Structure and Function
A great importance is based on this relationship. Anatomy, (Greek; cutting up) is structure,

The Human Tissues Act 2008,
- Voluntary Donation
- Donor works with relatives, who also have to consent
- Need the whole family support, they have the ability to withdraw
- No reference to the length of time that body tissues can be kept
- Avoid unnecessary mutilation/desecration of the body
- Operations on donations to be done in respect
- Bodies are cremated in separate coffins (No body mixing)
- The body viewed as the 'Ultimate Gift'
- A Whakawatea, a ‘clearing of the way’ ceremony is done to each body.

Levels of Organisation
- Body
- System, functionally related groups of organs
- Organ, collection of tissues
- Tissue, similar cells specialised by function
- Cell, consisting of organelles that assist the function of the cell e.g. Vesicles
- Molecules/atmos

Tissues
In general, tissues consist of specialised cells embedded in an extracellular matrix. The extracellular matrix contains water, proteins and proteoglycans. Proteins include cartilage and proteoglycans influence the ‘stiffness’ of the the matrix

There are four types:

Epithelial, e.g. The skin, linings of tracts and glands is formed of layers/sheets of cells with very little matrix. It functions to protect/cover/line body surfaces and cavities
Connective, e.g. Bones, cartilage, fat and blood are cells sparsely arranged in abundant extracellular matrix. It forms support and transport structures.
Muscle, e.g. Skeletal, smooth and cardiac; consist of long, strong and load bearing cells, which facilitate movement and heat production.
Nervous, e.g. Nerves (conducting), glial cells (supporting), sensory organs, brain and spinal cord tissue. The cells of this tissue are highly differential, but produce communication and coordination between different body parts.
Unicellular Organisms depend on the immediate external environment for nutrients, solute concentration, temperature, pH, and lack of toxins and predators. Thus unicellular organisms are limited to specific environments as their immediate environments much supply the appropriate nutrients and conditions.

Multicellular Organisms feature cell specialisation i.e. Tissues » organs » systems. These work together to form a stable internal environment, and thus the external environment is less crucial and a multicellular organism can survive in a range of environments. They still require the external environment as a source of nutrients and site for waste.

Internal Environment
Cells are bathed in Extracellular fluid (ECF) which contains 1/3 of the body's total water content (the remaining 2/3 resides in the cells themselves). The ECF provides a relatively constant temperature, pH and routes for nutrient delivery and waste disposal.

Claude Bernard (1813-1878) recognised the importance of the internal environment (ECF).
"La fixité du milieu intérieur est la condition d'une vie libre et indépendante"
"The constancy of the internal environment is the condition for a free and independent life".

Homeostasis
'Maintaining the constancy of the ECF allows multicellular organisms to explore, and function in, a diverse range of environments.' Walter Bradford Cannon (1871-1945) developed Bernard's ideas and coined the term homeostasis as; 'the maintenance of relatively constant conditions in the internal environment (ECF) in the face of external (or internal) change.'

Cannon suggested four general features of Homeostasis:
• In our bodies exist mechanisms that act to maintain constancy.
• Any tendency towards change automatically meets a factors and resistance against that change
• There are co-operating mechanisms that act collaboratively or successively to maintain homeostasis
• Homeostasis does not occur by chance, but via the result of self organised governance.

Constant ECF allows functionality in diverse environments e.g. extreme altitudes such as Machu Picu, where we would experience increased susceptibility to distressed states; hypoxia (oxygen), hypothermia (temperature), infection (disease), dehydration (water) and hypoglycaemia (nutrition).

At some point in our lives our normal body mechanisms are not sufficient enough to cope with maintaining homeostasis and we might need assistance; fluid/nutritional supplementation, antibiotics, drugs and surgery.

Climatisation is also important, we can get used to new environments if we are eased into it rather than experience the great amount bodily shock otherwise.

Important ECF Variables

Sodium (Na⁺) is the main ECF cation, which determines ECF volume and consequently blood pressure. It is also involved in action potential generation in nerve and muscle tissue. The normal Na⁺ ECF concentration is 135-145 mmol/L.

