

Human Biology 12

Endocrine system/Hormones

Introduction

- Cells, tissues, organs and systems work together in a coordinated manner.
- This coordination is achieved through the activities of the nervous and endocrine systems
- Nervous system exerts control by the transmission of nerve impulses to and from various tissues
- Endocrine system influenced the activity of cells by the release of chemical messengers known as hormones
- Homeostasis is the maintenance of a constant internal environment

Endocrine System

There are two types of glands:

Exocrine Glands: secrete into a duct that carries the secretion to the body surface or to one of the body cavities e.g. sweat glands, salivary glands and mucous

Endocrine Glands: secrete into extracellular fluid that surrounds the cells that make up the gland.

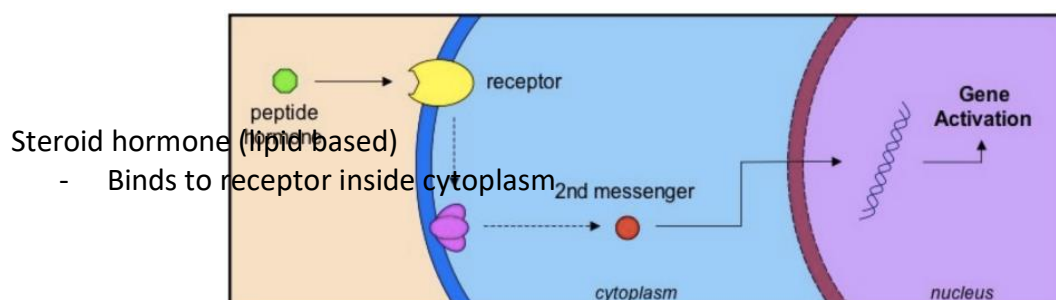
Hormones

- Hormones are a secretion of an endocrine glands
- Classified as either proteins and amines (water based) or steroid (lipid based)
- Transported through the body in the bloodstream
- May affect all the cells in the body or only one particular group of cells, target cells or particular organs, target organs
- Paracrine's are substances secreted by cells that diffuse to and effect adjacent cells
- Hormones are secreted by specialised cells and are transported by the bloodstream
- Hormone receptors are specific meaning they are only able to influence cells in the same tissue by secreting chemicals that diffuse to adjacent cells
- Saturation can occur which means once all the receptor molecules are occupied by hormone molecules the addition of more hormones does not produce any greater effect
- The mode of action of protein and amine hormones and steroid hormones is dependent on their ability to cross the cell membrane

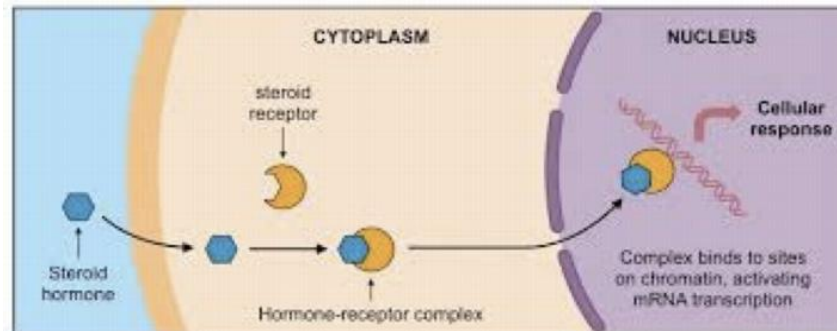
Mode of action of hormones

Protein and amine hormones (water based)

- Bind to the receptor on the surface of cell membrane
- Hormone receptor complex forms on cell membrane surface
- This produces a molecule that acts as a secondary messenger which diffuses through the cell and is activated within the cytoplasm, activating particular enzymes.



