclonal antibodies have already bound themselves to another part of the hCG complex

And finally the control zone contains more immobilised antibodies which will bind to the antibodies with the blue beads on, currently in the reaction zone. This means any of those first antibodies which don't bind in the testing zone (i.e. those without hCG) will move on and bind to the antibodies in the control zone



urine passes into the reaction zone and some of the monoclonal antibodies bind to the hCG, though some do not and carry on down the strip also

when the urine carrying the monoclonal antibodies (some bound to hCG and others not) reaches the testing zone, the hCG binds from a separate area to the polyclonal antibodies immobilised here, so that the blue beads on the original anditbodies are fixed – this zone goes blue

those monoclonal antibodies without hCG attached continue to move along the strip with the urine when they reach the control antibodies and bind to them, likewise here turning this zone blue

The above shows the positive testing strip for a pregnant woman. If she was not pregnant, there would be no hCG in the urine, and so the antibodies would not have bound in the testing zone (so no blue beads would show there) but only in the control zone. Therefore, as there is only a binding in the testing zone when hCG is present, two blue lines identify pregnancy, one blue line in the control zone does not

Dialysis and Kidney Failure

When kidney function fails, the two options available are kidney **dialysis** or a transplant. In **haemodialysis** a patient uses a special dialysis machine whereby their blood is taken from an artery or vein and enters the machine. The hormone **heparin** is added to prevent the blood from clotting whilst in the machine. The blood passes through the machine where **dialysis fluid** (separated from the blood by the **dialysis membrane**) exchanges materials with the blood. The concentrations of substances in the dialysis fluid are perfected so that the right amounts of unwanted substances leave the blood and enter the dialysis fluid, and vice versa required substances re-enter the blood from the fluid

With **peritoneal dialysis**, the process is managed internally, not hooked up to a machine. This allows the patient more freedom to walk around whilst the dialysis is taking place, although it still must be maintained often, and in both types diet must be carefully monitored. Peritoneal dialysis involves having a permanent catheter inserted into the patient's abdomen, and their abdominal wall, the **peritoneum** acts as the natural dialysis membrane. Dialysis fluid is inserted into the space between the abdominal walls and the surrounding organs, and the same exchange as with haemodialysis occurs here

The other option is a transplant, although these are not as common as availability of healthy organs is never high. This does involve major surgery and so the usual risks apply. Similarly, there is a chance that the new host will reject the donated kidney, and so it is required that **immunosuppressant drugs** are taken to temporarily shut down the responsiveness of the immune system to avoid rejection. On the other hand, post-transplant, life is much easier for the patient, as there is no burden of dialysis and the patient no longer feels ill, as they can largely return to living a normal life. However, there is a time attached to kidney transplants. A donated kidney will normally last the host five-to-ten years before it becomes useless