Calcium (Ca++) is important in bone and teeth and is involved in nerve transmission and muscle contraction, is essential for blood coagulation and regulates enzyme function. Its normal ECF concentration is 2-2.5 mmol/L.
**Glucose** is used by cells to produce ATP (especially neurons). High blood glucose (hyperglycaemia) causes other problems which are both acute and chronic. The normal fasting concentration of glucose is 3.5-6 mmol/L compared to its non-fasting concentration of 3.5-8 mmol/L. This can also be expressed in alternative units e.g. The textbook gives 80-100 mg/mL

**Potassium (K⁺)** is the most abundant intracellular cation and is described as the the main determinant of the Resting Membrane Potential (RMP). It is thus important for excitable tissue e.g. Nerves and muscle. Its normal ECF concentration is 3.5-5 mmol/L

**Acidity**, the normal pH of blood is 7.35-7.45 on the scale from 0 to 14. Acidosis results in loss of neuronal function and consciousness. Alkalosis results in the overexcitablity of nerve and muscle tissues; ‘pins and needles’, muscle spasms and convulsions.

**Core Body Temperature** is normally maintained around 37°C for optimum metabolic and physiological function. Peripheral temperatures vary quite a bit. Higher temperatures can result in the denaturation of enzymes and the rate of chemical reactions can become too slow at cooler ones. Nerves cells, and thus the control centres for many homeostatic functions, are very sensitive to temperature changes and thus a ‘vicious cycle’ can form, which rapidly leads to death.

**Membrane Transport**

**Diffusion** results from the random movement of individual particles as a consequence of their thermal energy. The distance travelled is proportional to the square root of time, and thus diffusion is rapid over short distances e.g. In and between cells and capillaries. The limitation of distance thus limits cell size; cells must have a high surface area to volume ratio. Substances diffuse from an area of high concentration to low concentration. This difference in concentration is called a concentration gradient.

**Simple Diffusion** occurs through the phospholipid bilayer of our cells by non-polar molecules like oxygen and carbon dioxide, and also steroid hormones and anaesthetic agents. Other molecules are too large or have awkward physiochemical substances like polarity and are not able to ‘dissolve’ across the membrane. They must cross the membrane via channel or carrier proteins embedded in the membrane, **Facilitated Diffusion**. Such particles needing this type of diffusion include ions and water. Aquaporins as channels allow the passage of water molecules that are otherwise lipid-insoluble and carrier proteins (Carrier Mediated Transport) bind to the particles they ferry across, changing shape in the process. Channels are usually specific and may be open/close spontaneously (leak channels) or in response to various stimuli e.g. chemicals (ligand gated), change in membrane potential (voltage gated)

Other transport across plasma membranes requires energy in that particles are moved against their concentration gradient, this is called **Active Transport**.

**Primary Transport** involves the use of enzymes embedded in the plasma membrane that utilise the energy produced in the hydrolysis of ATP to move molecules against the direction of their concentration gradient. An example of this is the Sodium-Potassium pump which transports three Na⁺ ions out of the cell for every two K⁺ ions in. This example is especially important in that it sets up an ionic gradient for RMP and regulates cell volume (due to movement of Na⁺ ions).

**Endocytosis and Exocytosis** is the bulk movement of material into and out of the cell via membranous (bilayer) vesicles. Phagocytosis is the uptake of large particles such as the ingestion of microbes via neutrophils and Pinocytosis is the uptake of fluid. Secretory cells expel excretions via the way of exocytosis.

**Osmosis** is the net movement of water down its concentration gradient (or toward a region of higher solute concentration).
Resting Membrane Potential (RMP)
This refers to the difference in ion concentration between the inside and outside of a cell, resulting in a potential difference of -70mV, where the inside is negative.