- Hormone receptor complex forms
- Hormone receptor complex enters the nucleus and binds to the DNA
- This interferes with the cells ability to read some genes, either switch on or switch off protein synthesis or particular genes



Effects of hormones

- Hormones change the functioning of cells by changing the type, activities or quantities of proteins produced
- Hormones are not enzymes, however, they can change the activity of enzymes or change the concentration of enzymes
- Enzyme amplification is the process whereby one hormone molecule activates thousands of enzyme molecules
- The hormone triggers a cascading effect in which the number of reacting molecules involved is increased hundred's or thousands of times for each step along the metabolic pathway
- A very small stimulus can produce a very large effect
- Once the hormone has achieved its required effect, it needs to be turned off. This occurs by breaking down the hormone molecule in the target cells. Most are broken down in the liver or kidneys
- Degraded hormones are excreted either in the bile or urine

Hormones:

1. Can activate certain genes in the nucleus so that a particular enzymes or structural protein is produced
2. Change the shape or structure of an enzyme so that it is turned on/off
3. Change the rate of production of an enzyme or structural protein by changing the rate of transcription/translation during protein production

Control of hormone secretions

- Hormone secretions are usually regulated by negative feedback systems
- Some negative feedback systems involve the nervous system
- The hypothalamus releases regulating factors which regulate the function of the pituitary glands
- Releasing factors stimulate the release of a hormone
- Inhibiting factors slow down the secretion of a hormone

Hormone	Target Organ	Main Effects
Anterior lobe of pituitary		
Follicle Stimulating Hormone	Ovaries, Testes	Growth follicles, production of sperm

Luteinising Hormone	Ovaries, Testes	Ovulation and maintenance of corpus luteum. Secretion of testosterone
Growth Hormone	All cells	Growth and protein synthesis
Thyroid Stimulating Hormone	Thyroid gland	Secretion of hormones from the thyroid
Adrenocorticotrophic Hormone	Adrenal cortex	Secretion of hormones from the adrenal cortex
Prolactin	Mammary glands	Milk production
Posterior lobe of pituitary		
Antidiuretic Hormone	Kidneys	Reabsorption of water
Oxytocin	Uterus, mammary glands	Contraction of uterus during childbirth. Release of milk

Gland	Hormone	Target Cells	Main Effects
Thyroid	Thyroxine	Most cells	Increases metabolic rate and therefore oxygen consumption and heat production
Parathyroid	Parathyroid Hormone	Bones, kidneys	Increase level of calcium in blood
Thymus	Thymosin's	T lymphocytes	Stimulates development and maturation of T lymphocytes
Adrenal Cortex	Corticosteroids including: - Aldosterone - Cortisol	Kidney, most cells	Increase reabsorption of sodium ions and excretion of potassium ions. Promotes normal metabolism
Adrenal Medulla	Adrenaline and noradrenaline	Most tissues	Prepares the body for fight or flight response
Pancreas	Insulin, glucagon	Most cells, liver and fat storage tissues	Stimulates uptake of Glucose; lowers blood glucose level. Stimulates breakdown of glycogen and fat; increases blood glucose level
Testes	Androgens	Many tissues	Stimulate sperm production; growth of skeleton and muscles; make sexual characteristics
Ovaries	Oestrogen, progesterone	Many tissues, uterus and mammary glands	Stimulate development of female characteristics; regulate the menstrual cycle. Regulates menstrual cycle and pregnancy; prepares mammary glands for milk secretion.

Relationship between hypothalamus and pituitary gland.

- The functions of the hypothalamus are carried out through the pituitary gland.
- The pituitary gland is joined to the hypothalamus by the infundibulum.
- The anterior pituitary gland is connected to the hypothalamus by a complex network of blood vessels referred to as the hypophyseal portal system
- The posterior pituitary gland is not a true gland as it does not secrete hormones.
- It joins to the hypothalamus by nerve fibres that come from nerve cell bodies in the hypothalamus and pass through the infundibulum to the posterior lobe

Hypothalamus produces different hormones:

- Some are carried by the blood to the anterior pituitary gland where they stimulate or inhibit the release of hormones made by in the anterior pituitary gland.
- Some pass along the nerve fibres from the hypothalamus to the posterior pituitary gland where they are released.

Recombinant DNA

- Gene technology is a broad field which includes analysis of DNA as well as genetic engineering and other forms of genetic modification
- Genetic engineering refers to the artificial manipulation of genes: adding or subtracting genes, or changing the way genes work
- Organisms with artificially altered DNA are referred to as genetically modified organisms.
- Gene technologies have great benefit to humanity through:
 1. Increasing crop production
 2. Increasing livestock production
 3. Preventing and fighting disease
 4. Reducing pollution and waste
 5. Producing new products
 6. Detecting and preventing crime

