The notes in this document are meant to cover IB topics 6.5 and 11.3 (HL ONLY).

**What is homeostasis?**

It is the maintenance of a constant internal environment (the immediate surrounding of cells) in response to:
- the changing conditions of the external environment
- the changing conditions of the internal environment

Homeostasis is a self-adjusting mechanism involving feedback where the response to a stimulus alters the internal conditions and may become a new stimulus.

**How is homeostasis achieved?**

To maintain cells, tissues and entire organisms within their biological tolerance limits, various mechanisms have evolved:

1. **Structural**: the organism has particular physical features which help its survival in an otherwise hostile environment
2. **Functional**: the metabolism of the organism is able to adjust to changes in conditions as they are detected
3. **Behavioural**: the actions and interactions of the individual, either alone or with others, help it to survive in its particular environment

Homeostasis is really the combined result of all of these, a failure of any one of them can result in the death of an individual.

The two systems of the body which are directly involved in maintaining homeostasis are the nervous system and the endocrine (hormone) system.

**Feedback Mechanisms**

Feedback mechanisms are the general mechanism of of nervous or hormonal regulation in animals. Feedback occurs when the response to a stimulus has an effect of some kind on the original stimulus. The nature of the response determines how the feedback is categorized:

- **Negative feedback** occurs when the response to a stimulus diminishes the original stimulus. Negative feedback is most common in biological systems.
  - Blood glucose concentrations rise after a meal (the stimulus) and insulin causes glucose to be removed from the bloodstream (the response), which decreases blood glucose.
  - Exercise creates metabolic heat which raises body temperature (the stimulus) and vasodilation and sweating (the response) cools the body.

- **Positive feedback** occurs when the response to a stimulus increases the original stimulus. It is rare in biological systems.
  - When a baby first suckles its mother's nipple, a small amount of breast milk is released (the stimulus) and a hormone is released which increases milk production (the response).
  - A ripening apple releases ethylene (the stimulus) which accelerates the ripening of unripe fruit near it, releasing more ethylene (the response).
Feedback Loops

- have certain essential components, whether they are positive or negative:
  - **stimulus**: the change from ideal or resting conditions
  - **receptor**: the cells or tissue which detects the change due to the stimulus
  - **relay**: transmission of the message, via nerves or hormones or both, to the effector
  - **effector**: the cells or tissue (gland or muscle) which cause the response to occur
  - **response**: an action, at cell, tissue, or whole organism level which would not have occurred in the absence of the stimulus
  - **feedback**: the consequence of the response on the stimulus – either positive or negative

*Negative Feedback and Osmoregulation*

![Diagram of blood water concentration and osmoregulation]

Image from [http://www.bbc.co.uk/scotland/education/bitesize/higher/img/biology/control_regulation/negative_feedback/02osmoregulation.gif](http://www.bbc.co.uk/scotland/education/bitesize/higher/img/biology/control_regulation/negative_feedback/02osmoregulation.gif)

The Endocrine System

- maintains homeostasis and long-term control using chemical signals
- works in parallel to the nervous system to control growth and maturation along with homeostasis
- a collection of glands that secrete chemical messengers called **hormones**
- hormones travel through the bloodstream to arrive at a target organ
  - cells of the target organ possess the appropriate receptor proteins
  - cells without these receptors are not affected by the hormone
- not all glands are part of the endocrine system
  - exocrine glands secrete products out of the body: sweat glands, salivary glands and digestive glands are all examples
- hormones are either steroids (e.g. testosterone), peptides (e.g. insulin) or amines (e.g. thyroid hormone)
Regulation of Hormones

Levels of hormones in the blood are controlled by the following mechanisms:

- When one hormone stimulates production of a second, the second supresses the production of the first.
  - Follicle stimulating hormone (FSH) stimulates release of estrogen, and high levels of estrogen suppress production of FSH.
- Antagonistic pairs of hormones.
  - Insulin causes the level of blood glucose to drop when it is too high, and glucagon causes it to rise when it has dropped too low.
- Hormone secretion is increased (or decreased) by the same substance whose level is decreased (or increased) by the hormone.
  - An increase in Ca\(^{2+}\) in the blood suppresses the production of parathyroid hormone. A low level of Ca\(^{2+}\) stimulates it.

Nervous Regulation of Homeostasis

Sensory receptors are constantly monitoring both the external and internal environments:

- These receptors pass impulses along sensory neurons to the CNS in response to stimuli (e.g. change in body temperature or a visual stimulus).
- The brain processes sensory input and coordinate a response.
- Motor neurons carry impulses to the effectors, the muscles and glands.