An equation that quantifies the membrane potential is the Goldman-Hodgkin-Katz equation. But we don’t have to know this:

\[ E_m = \frac{RT}{F} \ln \left( \frac{P_{Na^+}[Na^+]_{out} + P_{K^+}[K^+]_{out} + P_{Cl^{-}}[Cl^{-}]_{in}}{P_{Na^+}[Na^+]_{in} + P_{K^+}[K^+]_{in} + P_{Cl^{-}}[Cl^{-}]_{out}} \right) \]

Being the most permeable, K\(^+\) ions are the main determinant of the membrane potential. The normal membrane potential is -70mV, but this necessarily changeable for excitable tissues such as muscle and nerves and is controlled by the opening and closing of channels. If this were not to occur, muscle weakness, or cardiac arrest would ensue.

Important Terms
- The **Controlled Variable** is the variable/constituent of the environment that the systems tries to keep stable.
- The **Set Point** is the target value for the controlled variable.
- The **Reference Range** (normal) is the range of values (limits) that are acceptable for that value.

   The measurement for these values are taken from ‘healthy’ people, and the ‘normal’ range is defined as two standard deviations around the ‘normal’ mean

Variation exists between individuals in both set point and reference range. This variation is largely due to genetic factors, and can even be intra-individual, e.g. Difference in blood glucose level during fasting/non-fasting and due to biological rhythms (e.g. Cortisol concentrations which is involved in blood sugar level and hormone levels during the menstrual cycle). Other examples include variation due to Thus when analysing test results one must take this variability into account.

Control Systems for Homeostasis
Homeostasis is achieved via a combination of feedforward and feedback systems.

Negative
The most important type of feedback for physiological control is **negative feedback**. **Negative feedback** systems oppose the change in the controlled variable and move it back toward the ‘set-point’.

The key components of a negative feedback control system are….  
- The **Sensor** which monitors the actual value of the controlled variable  
- The **Integrator** which compares the actual and set point values, and then determines and controls the response  
- The **Effector** produces the response to restore the controlled variable.  
- **Communication Pathways** carry signals between other components.

An example of a negative feedback system is the one involving body temperature as the variable. Temperature receptors as sensors in the skin detect changes in temperature. Sensory nerve fibres relay this signal as a communication pathway to the hypothalamus in the brain as an integrator, which then signal effector via nerve fibres and hormones to effectors which are stimulated to rectify the change. Effectors and their actions in this case may be the muscles being stimulated to shiver when too cold, or the capillaries of the skins stimulated to dilate when too hot.
Treatment
Type I diabetes can be treated with injections of insulin. Grant Banting, Charles Best (and colleagues) at University of Toronto developed methods for extracting and purifying insulin from bovine pancreases in 1922.

A ‘Typical’ Regime might involve:
• A daily injection of a long acting insulin based on anticipated food intake and energy expenditure, feed-forward control
• Additional doses of short acting insulin based on actual blood glucose measurements, negative feedback control

Homeostatic Mechanisms restoring Blood Pressure and Volume after Haemorrhage
1. Activation of platelets and coagulation cascade:
   • Clot formation and cessation of blood loss begins

2. Changes to heart rate, cardiac contractility and vascular tone:
   • Drop in blood pressure detected by sensors in large arteries
   • Information sent by nerves back to cardiovascular control centres in brainstem
   • Nerves impulses sent from brain to heart (effector) to increase HR and force of contraction, which increases cardiac output and BP
   • Nerve impulses also sent from brain to blood vessels (effectors) causing them to constrict increasing arterial BP and venous return to heart, diversion of blood away from ‘non-essential’ organs

3. Restoration of blood volume
   • Arterioles in kidney detect reduced BP
   • Renin (enzyme) released into blood by specialised renal cells and results in formation of Angiotensin II
   • Angiotensin II has several effects which help restore actual blood volume (and pressure)
     • Secretion of aldosterone hormone from adrenal glands increase Na\(^+\) reabsorption
     • Secretion of antiuretic hormone (ADH) from pituitary gland increases water reabsorption
     • Constriction of arteries and veins
     • Simulation of thirst

4. Restoration of red blood cells
   • We don’t have a mechanism for actually counting red blood cells (erythrocytes) but since they transport oxygen the kidney can detect when there is a reduction in oxygen delivery
   • A hormone (erythropoietin or EPO) is then secreted into the blood and stimulates their production of new RBCs in the bone marrow
   • Complete restoration of red cell numbers to original levels may take a number of weeks and will also depend on availability of nutrients such as iron and B12
HUBS191 - Lecture 15, Complex Movements

Movement analysis involves joint position, muscle action, movement and role.