Method

- Methods were developed to insert foreign DNA into cells using vectors. New recombinant DNA technology involved recombining DNA from different individuals and even different species.
 1. A gene of interest is isolated from human tissue cells
 2. Human DNA and plasmid are treated with the same restriction enzyme to produce identical sticky ends
 3. Restriction enzyme cuts the plasmid DNA at its single recognition sequence, disrupting the tetracycline resistance gene
 4. Mix the DNAs together and add the enzyme DNA ligase to bond the sticky ends
 5. Recombinant plasmid is introduced into a bacterial cell by simply adding the DNA to a bacterial culture where some bacteria take up the plasmid from solution

Producing GMOs

- GMOs may be created by modifying their DNA in one of three ways:
 1. Adding a foreign gene
 2. Alter an existing gene
 3. Delete or turn off a gene

Restriction enzymes

- Purified forms of these naturally occurring bacterial enzymes are used as molecular scalpels allowing genetic engineers to cut up DNA in a controlled way.

Specific recognition sites

- Restriction enzymes are named according to the bacterial species they were first isolated from, followed by a number to distinguish different enzymes isolated from the same organism
- A restriction enzyme cuts the double stranded DNA molecule at its specific recognition site

Sticky ends

- Restriction enzymes that cut leaving an overhang is called a sticky end
- DNA cuts in such a way that produces ends which may only be joined to other sticky ends with a complementary base sequence

Blunt ends

- Restriction enzymes can cut leaving no overhang which is called a blunt end
- DNA cut in such a way able to be joined to any other blunt end fragment, but tends to be non specific because there are no sticky ends as recognition sites.

Ligation

- DNA fragments produced using restriction enzymes may be reassembled by a process called ligation
- Pieces of DNA are joined together using an enzyme DNA ligase
- DNA of different origins produced in this way is called recombinant DNA because it is DNA that has been recombined from different sources

Annealing

- When the two matching sticky ends come together, they join by base pairing. This is called annealing
- This can allow DNA fragments from a different source, perhaps a plasmid, to be joined to the DNA fragments
- The joined fragments will usually form either a linear molecule or a circular one, as shown here for a plasmid

Divisions of the nervous system

- Nervous system
- Central nervous system
- Brain, spinal cord
- Peripheral nervous system
- Motor nerves, sensory nerves
- Somatic, autonomic
- Sympathetic, parasympathetic

The nervous system

- One of the body's communications network
- Involved in maintaining homeostasis
- Involves the use of electrical impulses to send messages around the body
- Body's nervous system consists of the brain, spinal cord and all the nerves
- Two main parts of the nervous system are the central nervous system and peripheral nervous system

Ganglia

- Groups of nerve cell bodies which lie outside the brain and spinal cord
- These nerve fibres are arranged into nerves which arise from the brain and spinal cord

Cranial nerves

- 12 pairs of nerves that arise from the brain
- Most are mixed nerves meaning they contain fibres that carry impulses to the brain and away from the brain
- Sensory fibres, carry impulses into the central nervous system
- Motor fibres, carry impulses away from the central nervous system

Spinal nerves

- 31 pairs of nerves that arise from the spinal cord
- Mixed nerves containing both motor and sensory fibres
- Each is joined to the spinal cord by two roots:
 1. Ventral root, contains axons of motor neurons that have their cell bodies in the grey matter of the spinal cord
 2. Dorsal root, contain axons of sensory neurons that have their cell bodies in a swelling on the dorsal root ganglion

Peripheral nervous system

- Can be divided and subdivided further.
 1. Afferent division, fibres that carry impulses into the CNS. Carried by sensory nerve cells from receptors in the skin and around muscles and joints. Somatic sensory neurons are nerve cells from the body. visceral sensory neurons take impulses from internal organs into CNS.
 2. Efferent division, fibres that carry impulses away from the CNS. Subdivided into somatic and autonomic. Somatic division takes impulses from CNS to skeletal muscles. Autonomic carries impulses from CNS to heart muscle, involuntary muscle and glands
 3. Autonomic subdivided into sympathetic and parasympathetic division.