Comparison of Hormonal and Nervous Control:

<table>
<thead>
<tr>
<th></th>
<th>Nervous Control</th>
<th>Hormone Control</th>
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</thead>
<tbody>
<tr>
<td>Communication</td>
<td>Impulses across synapses</td>
<td>Hormones in the blood</td>
</tr>
<tr>
<td>Speed</td>
<td>Very rapid (within a few milliseconds)</td>
<td>Relatively slow (over minutes, hours or longer)</td>
</tr>
<tr>
<td>Duration</td>
<td>Short term and reversible</td>
<td>Longer lasting effects</td>
</tr>
<tr>
<td>Target pathway</td>
<td>Specific (through nerves to specific cells)</td>
<td>Hormones broadcast to target cells everywhere</td>
</tr>
<tr>
<td>Action</td>
<td>Causes glands to secrete or muscles to contract</td>
<td>Causes changes in metabolic activity</td>
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Control of Blood Glucose
Blood glucose is maintained within a very narrow range. **Insulin** and **glucagon**, produced by the pancreas, are responsible for control of blood glucose levels, which is actually monitored by the pancreas.

**Insulin:**
- secreted by β-cells in the Islets of Langerhans (in the pancreas)
- stimulated by high blood glucose (but always produced)
- causes skeletal muscles, liver and fat cells to absorb glucose from the bloodstream and convert it to glycogen or fat (for storage)

**Glucagon:**
- secreted by α-cells in the Islets of Langerhans
- stimulated by low blood glucose
- causes skeletal muscles and liver to convert glycogen to glucose, which is released into the blood

The normal range for blood glucose is between 70 mg/dl and 110 mg/dl:
- <70 mg/dl indicates hypoglycemia (low blood sugar)
- >110 mg/dl may occur 2-3 h after a meal
- >180 mg/dl indicates hyperglycemia, and may indicate diabetes
Diabetes

Type 1 Diabetes is a condition where the pancreas produces insufficient amounts of insulin. Glucose builds up in the body instead of being used for energy. Often called juvenile diabetes because it is diagnosed in childhood/early teens. People with type 1 diabetes need to monitor their blood sugar levels, and keep it within narrow limits by:

- taking insulin as required (other medications may also be prescribed)
- eating healthy meals and snacks
- enjoying regular physical activity

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Treatment</th>
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<tr>
<td>- constant thirst</td>
<td>- injection of insulin into the bloodstream daily</td>
</tr>
<tr>
<td>- undiminished hunger</td>
<td>- regular measurement of blood glucose level</td>
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<tr>
<td>- excessive urination</td>
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Type 2 Diabetes is a progressive, life-long condition in which the pancreas either does not produce enough insulin, or the body does not properly use the insulin it makes. Over time it may be more difficult to manage symptoms and keep blood sugar within the prescribed range.

<table>
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<th>Treatment</th>
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<tbody>
<tr>
<td>- mild – sufferers usually have sufficient blood insulin, but insulin receptors on cells have become defective</td>
<td>- largely by diet/exercise alone</td>
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<tr>
<td></td>
<td>- may require insulin therapy and other medications later in life</td>
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Thermoregulation

Poikilotherms are animals which cannot control body temperature internally and do not maintain a constant body temperature.

- may be called ectotherms or “cold-blooded”
- invertebrates, fish, amphibians and reptiles

Homeotherms are animals which do maintain a constant body temperature through internal mechanisms and behaviour.

- may be called endotherms or “warm-blooded”
- thermoreceptors are located in the skin and heat centre of the brain
- birds and mammals

When body temperature is too high, it is known as hyperthermia.

- vasodilation increases the diameter of blood vessels in the skin, allowing heat to escape to the environment
- sweating removes heat from the body when sweat evaporates – in animals without sweat glands, panting does the same thing
- hairs (or feathers) lie flat to minimize insulation
- decreased metabolism slows production of heat by cellular respiration
- behavioural adaptations such as seeking shade or shelter from the Sun, or swimming/bathing can help decrease body temperature

Prolonged hyperthermia can damage cells and denature proteins.
When body temperature is too low, it is known as hypothermia.

