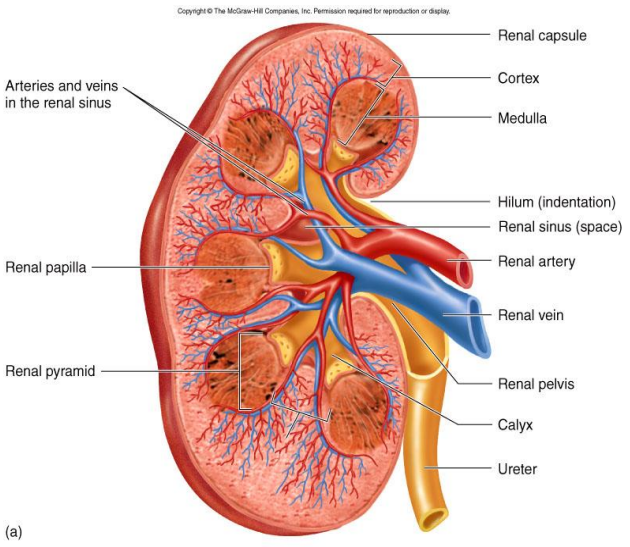
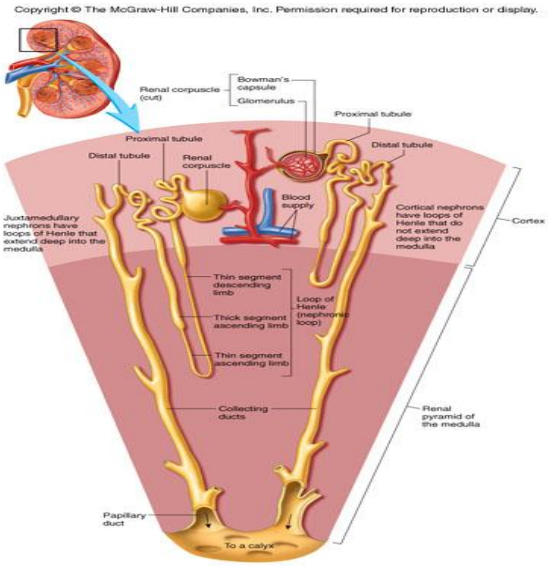
The Renal system

1. Structure

The 2 kidneys are each made up of an outer cortex and inner medulla. The center of the kidney is a cavity, the pelvis in which the urine collects before exiting through the ureters to the bladder for storage. The urine leaves the bladder through the urethra.

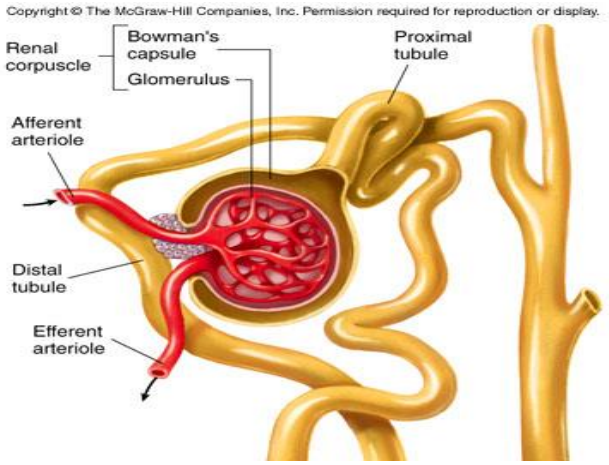


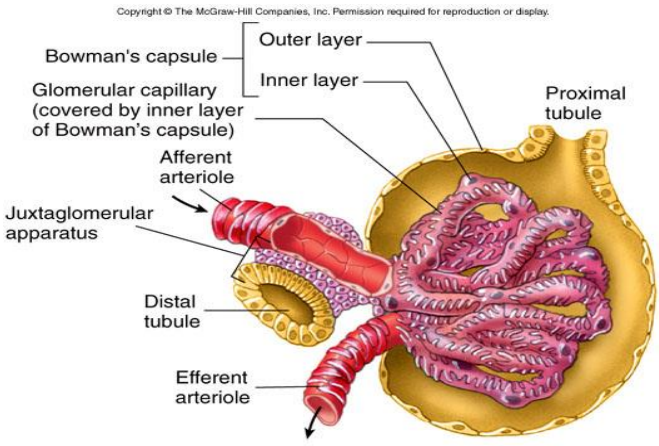


The kidneys are made up of around 1,300,000 nephrons, each of which is a long tube looping backwards and forwards between the cortex and medulla. There are 2 types of nephrons: 85% are **cortical nephrons** with short loops of Henle, but 15% are **juxtamedullary nephrons** with much longer loops, giving more efficient dehydration of the urine.