Autonomic nervous system

- Responsible for control of body's internal environment and involved in many homeostatic mechanisms that keep internal environment constant
- Usually operates without conscious control
- Regulated by groups of nerve cells in the medulla oblongata, hypothalamus and cerebral cortex
- Nerve fibres of ANS make up part of the spinal nerves and part of some of the cranial nerves
- Impulses are carried to the heart muscles, muscles of internal organs and glands

Sympathetic

- Prepares the body for action
- Enables body to respond to stress
- In extreme situations it functions the response of fight or flight

Parasympathetic

- Steadies the body
- Maintains the body during relatively quiet time

ANS (involuntary)

- Pathway consists of 2 motor neurons, 1 has its cell body in the CNS the other cell body is a ganglion
- Most organs receive 2 sets of nerve fibres, sympathetic and parasympathetic

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- Neurotransmitter that carries messages from neuron to skeletal muscle is either acetylcholine or noradrenaline.

Somatic to skeletal (voluntary)

- Pathway consist of 1 motor neuron
- Neurotransmitter is acetylcholine

Hypothalamus involvement

- Hypothalamus sorts the impulse that warn of these variations and adjust the balance of the sympathetic and parasympathetic stimulations in order to maintain a stable internal environment
- Actions of the ANS may be influenced by impulses from the cerebral cortex

Brain and spinal cord

- Nervous system is the communication network and control centre of the body
- CNS consists of both grey matter and white matter
- Grey matter, consists of nerve cell bodies and unmyelinated fibres
- White matter, composed of myelinated fibres

Protection mechanisms

- Cranium, outermost bone structure
- Meninges, 3 layers of connective tissue covering the surface of the brain
- Cerebrospinal fluid, occupies a space between the middle and inner meningeal layers and circulate through cavities in the brain. Also found around the spinal cord.

Meninges

- Dura mater, tough and fibrous
- Arachnoid mater, loose mesh of fibres containing blood vessels
- Pia mater, delicate structure where many blood vessels pass through

Cerebrospinal fluid

- Clear watery fluid between arachnoid mater and pia mater
- Contains few cells
- Contains some glucose, protein, urea and salts
- Acts as shock absorber
- Supports brain
- Transports nutrients towards and away from brain

The brain

Human brain consists of four parts

- Brain stem
- Diencephalon
- Cerebellum
- Cerebrum

Cerebrum

- Made up of cerebral cortex, folder outer layer of grey matter
- Divided into four main lobes
- Can be divided into three main functional areas

Lobes of the cerebrum

Frontal lobe

- Primary motor cortex
- Voluntary motor function
- Concentration
- Verbal communication

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- Decision making
- Planning
- Personality

Parietal lobe

- Primary somatosensory cortex
- Sensory functions
- Comprehension of language

Occipital lobe

- Primary visual cortex
- Processing visual information
- Storing visual memories

Temporal lobe

- Understanding speech
- Interpretation and storage of auditory and olfactory sensations

Cerebrum internal structure

- Also made up of basal ganglia: mass of grey matter inside brain
- Contains nerve cell bodies associated with skeletal movements, eye movements, cognition and emotion
- Corpus callosum: wide band of nerve fibres beneath cerebral cortex
- Bridge between left and right hemisphere
- Provides communication between hemispheres

3 functional areas of the brain

- Sensory areas, receive and process nerve impulses from the senses
- Motor areas, send impulses to muscles, especially for voluntary movement
- Association areas interpret information from the senses and make it useful.

Diencephalon

- Located beneath cerebrum and part of basal ganglia
- Consists of:
- Thalamus, sensory relay in visual, auditory, somatosensory and gustatory systems. Translate various receptors to cerebral cortex. Motor activity, emotions, memory
- Hypothalamus, mostly controls homeostasis, regulates ANS, body temperature, food/water intake, sleeping patterns, emotional responses, contraction of urinary bladder, secretion of hormones

Cerebellum

- Located underneath occipital and temporal lobes
- Folded into parallel ridges
- Grey matter on outside and white matter inside
- Functions include controlling coordination's of body, fine coordination of voluntary muscle motor movement. Posture, balance and speech, stores previously learned movement patterns.

Brain stem

Three main parts

Midbrain

- motor movements, auditory and visual processing

Pons,

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- connects spinal cord with brain and relays messages between cerebrum and cerebellum

Medulla oblongata

- regulates heart rate and diameter of blood vessels
- controls breathing
- regulates swallowing, sneezing, coughing and vomiting reflex

The spinal cord

- cylindrical structure extending from the foramen magnum to the 2nd lumbar vertebrae
- approx. 44 cm length

heavily protected

1. enclosed in vertebral column
 2. meningeal layers inside the ring of bone, outermost meningeal layer is not joined to bone, there is a space containing fat, connective tissue and blood vessels. This serves as padding around the spinal cord, allowing spinal cord to bend
 3. cerebrospinal fluid
- myelinated fibres of the white matter arranged in bundles known as ascending and descending tracts
 - ascending tracts, sensory axons, carry impulses up towards the brain
 - descending tracts, motor axons carry impulses downwards away from the brain.