- **vasoconstriction** decreases the diameter of blood vessels in the skin, in order to keep heat in the body core (where vital organs are)
- **shivering** produces heat by rapid contractions of skeletal muscles
- **increasing metabolism** produces heat by cellular respiration
- the **pilomotor reflex** causes hairs (or feathers) to stand perpendicular to the skin, trapping an insulating layer of air
  - in humans, this reflex produces **goose bumps**, which only make us warmer by telling us to put on a sweater
- **structural adaptations** may help counteract hypothermia
  - polar bears have transparent hair and black skin to absorb sunlight
  - some animals have brown fat/blubber for insulation
- **behavioural adaptations** such as herding behaviour (to share body heat) or putting on a sweater may help conserve heat

Prolonged hypothermia can damage cells and cause death.

**Excretion in Organisms**

Plants excrete oxygen gas during the day.

Animals excrete nitrogenous waste in urine, and excrete carbon dioxide from the lungs.

**Effect of Habitat on Excretion**

Ammonia (NH₃) is produced by the metabolism of proteins, when amino acids are deaminated.

- **Fresh water animals** take in a surplus of water by osmosis. Excess water is used to dilute ammonia and flush it out of the organism.
- **Marine (salt water) animals** do not have excess water. Instead, they convert NH₃ to urea [(NH₂)₂CO] and trimethylamine oxide [(CH₃)₃NO]. Both these compounds are less toxic than ammonia, and are excreted in urine.
- **Amphibians** live in fresh water as juveniles and excrete dilute ammonia. Adults need to conserve water, and convert ammonia to urea.
- **Birds** cannot carry much water due to weight restrictions imposed by flight. They convert ammonia to uric acid, which is insoluble in water (it's the white part in bird droppings).
- **Mammals** excrete urea, which is produced by the liver in the ornithine cycle. The extent to which they can concentrate their urine is dependent upon the length of the nephron (the loop of Henle) – this determines potential habitat. Desert mammals have a very long loop of Henle, and produce very concentrated urine.

**Excretion and Water Balance in Humans**

**Excretion** = removal from an organism of toxic waste products of metabolism

**Osmoregulation** = control of water balance of blood, tissues and cytoplasm of living organisms
The primary organ of excretion and water balance in humans and all other vertebrates is the kidney. Human kidneys:

- are two bean-shaped organs found on either side of the spine
- represent 0.5% of the total weight of the body, but receive 20-25% of the total arterial blood pumped by the heart
- each contain one to two million nephrons

Why is excretion necessary?

In addition to ATP (energy), metabolism creates waste products which, if they build up inside the body, are toxic to cells.

Osmoregulation is a two-stage process in the kidney:

- **ultrafiltration** removes tiny particles from the bloodstream
- **reabsorption** returns glucose, amino acids and ions to the bloodstream
The nephron is the functional unit of the kidney. It is essentially a long tube, open at one end and closed at the other:

- **Bowman’s Capsule** is located at the closed end of the nephron, and is pushed in to form a double-walled chamber.
- The **glomerulus** is a network of capillaries found inside Bowman’s capsule. Blood leaving the glomerulus passes into a second capillary network surrounding the proximal convoluted tubule.
- The **Proximal convoluted tubule** is coiled and lined with cells carpeted with microvilli and stuffed with mitochondria.
- The **Loop of Henle** makes a hairpin turn and returns to the distal convoluted tubule.
- The **Distal convoluted tubule** is also highly coiled and surrounded by capillaries.
- The **collecting tubule** leads to the pelvis of the kidney from where urine flows to the bladder and, periodically, on to the outside world.

**Aldosterone** regulates absorption of Na\(^+\) in the distal convoluted tubule.

**Anti-diuretic hormone** (ADH) regulates absorption of water from nephric filtrate.
Formation of Urine

The nephron makes about 2 L of urine daily by filtering small molecules and ions from the blood, then reclaiming the needed amounts of useful materials. Surplus or waste molecules and ions are left to flow out as urine.

In 24 hours the kidneys reclaim:

- ~650 g of NaCl
- ~400 g NaHCO₃
- ~180 g glucose
- almost all of the 170 litres of water that entered the tubules.