2. Ultrafiltration in the renal corpuscles.

Each nephron starts with a renal corpuscle, consisting of a glomerulus surrounded by a Bowman's capsule. The glomerulus is made up of a mass of capillaries, each surrounded by podocytes.



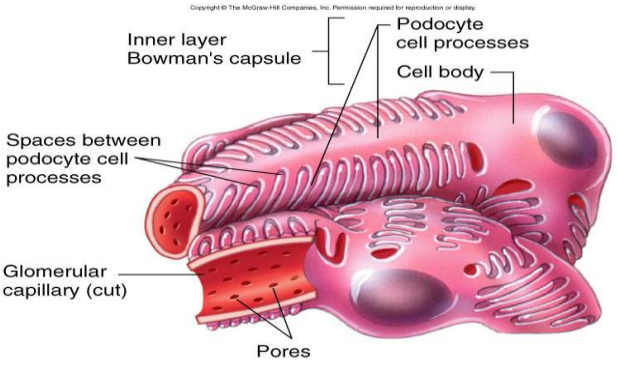


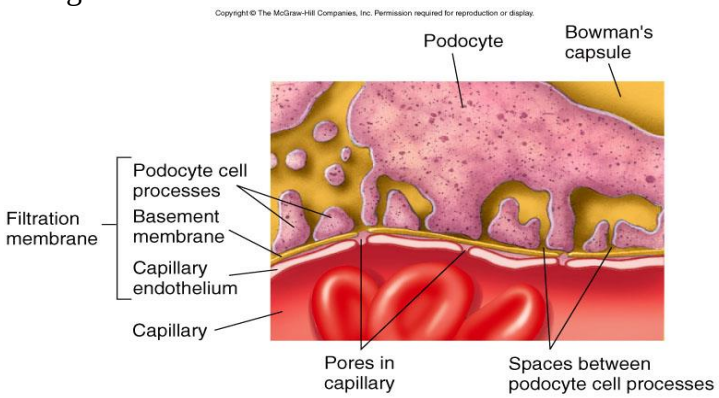
Ultrafiltration is the filtering of the blood through a molecular filter, so that large molecules (e.g. proteins) cannot pass through and remain in the blood; small molecules are filtered in to the nephron. Ultrafiltration requires:

- **An ultrafilter made of 2 layers:**
  - The endothelial cells making up the glomerular capillaries have large numbers of **tiny pores passing through the cell**.
  - Surrounding the capillary are podocytes, but there are narrow gaps between podocytes known as **filtration slits**.

The plasma thus 1st escapes out of the capillary through the pores, then passes through the filtration slits between the podocytes and enters Bowman's capsule and thus the proximal tubule.

- **A very high blood pressure in the capillaries of the glomerulus**. Normally, capillaries have a lower pressure than the arteriole leading in to them, because the capillaries lead in to a much wider venule. However, in the glomerulus, the capillaries collect blood from an arteriole (as usual) but lead in to a 2nd smaller arteriole. This raises the blood pressure above normal (as the blood is forced in to a narrower tube). This very high pressure forces the blood plasma through the filter.





Opposing the blood pressure is the colloidal OP: the blood contains proteins, while the filtrate does not, so the higher blood OP tends to suck water back in.

The amount of filtrate will thus depend on changes in the overall blood pressure, but to compensate for this, the afferent arteriole (going in) constricts when the body pressure rises and dilates as the body pressure drops to keep the ultrafiltration pressure constant.

Only **19%** of the blood plasma entering the glomerulus is actually filtered into the nephron. If it were higher, there would be insufficient blood carrying on through the renal artery into the rest of the kidney. This 19% filtered results in **180 l of filtrate/ day**, almost all of which has to be reabsorbed in the rest of the nephron.