**Quadrapedal Standing**
- Involves using four limbs for support
- Is not very energy efficient; as a lot of energy is expended in the legs being in a continual flexed state at several joints.
- Has a very large support base, due to wide stance.

**Bipedal Standing**
- Utilises only two limbs
- Is far more energy efficient, allow long periods of standing
- Is unique to humans (sustained standing)
- Has a small base of support that is the circle that encloses the feet, not as stable as quadrapedal

**Effect of Gravity**
Especially in standing and walking, gravity acts as both an agonist and antagonist. It acts through the 'line of gravity', an imaginary vertical line that descends from the centre of mass. In the anatomical position, the hip joint is extended. In the sitting position, it is flexed. To sit down, gravity works as an agonist, whilst muscles acting as antagonists, such as the gluteus maximus and hamstring muscles, work to slow the movement down. In standing up, the roles are reversed, where the gluteus maximus produces the extension of the hip joint as an agonist, whilst gravity counteracts this motion as an antagonist. Gravity acts on three major joints when in a stable, upright stance:

**Hip Joint**
- Relative to the joint, the line of gravity lies posteriorly, forcing an extension of the joint
- In this position, the capsular ligaments of the joint are tight (three part of ligament), and thus they take most of the strain as opposed to muscle. Conversely, when in the seated position, the ligaments are loose.
- The joint is in a locked position.
- Not much energy is required at the hip, due to most of the force being transferred to ligamentation that isn’t energy consumptive.

**Knee Joint**
- Relative to the joint, the line of gravity lies anteriorly, forcing again an extension of the knee joint.
- In this position, the capsular ligaments of the joint are tight, creating stability. They take most of the strain as opposed to muscle. Conversely flexed, the ligaments are loose.
- The joint is in a locked position.
- Not much energy is required at the knee, due to most of the force being transferred to ligamentation that isn’t energy consumptive.

**Ankle Joint**
- Line of gravity lies anterior to the joint, producing a ‘falling’ into dorsiflexion. This join is not locked.
- Plantarflexors must then stabilise the joint. The soleus in the triceps surae performs this role.
- Energy is thus required at the ankle

Standing is thus achieved with very little muscular effort (most at the ankle joint). This is because of the development of bones, joints and muscles with specialised anatomical features that assist to solve the problem of balance.