Spinal cord cross section

- contains areas of grey matter and white matter
- composition is same as in brain
- difference, grey matter is central, surrounded by white matter
- grey matter, roughly shape of letter H

spinal cord functions

- carry sensory impulses via ascending tracts up to the brain and motor impulses via descending tracts down from the brain

Neurons structure and function

Nerve cells

Neuron

- basic structural and functional unit of the nervous system
- varies in size and shape, but all consist of a cell body and two different types of extensions from the cell

Nerve fibre

- any long extension of the cytoplasm of a nerve cell body

Nerve

- a bundle of nerve fibres

Parts of the neuron

Cell body, contains the nucleus and many other cell organelles

Dendrites, often contain many branches, receive messages from other neurons and carry impulses towards the cell body.

Axon, only one, often long and unbranched for most of its length, carry impulses away from the cell body.

Myelin sheath, layer of fatty material that covers the axon.

3 important functions

- helps insulate the axon
- protect from damage

- speeds up the movement of nerve impulses along the axon

Myelinated fibres, fibres containing myelin sheath.

Unmyelinated fibres, fibres not containing myelin sheath.

Schwann cells, special cells of myelin sheath, occur outside the brain and spinal cord.

Nodes of Ranvier, gaps within the myelin sheath along the axon.

Neurilemma, membrane that surrounds the myelin sheath which helps repair injured fibres.

Types of neurons

Neurons can be classified according to their function or structure

Functional neurons:

- sensory/afferent neurons, carry messages from receptors to the brain and spinal cord
- motor/ efferent neurons, carry messages from the brain and spinal cord to effectors
- connector/interneurons/association/relay neurons, located in the brain and spinal cord, a link between sensory and motor neurons

Structural neurons

- classification is based on the number of extensions from the cell body
- **multipolar neuron**, have one axon and multiple dendrites extending from the cell body, most common type of neuron, includes most of the interneurons in the brain and spinal cord and motor neurons that carry messages to the skeletal muscles
- **Bipolar neuron**, have one axon and one dendrite, both axon and dendrite may have many branches at their ends. Occur in the eye, ear and nose where impulses are taken from the receptor cells to other neurons
- **Unipolar neuron**, have just one extension, an axon, cell body is to one side of the axon. Most sensory neurons that carry messages to the spinal cord are unipolar.

Synapses

- A synapse is the junction between the branches of adjacent neurons
- Neurons do not touch at the synapse, there is a small gap between them
- Most synapses occur between the end branches of an axon of one neuron and a dendrite or the cell body of another neuron
- Messages are carried across the synapse

Receptors

- Structures that are able to detect a change in the body's internal or external structure

Receptors can be found in:

- Sense organs (light receptor in the eye)
- Simple nerve endings which are spread throughout parts or the whole of the body

Types of receptors

1. Thermoreceptors
 - Found in the skin, nerve endings that are sensitive to either heat or cold but not both
 - Responds to heat and cold informs brain of changes in the temperature outside the body
 - Temperature inside body is monitored by thermoreceptors in hypothalamus
 - Detects temperature of blood flowing to the brain
2. Osmoreceptors
 - Located in the hypothalamus
 - Sensitive to osmotic pressure
 - Responds to very small changes in osmotic pressure and are able to stimulate the hypothalamus so body's water content is maintained within narrow limits
3. Chemoreceptors

- Located in the nose, mouth, blood vessels
- Stimulated by particular chemicals and sensitive to odours, taste, pH of blood, composition of body fluids and concentrations of oxygen and carbon dioxide.
- Regulation of heartbeat and breathing
- 4. Touch receptors
 - Located in the skin, lips, fingertips, eyelids, external genital organs, base of hair follicle, deeper in skin
 - Receptors close to skin are sensitive to very light touches
 - These receptors adapt quickly after a short time, no longer aware of touch
- 5. Pain receptors
 - Found in the skin, mucous membranes and in most organs except the brain
 - Stimulated by damage to the tissues, such as a cut, heavy bump, excessive stimulation from heat or chemicals.
 - Important receptor, warns if tissue is being damaged and allows individuals to take evasive action
 - Pain receptors adapt little or not at all so pain continues as long as the stimulus is present