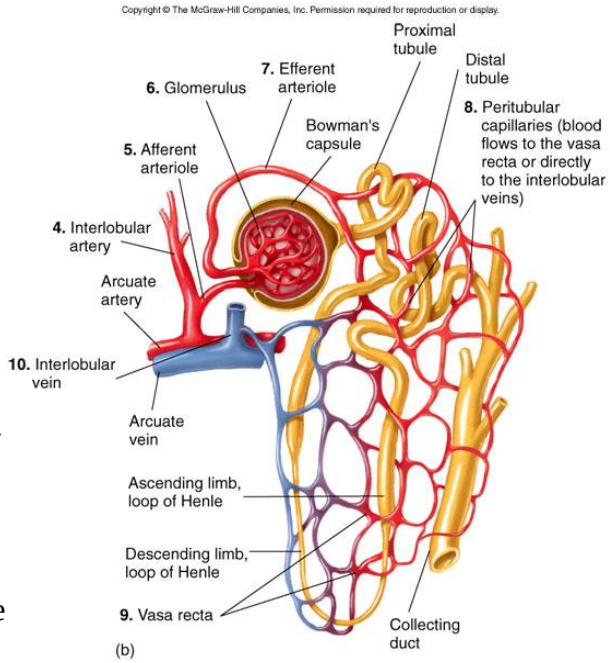
3. Nephron blood supply.

The efferent arteriole leaving the renal corpuscle enters the **peritubular capillaries** in the cortex (surrounding the proximal and distal tubules), which then flow in to the **vasa recta** capillaries in the medulla (around the loop of Henle and collecting ducts). Because of their arrangement (see below), the vasa recta perform differently from the peritubular capillaries.

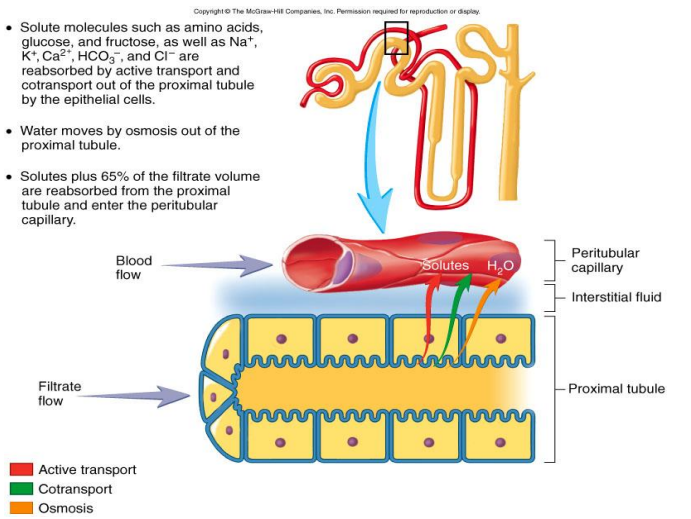
4. Reabsorption.

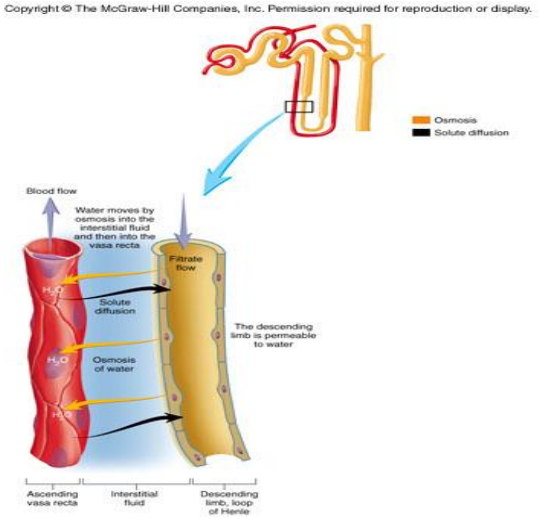
- **The Proximal tubule**

Useful substances are reabsorbed by **active transport and cotransport**. Thus the cells of the proximal tubule have microvilli (give a large surface area) and large numbers of mitochondria (ATP for active transport). Separate pumps are found for each of the different types of foods e.g. glucose, fructose, aminoacids, and for different ions e.g. Na^+, Ca^{2+}, HCO_3^-. Foods are thus normally completely reabsorbed, unless the capability of the pump is exceeded. Thus the maximum reabsorption of glucose produces a blood concentration of 150mg/ 100ml, so if a higher level of glucose enters the kidney (after eating too many sweets), the excess will be excreted in the urine. The ionic pumps increase the concentrations of ions outside the nephron and produce a low concentration inside the tubule