**Bipedal Walking**
<table>
<thead>
<tr>
<th>Hormone</th>
<th>Source</th>
<th>Solubility/Type</th>
<th>Receptor Location</th>
<th>Mechanism of Action</th>
<th>Secretion Influenced By</th>
<th>Target Cell and Principal Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Beta Cells in Pancreatic Islets</td>
<td>Water-soluble</td>
<td>Muscle, Adipose and Liver cells</td>
<td>Activates 2nd</td>
<td>Stimulated by increased blood glucose level</td>
<td>Decreases blood glucose concentration. Stimulates the increased uptake of glucose in muscle, adipose and fat cells; glycogen and fat synthesis. Stops glucose output from the liver.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protein Hormone</td>
<td></td>
<td>Messenger</td>
<td></td>
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<tr>
<td>Glucagon</td>
<td>Alpha Cells in Pancreatic Islets</td>
<td>Water-soluble</td>
<td>Liver Cells</td>
<td>Activates 2nd</td>
<td>Stimulated by decreased blood glucose level</td>
<td>Increases blood glucose (and ketone) concentration. Stimulates the liver to increase breakdown of glycogen (glycogenolysis), increase glucose synthesis (gluconeogenesis) and increase ketone synthesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protein Hormone</td>
<td></td>
<td>Messenger</td>
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<tr>
<td>Antidiuretic Hormone (ADH, Vasopressin)</td>
<td>Posterior Pituitary Gland</td>
<td>Water-soluble</td>
<td>Kidneys</td>
<td>Activates 2nd</td>
<td>Stimulated by increased blood osmolality</td>
<td>Stimulates the kidneys to reabsorb water (Decreases plasma osmolality)</td>
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<td></td>
<td></td>
<td>Peptide Hormone</td>
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<td>Messenger</td>
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<tr>
<td>Oxytocin</td>
<td>Posterior Pituitary Gland</td>
<td>Water-soluble</td>
<td>Uterine Muscle Breast Milk Ducts</td>
<td>Activates 2nd</td>
<td>Stimulated by stretch receptors in breasts</td>
<td>Stimulates the contraction of uterine muscles during childbirth and stimulates milk release in breastfeeding</td>
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<td></td>
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<td>Peptide Hormone</td>
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<td>Messenger</td>
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<tr>
<td>Prolactin-Releasing Hormone (PRH)</td>
<td>Hypothalamus</td>
<td>Water-soluble</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2nd</td>
<td>Stimulated by stretch receptors in breasts</td>
<td>Stimulates the secretion of prolactin from the anterior pituitary gland</td>
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<td></td>
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<td>Peptide Hormone</td>
<td></td>
<td>Messenger</td>
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<tr>
<td>Prolactin-Inhibiting Hormone (PIH, Dopamine)</td>
<td>Hypothalamus</td>
<td>Water-soluble</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2nd</td>
<td>Stimulated by Prolactin</td>
<td>Inhibits the secretion of prolactin from the anterior pituitary gland</td>
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<td></td>
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<td>Catecholamine</td>
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<td>Messenger</td>
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<td>Hormone</td>
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<tr>
<td>Prolactin</td>
<td>Anterior Pituitary Gland</td>
<td>Water-soluble</td>
<td>Breasts</td>
<td>Activates 2nd</td>
<td>Inhibited by PIH Stimulated by PRH</td>
<td>Stimulates breast development and milk synthesis</td>
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<td></td>
<td></td>
<td>Protein Hormone</td>
<td></td>
<td>Messenger</td>
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<tr>
<td>Growth Hormone-Releasing Hormone (GHRH)</td>
<td>Hypothalamus</td>
<td>Water-soluble</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2nd</td>
<td>Inhibited by IGF-1</td>
<td>Stimulates the secretion of growth hormone by the anterior pituitary gland</td>
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<td></td>
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<td>Peptide Hormone</td>
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<td>Messenger</td>
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<tr>
<td>Growth Hormone-Inhibiting Hormone (SS, Somatostatin)</td>
<td>Hypothalamus</td>
<td>Water-soluble</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2nd</td>
<td>Stimulated by IGF-1</td>
<td>Inhibits the secretion of growth hormone by the anterior pituitary gland</td>
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<td></td>
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<td>Peptide Hormone</td>
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<td>Messenger</td>
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<tr>
<td>Insulin-like Growth Factor-1 (IGF-1)</td>
<td>Liver</td>
<td>Water-soluble</td>
<td>SS and GHRH Neurons in Hypothalamus</td>
<td>Activates 2nd</td>