Reflexes

- A reflex is a rapid, automatic response to a change in the external or internal environment
- Many reflexes protect the body from injury. (blinking, sneezing, coughing etc)
- Reflexes can be learned during a baby's development, suckling, chewing, following movements with eyes. Complex motor patterns are acquired reflexes such as balance while riding a bike.
- All reflexes have four important properties:
 1. Stimulus, required to trigger a reflex, reflex is not spontaneous
 2. Involuntary, occurs without conscious thought
 3. Rapid, only a small number of neurons are involved
 4. Stereotyped, occurs in the same way each time it happens
- Some reflexes involve the unconscious parts of the brain, the majority are coordinated by the spinal cord
- Spinal reflex, reflex involving the spinal cord
- Pathway a nerve impulse follows in travelling from a receptor to an effector is known as a reflex arc
- Spinal reflex is involuntary as it does not involve the brain
- Impulses usually sent to the brain so that we are aware of what is happening, but this occurs after the response has been initiated

Reflex arc

- Receptor, either the ending of a sensory neuron or a specialised cell associated with the end of a sensory neuron
- Sensory neuron carries impulses from the receptor to the CNS
- Synapse at least one
- Motor neuron carries the impulse to an effector
- Effector receives the nerve impulse and carries out the appropriate response. Effectors are muscle cells or secretory cells.

Nerve impulse

- A nerve impulse is a message that travels along a nerve fibre.

- It is described as electromechanical as it involves changes in electrical voltage that is brought about by changes in the concentration of ions inside and outside of the membrane of a neuron

Speed of transmission depends on

1. Whether the nerve fibre is myelinated or unmyelinated
2. Diameter of the fibre

Maintenance of resting membrane potential

- Resting membrane potential of a nerves cell is measured to be -70 millivolts
- As long as the resting membrane potential is undisturbed, it remains polarised.
- A depolarised membrane occurs when a strong stimulus is applied to the nerve fibre, membrane becomes more permeable to Na ions so that Na can move across the cell membrane into the cell
- In order for a nerve impulse to be started or propagated in a nerve cell, this resting membrane potential must be disturbed

local potential changes

- Resting membrane potential of -70 mV can be disrupted or changed in one of two directions
1. More negative, hyperpolarisation
 2. Less negative, depolarisation

Action potential

- When the resting membrane potential of a neuron is depolarised to -55 mV threshold potential is reached
- Threshold potential for a neuron is -55mV
- Therefore, a threshold stimulus is +15mV
- When threshold potential is reached, the rapid opening of Na channels result in rapid depolarisation
- This event is called action potential
- Action potential represents the start of the nerve impulse on a neuron
- K channels open, while Na channels close and repolarisation occurs
- Repolarisation, membrane returns to -70mV
- This occurs rapidly
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Sodium potassium pump

- Active transport method, requires energy
- 3 Na bind to protein channel; ATP provides the energy for the channel to change shape, allowing the 3 Na to move through the channel and released outside of the cell
- 2 K bind to the protein channel, changing the shape of the protein channel, allowing the 2K to move inside the cell
- Both Na and K are moving from an area of LOW concentration to an area of HIGH concentration
- This type of movement can only be achieved by the constant expenditure of ATP energy

Thermoregulation

- Internal body temperature of humans is relatively constant
- In the body, heat gained is heat lost
- Thermoregulation, process that maintain the balance between heat production and heat loss to maintain a relatively constant internal body temperature

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- Metabolic reactions produce heat
- Heat produced from metabolism helps ensure that internal body temperature is warmer than the environment
- When internal temperature changes, range of processes occur to return internal temperature
- Internal temperature never consistently at 37

Detecting heat changes

- Central thermoreceptors, located in hypothalamus
- Peripheral thermoreceptors found in skin and mucous membranes
- Provide hypothalamus with information about external temperature changes
- Cold receptors stimulated by lower than normal environmental temperatures
- Hypothalamus receives information and initiates heat production
- Hot receptors, stimulated by higher than normal environmental temperatures
- Hypothalamus receives information and initiates heat reduction/loss