This produces an osmotic pressure sucking water out of the tubule into the plasma surrounding the tubule. In this way, **65% of the water** in the filtrate is reabsorbed by osmosis. The reabsorbed substances are taken up by the peritubular capillaries and so removed from the cortex back in to the blood. The filtrate leaving the **proximal tubule is isotonic** (has the same osmotic pressure as the blood plasma = **300 mOsm**). This is because salt and water were removed at the same rate from the filtrate.



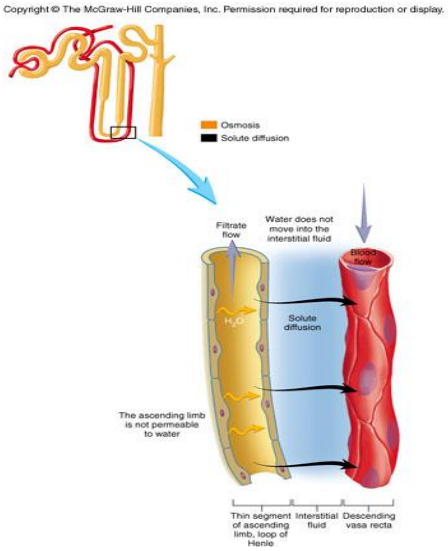


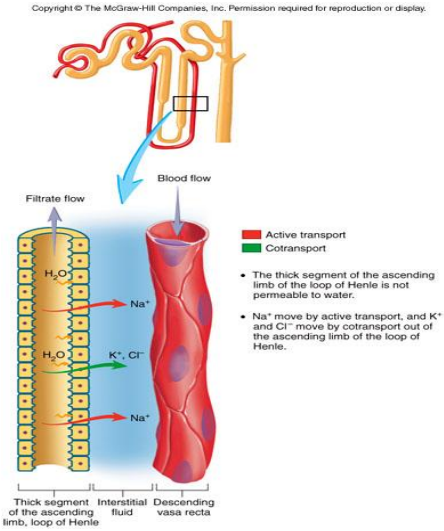
▪ Loop of Henle

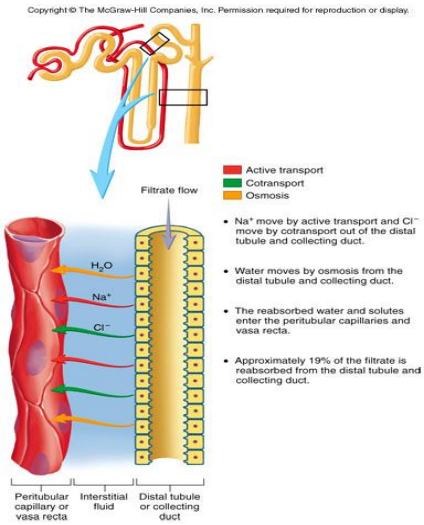
The loop of Henle consists of a descending loop, descending deep in to the medulla, and an ascending loop, returning back towards the cortex. The ascending loop is subdivided into a short section of thin segment and a longer thick segment.

The medulla has **high concentrations of NaCl** + **small quantities of urea** (that have leaked out of the collecting ducts), so that its osmotic pressure increases from 300 mOsm (near the cortex) to 1200 near the central pelvis. This is because the vasa recta only remove water from the medulla, leaving behind most of the salt (unlike the peritubular capillaries of the cortex). Thus water reabsorption occurs in 3 stages:

- The **descending loop** has walls **permeable to water**, but only a very low permeability to salts. As the filtrate descends in to progressively higher and higher OP's, water is sucked out, but only small quantities of salt can diffuse in. By the **bottom** of the loop, the OP of the filtrate has increased to **1200 mOsm**. **15% of the water is reabsorbed in the descending loop of Henle**, so the volume of filtrate is now only 20% of the original.
- In the **thin segment** of the ascending loop, the walls are not permeable to water, so as it moves up through progressively lower salt concentrations, some **salt will diffuse out**, to reduce its OP (but not change its volume).
- In the **thick segment** of the ascending loop, there are Na^+ pumps (like in the proximal tubule). **Na^+ is pumped out**, while **Cl^- follows passively**; **K^+ also moves out by cotransport**. This progressively dilutes the filtrate (water will not be removed because the walls throughout the ascending loop are not permeable). By the **top** of the loop (as the tubule re-enters the cortex), the filtrate will now be hypotonic (**100 mOsm**).







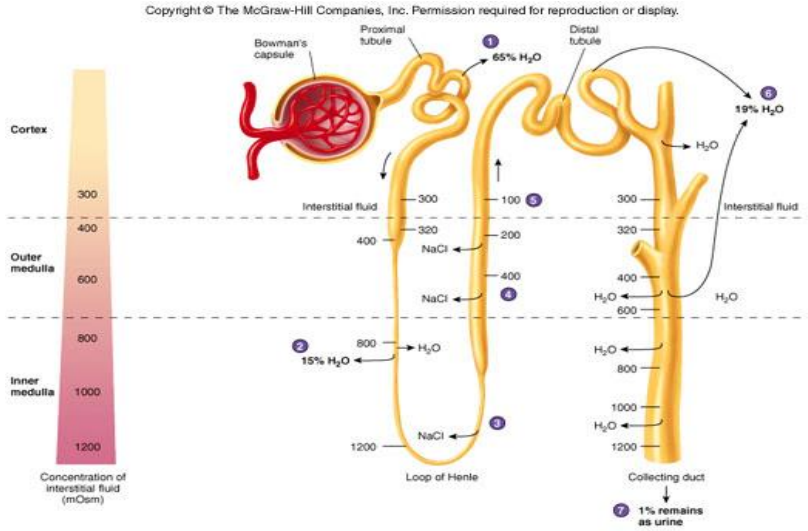
The descending loop thus loses water (and thus reduces its volume); the ascending loop loses salt (no further change in volume).

- **Distal tubule.**

Because the OP of the filtrate is now less than the surrounding plasma, **some water will diffuse out** (and some salt diffuse in) to return the OP to 300 mOsm. However, **aldosterone** can act in this section (and the collecting duct) by activating Na^+/K^+ pumps (so Na^+ out, but K^+ in - unlike loop of Henle)

- **Collecting duct.**

The **collecting duct** re-enters the medulla, but this time passes right through the medulla. As it passes through the deepest layers of the medulla, which have the very highest concentrations of NaCl, the maximum reabsorption of water by osmosis will occur (raising the OP of the filtrate to over **1200 mOsm**). A further **19%** of the filtrate may be reabsorbed, leaving just 1% of the original remaining. However, the permeability to water of the collecting duct walls is controlled by the hormone **ADH**.



Changes in osmotic pressure in the filtrate

5. Active secretion.

The distal tubule secretes **toxins** in to the tubule by **active transport**. These include $\mathbf{H^+}$ (which interferes with respiration and enzyme activity), $\mathbf{K^+}$ (nerve conduction requires a low conc of K^+ in the plasma), **histamine** (acts locally in the body, so should then be removed), **creatinine**, etc. In addition, some toxins, such as **ammonia** (produced by the breakdown of aminoacids), will passively diffuse into the tubule.

6. Control of urine production.

Your body needs to control:

- Your **blood volume** = reduce water loss when dehydrated; increase loss when over-hydrated. This is mainly due to **ADH** and to **aldosterone/ ANH**, but is affected by **blood pressure** (through ultrafiltration).
- The **amount of salts in the blood** and therefore lost in the urine e.g. Na^+, K^+. This is mainly controlled by **aldosterone** and **ANH**.