<td>Stimulated by GH</td>
<td>Stimulates the growth of bones, muscles and other tissues by cell division (mitogenesis). Simultaneously stimulates the secretion of SS and inhibits the secretion of GHRH.</td>
</tr>
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<td></td>
<td></td>
<td>Peptide Hormone</td>
<td></td>
<td>Messenger</td>
<td></td>
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</tr>
<tr>
<td>Growth Hormone (GH, Somatotrophin)</td>
<td>Anterior Pituitary Gland (Somatotrophs)</td>
<td>Water-soluble</td>
<td>Bones, Muscles and Fat</td>
<td>Activates 2nd</td>
<td>Stimulated by GHRH Inhibited by SS</td>
<td>Indirectly via IGF-1, stimulates the growth of bones, muscles and other tissues by cell division (mitogenesis). Increases blood glucose by stimulating glucose synthesis in liver and inhibiting cellular uptake of glucose (textbook indirect). Also stimulates protein synthesis in muscles and triglyceride breakdown and fatty acid mobilisation in adipose tissue.</td>
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<td></td>
<td></td>
<td>Protein Hormone</td>
<td></td>
<td>Messenger</td>
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<td>Hormone</td>
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<tr>
<td><strong>Corticotropin-Releasing Hormone (CRH)</strong></td>
<td>Hypothalamus</td>
<td>Water-soluble Peptide Hormone</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Stimulated by abnormal stress, due to circadian rhythm. Inhibited by cortisol</td>
<td>Stimulates the anterior pituitary hormone to produce adrenocorticotrophic hormone (ACTH)</td>
</tr>
<tr>
<td><strong>Adrenocorticotropic Hormone (ACTH)</strong></td>
<td>Anterior Pituitary Gland</td>
<td>Water-soluble Protein Hormone</td>
<td>Adrenal Cortex</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Stimulated by CRH. Inhibited by cortisol</td>
<td>Stimulates the adrenal cortex to produce cortisol</td>
</tr>
<tr>
<td><strong>Cortisol</strong></td>
<td>Adrenal Cortex</td>
<td>Lipid-soluble Steroid Hormone</td>
<td>Cytoplasmic Receptors in Muscle, Fat and Liver Cells</td>
<td>Binds to receptors in the cytoplasm; activates or inhibits genes</td>
<td>Stimulated by adrenocorticotropic hormone (ACTH)</td>
<td>Stimulates protein and fat breakdown, and glucose synthesis, and decreases glucose uptake in muscle, fat and liver cells. Also helps to cope with stress; in the long term, suppresses the immune system and is essential for maintaining normal blood pressure.</td>
</tr>
<tr>
<td><strong>Adrenaline (Epinephrine)</strong></td>
<td>Adrenal Medulla</td>
<td>Water-soluble Catecholamine Hormone</td>
<td>Skeletal Muscle, Liver and Fat Cells</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Stimulated sympathetic preganglionic fibres in response to stress</td>
<td>Stimulates skeletal muscle and the liver to breakdown glycogen to glucose and fat to breakdown fat to fatty acids</td>
</tr>
<tr>
<td><strong>Thyrotropin-Releasing Hormone (TRH)</strong></td>
<td>Hypothalamus</td>
<td>Water-soluble Peptide Hormone</td>
<td>Anterior Pituitary Gland</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Inhibited by TRH, TSH and TH Stimulated by decreased BMR</td>
<td>Stimulates anterior pituitary gland to produce thyroid stimulating hormone</td>
</tr>
<tr>
<td><strong>Thyroid-Stimulating Hormone (TSH)</strong></td>
<td>Anterior Pituitary Gland</td>
<td>Water-soluble Glycoprotein Hormone</td>
<td>Thyroid Gland</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Inhibited by TH Stimulated by TRH</td>
<td>Stimulates the thyroid gland to secrete thyroid hormones T(_3) and T(_4)</td>
</tr>
<tr>
<td><strong>Thyroid Hormone (TH)</strong></td>
<td>Follicles in the Thyroid Gland</td>
<td>Lipid-soluble Iodinated Amino Acid Hormone</td>
<td>Cells</td>
<td>Binds to receptors in the nucleus; activates or inhibits genes</td>
<td>Stimulated by TSH</td>
<td>Increases basal metabolic rate (by increased synthesis and activity of the Na(^+)/K(^+) pump). Also stimulates growth (fetus and early childhood) and facilitates normal alertness and reflexes in the nervous system.</td>
</tr>
<tr>
<td><strong>Parathyroid Hormone (PTH)</strong></td>
<td>Parathyroid Glands</td>
<td>Water-soluble Protein Hormone</td>
<td>Bone and Kidney Cells</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Inhibited by increased blood calcium levels Stimulated by decreased blood calcium levels</td>
<td>Stimulates bone cells to increase bone breakdown, which releases calcium into the blood. Stimulates the kidneys to reabsorb calcium and to activate vitamin D, decreasing urinary ecretion of calcium</td>
</tr>
<tr>
<td><strong>Calcitonin (CT)</strong></td>
<td>Parafollicular Cells (C Cells) in the Thyroid Gland</td>
<td>Water-soluble Protein Hormone</td>
<td>Bone</td>
<td>Activates 2(^{nd}) Messenger</td>
<td>Inhibited by decreased blood calcium levels Stimulated by increased blood calcium levels</td>
<td>Inhibits the breakdown of bone. Decreases the rate of release of calcium into bone. Decreases blood calcium concentration.</td>
</tr>
</tbody>
</table>
34. The antibody that most effectively activates the complement system is:
A) IgD  B) IgG  C) IgA  D) IgE  E) IgM