The steps:

- Blood enters the glomerulus under pressure.
- This causes water, small molecules (but not macromolecules like proteins) and ions to filter through the capillary walls into the Bowman’s capsule. The basement membrane determines the size of particles allowed through into the nephron.
  - This is known as ultrafiltration and produces a fluid called nephric filtrate. It is simply blood plasma minus almost all of the plasma proteins. Essentially it is no different from extracellular fluid.
  - Ultrafiltration removes particles from the blood by size (<65 000 u); proteins and blood cells remain in the capillaries.
  - Ultrafiltration is a three-step process:
    - Pores (fenestrations) in the capillary walls (between cells) are 100 nm in diameter – anything smaller than this passes through.
    - A basement membrane covers & supports the wall of the capillaries. It is a mesh network of glycoproteins that prevents plasma proteins from leaving the bloodstream.
    - Podocytes form the inner wall of Bowman’s capsule. These cells have extensions that wrap around the capillaries of the glomerulus. There are very narrow gaps between, preventing all but the smallest particles from being filtered out of the blood.

- Nephric filtrate collects within the Bowman’s capsule and then flows into the proximal tubule.
- Here all of the glucose, and amino acids, >90% of the uric acid, and ~70% of inorganic salts are reabsorbed by active transport.
  - The active transport of Na⁺ out of the proximal tubule is controlled by angiotensin II.
The active transport of phosphate ($\text{PO}_4^{3-}$) is regulated (suppressed by) the parathyroid hormone.

- As these solutes are removed from the nephric filtrate, a large volume of the water follows them by osmosis (80-85% of the 170 litres deposited in the Bowman's capsules in 24 hours).
- Microvilli increase the surface area of in the renal tubule.
- As the fluid flows into the descending segment of the loop of Henle, water continues to leave by osmosis because the interstitial fluid is very hypertonic. This is caused by the active transport of $\text{Na}^+$ out of the tubular fluid as it moves up the ascending segment of the loop of Henle.
- In the distal tubules, more sodium is reclaimed by active transport, and still more water follows by osmosis.
- Final adjustment of the sodium and water content of the body occurs in the collecting tubules.

**Composition of Blood, Filtrate and Urine**

**Blood:**
- In the renal artery, blood is oxygen-rich, and contains high levels of urea, salt and may have excess water.
- In the renal vein, blood is deoxygenated, contains a high amount of carbon dioxide, the correct amounts of water and salts, and very little urea.

**Nephric Filtrate:**
- Has a similar composition to blood plasma, without the large proteins. Particles are only “selected” based on size (by ultrafiltration).

**Urine:**
- Contains less water and salt than nephric filtrate, and more urea. In healthy individuals, there should be no glucose, proteins or amino acids.

**Diabetes:** One sign that a patient may be diabetic is the presence of glucose in the urine – because blood sugar levels are so high, the kidney cannot reabsorb it all. Presence of glucose in urine could be especially high after a meal.

**The Kidney and Homeostasis**

While we think of the kidney as an organ of excretion, it is more than that. It does remove wastes, but it also removes normal components of the blood that are present in greater-than-normal concentrations. When excess water, sodium ions, calcium ions, and so on are present, the excess quickly passes out in the urine. On the other hand, the kidneys step up their reclamation of these same substances when they are present in the blood in less-than-normal amounts. Thus the kidney continuously regulates the chemical composition of the blood within narrow limits. The kidney is one of the major homeostatic devices of the body.
Kidney Dialysis

Humans cannot survive for long without a functioning kidney. Artificial kidney machines must be used to clean the blood must be used, until a kidney transplant becomes available.

Dialysis machines use semi-permeable membranes to filter the blood:

- membrane is made of cellulose acetate or nitrate
- it has pores that let small solute particles pass through, but not large particles such as plasma proteins or blood cells
- blood flows on one side of the dialysis membrane and dialysis fluid on the other side
- the formulation of dialysis fluid ensures that only some substances diffuse into it from the blood:
  - it contains no urea or other excretory products, so these diffuse into it rapidly
  - it has the same concentration of glucose, mineral ions and other desirable substances as normal blood plasma, so these substances do not diffuse unless the level in the blood is above or below normal
  - it contains dextran, a solute that cannot pass through the dialysis membrane and so causes excess water to move by osmosis from the blood to the dialysis fluid
- during dialysis, the patient's blood flows through tubes or between sheets of dialysis membrane
  - blood is taken from the patient and returned via needles inserted into a blood vessel in the arm
- dialysis fluid must be replaced gradually through the session in order to maintain the concentration gradients
  - a large volume of fluid is used, in contrast to the kidney, which can excrete waste products with very little loss of fluid

Image from [http://www.ivy-rose.co.uk/Topics/Urinary/Kidney_Dialysis_cIvyRose.jpg](http://www.ivy-rose.co.uk/Topics/Urinary/Kidney_Dialysis_cIvyRose.jpg)