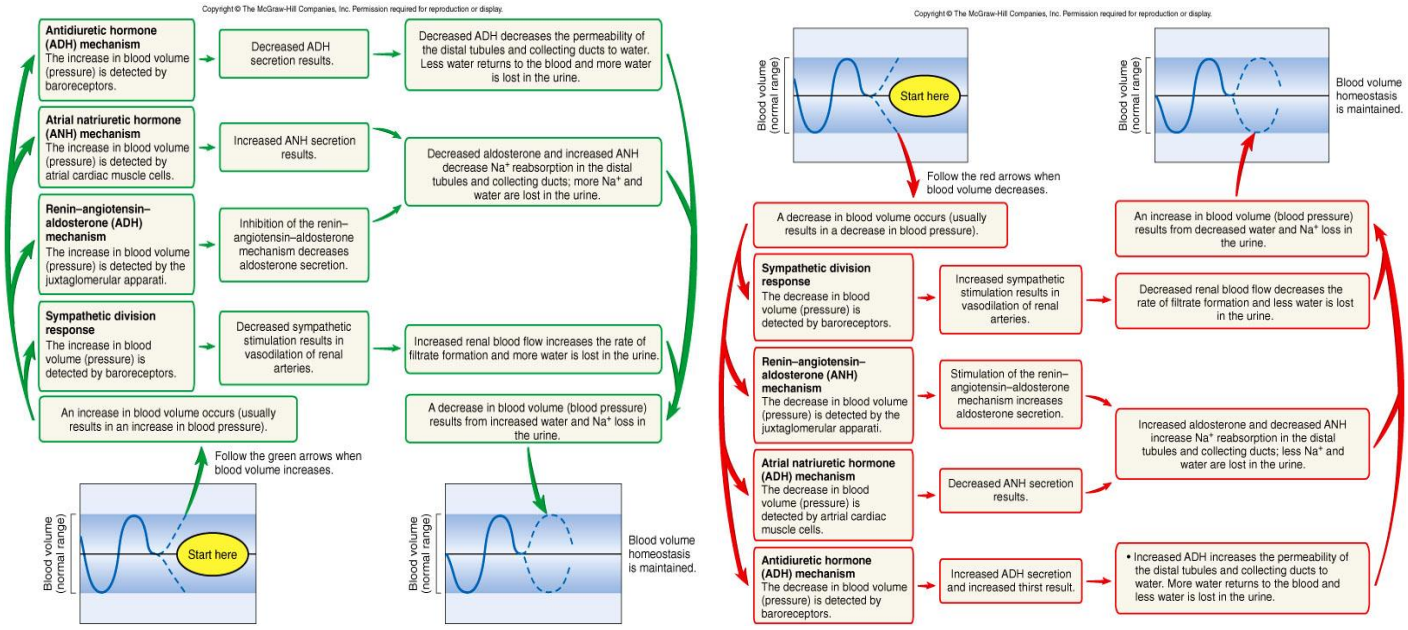
- **ADH**

ADH is secreted by the **hypothalamus** and stored and released from the posterior pituitary, in response to either **high blood OP** or **low blood pressure** detected by the hypothalamus (both indicate dehydration).

ADH makes the **walls of the collecting duct permeable to water**, so that a total of 99% of the water in the urine is reabsorbed. When over-hydrated, the absence of ADH results in 20% water loss (= 19% from the collecting duct + the 1% unrecoverable water).

- **Controlling sodium chloride by Aldosterone + ANH.**

A **low blood pressure** results in the **juxtamedullary apparatus** (attached to the glomerulus) releasing the enzyme **renin** into the blood. This activates the hormone **angiotensin**, which cause the adrenal glands to release **aldosterone**. Aldosterone increases **reabsorption of sodium ions from the distal tubule and collecting duct** (Note: the Na^+ pumps in the proximal tubule and loop of Henle are unaffected). As well as increasing blood Na^+, it increases the blood volume by increasing reabsorption of water alongside the Na^+.



If **blood pressure is high**, then no aldosterone is secreted. Instead, **cardiac cells in the heart secrete ANH (atrial natriuretic hormone)**, which inhibits absorption of sodium from the urine. The resulting high sodium in the filtrate increases its osmotic pressure, so less water is reabsorbed from the filtrate and thus **more water is excreted** in the urine.

Aldosterone and ANH are thus antagonistic hormones responsible for controlling blood sodium, but in doing so, they alter water reabsorption by the kidney.