35. The antibody that most effectively destroys multicellular parasites is:
1. A) IgD
2. B) IgG
3. C) IgA
4. D) IgE
5. E) IgM

36. The BCR on naïve B cells is mainly composed of:
A) IgE and IgG  B) IgG and IgA  C) IgA and IgE  D) IgD and IgM  E) IgM and IgG

37. 1. A) is pentameric
2. B) has a J-chain
C) is present as a cell surface receptor
1. D) is often present in myelomas (plasma cell cancer)
2. E) is abundant in milk

IgD:

38. My function is still unknown. What am I?
A) IgA  B) IgG  C) IgD  D) IgE  E) IgM

39. The process of coating a microbe in antibody (or complement) is called:
A) Alliteration
B) Procrastination  C) Opsonisation  D) Pontification  E) Saponification

40. B cells recognise ____ via their _____, while T cells recognise ____ in the context of _____:
A) Peptide antigens / BCR / Native antigens / BCR  B) Peptide antigens / TCR / Native antigens / MHC
C) Antibody / BCR / Native antigens / MHC  D) Native antigens / BCR / peptides / TCR
E) Native antigens / BCR / peptides / MHC

41. A patient is admitted to your ward with a severe skin reaction. The 2 days before, the patient was administered penicillin for a minor skin infection.
- PCV, pneumococci producing meningitis
- MMR; measles/mumps/rubella, rubella affects pregnant women
- Influenza

**Opposition to Vaccination**
- Not My Problem
- We are Special
- Personal risk vs communal benefit
- They don't work!
- Underestimate impact of disease; polio
- Side effects; inflammation, fever, headache (which are actually good; they imply the vaccine is working, stimulating an immune response)
- Disinformation; vaccines cause autism
- Alternative medicines; But vaccines come from nature!

**Some Vaccines Cannot Work... Yet**
- Multiple strains of Rhinovirus make it impossible to develop vaccines against common cold virus
- HIV Changes its Surface Antigens (Reverse transcriptase - low fidelity); two recent HIV Vaccines (STEP and HVTN-505) have failed
- Vaccines may cause side-effects
- Vaccines don't work if there is not public acceptance
- Our new reality is the difficulty of the use of live vaccines in 'compromised' patients; nature used to screen them out.

**Pathways of Immunity**
- Live vaccines
  - Stimulate Cell Mediated Immunity (TC) and IgA production
  - Essential to give at least 2 doses of live vaccines (8 week interval)
- Killed vaccines
  - stimulate IgM/IgG production, causing opsonisation of bacteria and the neutralisation of toxins/virus
  - May give 3 or more doses if vaccine is killed/subunit/conjugate

**Vaccine Failures**
- Poor vaccine potency
- Inadequate vaccine storage; live vaccines need to be stored properly to be kept alive
- Immunocomprised patients: (Pregnant, Malnourished, AIDS)
- Genetic susceptible; modern medicine has stopped

**New Generation Vaccines**
- Cancer
- Allergy
- Autoimmunity
- Immunocontraception
First line of defense is the physical and barriers, e.g. Epithelial linings. 
Second defense cellular, macrophage, mast cells release amines.