- **Blood pressure**

When there are temporary changes in blood pressure, the afferent arteriole in to the renal corpuscle stabilises ultrafiltration by constricting when pressure rises and dilating when pressure drops.

However, the arteriole is also controlled by the sympathetic nervous system from the hypothalamus (measuring the overall blood pressure). If there is a **severe drop in pressure** due to heavy bleeding or extensive inflammation, **increased sympathetic stimulation** increases vasoconstriction to reduce filtration and thus reduce further urine loss. This also happens during **intense physical activity**, when there is a high blood pressure, in order to maintain the high pressure and thus rapid O_2 transport.

Conversely, **continuous high pressure** (when not active) **decreases sympathetic stimulation** → vasodilation → greater urine production → reduced blood volume and thus pressure.

- **Thirst center in hypothalamus.**

Overall control of water balance is by the hypothalamus. The Thirst center in the hypothalamus responds to:

- Low blood pressure.
- High osmotic pressure of the blood.
- Dehydration of the mucosa of the mouth.

These all stimulate the feeling of "thirst" so you drink water and increase your blood volume.

7. Regulation of ions (summary).

- **Sodium ions.**

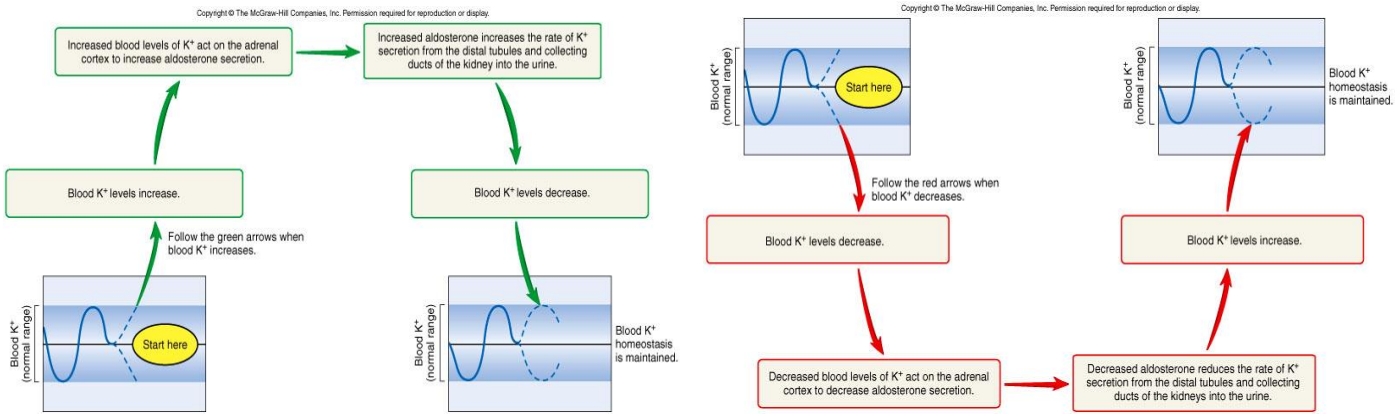
This is the major cation in the extracellular fluid and thus gives 90% of its OP. Low bp → increased angiotensin → increased **aldosterone** → increased reabsorption in the distal tubules and collecting ducts, so less Na^+ is lost. High bp → increased **ANH** → opposite effect.

Some Na^+ is also lost during **sweating,** but the concentration varies depending on body availability.

- **Potassium ions.**

Extracellular K^+ must be kept low to maintain the resting potential of the body cells, but is required inside the cell. Dehydration increases the conc of plasma K^+, which must thus be excreted.

Aldosterone → increased loss from the distal tubules and collecting ducts (at the same time as Na^+ is reabsorbed).



- **Calcium ions.**

Ca^{2+} conc is of major importance in nerves (especially the synapses) and muscles, and affects the permeability of the cell membrane to Na^+ and so is closely controlled.

Parathyroid hormone increases as Ca^{2+} decreases to stimulate osteoclasts to release Ca^{2+} from bones, reduce loss in the urine and increase uptake from the gut (by stimulating vitamin D).

Excessive Ca^{2+} reduces PTH but increases calcitonin to reverse these 3 processes.