An amazing amount of mucosal linings
Secretions
Ea secretions
Sebaceous secretions

Cellular response, innate
Phagocytosis
- Taken up into phagosome
- Fuses with lysosome
- Breaks down bacteria

Phagocytes recognise pathogens via toll like receptors
Recognises unique things common to pathogens
TL9 etc

We want to make the phagocytosis function as efficient as possible; inflammation
MesAT cells are stimulated to produce vasodilatory chemicals
Stimulates blood dilation
Macrophages release IL-1 IL-6 and TNF-alpha
IL-1 acts on hypothalamus and causes fever
In the blood, neutrophilia, increased fibrinogen and haptoglobin, complement (3a, 3b and 5a) also acute phase proteins
Increased permeability of the blood vessel walls allow diapedesis

Inflammation; calor (heat), rubor (redness), tumor (swelling), dolor (pain) and loss of function

Antimicrobial peptide and protein are produced; interferon, activation of complement

C3a and C5a act as peptide mediator of inflammation recruit phagocyte
C3b, opsonisation (sticking to organisms)
C6,7,8,9, Lysis (MAC complex)

Opsonisation

Organisms have adapted to become resistant to inflammatory systems

How we respond to natys that get into our body
Adaptive immune system
Highly specific
Work against antigens
Cells are produced in the bone marrow
- B cells mature in bone marrow
- T cells mature in the thymus
Secondary lymph nodes, lymph follicles and spleen

Blood system transports stuff from spleen
Lymphatic system drains from tissue

Supermacrophages; dendritic cells
Transport foreign materials to lymph nodes
Antigen presenting cell.

Special display system MHC -1 and MHC-II
MHC-II displayed on dendritic cells
Antigen developing inside cells are displayed on MHC-I, displayed on every nucleated cell.

- B cell response
  - Each has a BCR, which is a IgM antibody
  - Cd4 cells recognise MHC-II displayed peptides on APCs (via TCR)
  - B cell recognise via BCR
  - Need help from helper cytokines released by CD4
  - Stimulates the clonal selection of B cells
  - B cells recognise native antigen

- Plasma cells
- Memory cells

Antibody response matures with increased frequency of stimulation.

- T cells are essential to switch between isotopes
- Antibody feature different function
  - IgM
  - IgG, does everything
  - IgA, mucous, neutralises things in secretory system
  - IgE, response to
  - IgD, immature cells, tolerance

Cell mediated response
- CTL
  - Up regulate macrophages to enhance their killing of intracellular bacter
  - Both are effector cells
  - Cytotoxic cells produce specialised molecules
    - Performs, which form complexes in the membrane of infected cells, form a channel
    - Granzymes activate apoptotic enzymes
  - Cause apoptosis

- Chronic infections upregulate via gamma IFN to

  - IgM/IgG, motility

- Develop or acquire immunity
  - Active by getting an infection and then recovering e.g. Mumps., after recovering from them, you never get mumps again. Permanant protection.
  - Vaccination either attenuated, killed or antigens from the organism are inoculated to produce a response, gives you memory which allows you to response better.
  - Passive via placenta or milk, colostrum
  - Injection of antibodies to combat antigens. First example is the injection of horse serum to combat tetanus.
  - Serums re mainly IgG

- Passive immunity helps you immediate, but then disappears, limited half life.
- Active immunisation, boosters contribute to a long lasting response.
- Vaccines have decreased the rate of many diseases, mostly in children.

- Live vaccines are more effective (but sometime have side effects) that killed vaccines.
- Tetanus, first passive, now active, which is more effective.

Milestones

Attenuation where pathogen loses its virulence after being cultured not in the host environment.

Conjugate vaccines.