The skin

- Sweating helps lose additional heat
- Stimulated by sympathetic nerves, sweat glands secrete fluid
- Sweat consists of water, sodium chloride, urea, lactic acid, potassium ions
- Sweat evaporates from skin, cools blood close to skin surface and reduces internal body temp
- Effective sweating occurs when environmental temp, body temp and when humidity is low

Heat transfer methods

Conduction

- Heat transfer between two objects in contact with each other
- Heat flows, high temp -> low temp

Convection

- Heat transfer due to currents of air and water
- In air, clothes reduce heat loss by trapping air near skin
- In water, divers wear wetsuits to reduce heat loss by convection

Radiation

- Heat loss into surrounding environment cool room, body radiates heat into air from exposed skin

Evaporation

- State change from liquid to gas
- Evaporation involves immense amounts of energy, very effective for heat loss
- Water evaporation generates cooling effect

Falling body temperature

- Occurs when environmental temperature decreases
- Hypothalamus sends impulses prompting following changes:
 1. Vasoconstriction
 2. Stimulation of adrenal medulla
 3. Shivering
 4. Increased production of thyroxine
 5. Behavioural responses
- Responses are to increase internal body temperature

Vasoconstriction

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- Impulses from hypothalamus stimulates sympathetic nerves
- Blood vessels in skin constrict
- Warm blood flow decreases to skin
- Less heat is lost from body' surface

Stimulation of adrenal medulla

- Hypothalamus stimulates adrenal medulla via sympathetic nerves
- Adrenal medulla secretes adrenaline and noradrenaline
- Cellular metabolism increases -> increases heat production

Shivering

- Hypothalamus impulses stimulates part of the brain that lead to increased skeletal muscle tone
- Causes muscle tremors
- Increases body heat production
- Can be consciously suppressed

Increased thyroxine production

- Hypothalamus stimulates anterior pituitary gland
- Anterior pituitary secretes thyroid stimulating hormone
- TSH targets thyroid gland
- Thyroid gland secretes thyroxine into blood
- Metabolic rate increases
- Occurs often in winter

Behavioural responses

- Huddling
- Curling into a ball
- Putting on layers of warm clothing
- Using heat devices
- Sheltering in warmer environment

Rising body temperature

- Occurs when environmental temperature increases
- Hypothalamus sends impulses prompting following changes:
 1. Vasodilation
 2. Sweating
 3. Decrease in metabolic rate
 4. Behavioural responses
- Responses are to decrease internal body temperature

Vasodilation

- Blood vessels in skin dilate
- Warm blood flow through skin increases
- Skin begins to turn red and warms up
- Increase heat loss via radiation and convection

Sweating

- Excretion of sweat from sweat glands
- Increases evaporation of heat
- Blood near skins surface cools down

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- Not effective in high humidity

Decreased metabolic rate

- Decrease in thyroxine production
- Reduces metabolism
- Occurs often in summer

Behavioural responses

- Decreasing body movement
- Less exposure to sun
- Air conditioning wearing less clothing
- Swimming

Blood glucose regulation

Hormones involved

Insulin:

- A hormone, secreted by beta cells of the islets of langerhans, in the pancreas, designed to reduce blood glucose levels

Glucagon:

- A hormone, secreted by alpha cells of the islets of langerhans, in the pancreas, designed to increase blood glucose levels

Role of liver

The liver's role in regulating blood glucose levels is to either:

1. Convert glucose to glycogen (storage)
 2. Convert glycogen to glucose (use)
- Much of the liver's blood supply comes from the hepatic portal vein, which brings blood from the stomach, spleen, pancreas and small and large intestines
 - After consuming a high proportion of carbohydrates, breakdown products, mainly glucose, are absorbed into blood capillaries of villi of the small intestines.

Role of pancreas

- Islets of langerhans are clusters of hormone secreting cells found in the pancreas

There are two types of cells in islets of langerhans:

1. Alpha cells secrete glucagon
2. Beta cells secrete insulin

Insulin

Insulin causes a decrease in blood sugar levels by:

1. Accelerating the transport of glucose from blood into cells
2. Accelerating the conversion of glucose into glycogen
3. Stimulating the conversion of glucose into fat and causes an increase in protein synthesis

Glucagon

Glucagon causes an increase in blood glucose levels by

- Stimulating glycogenolysis, conversion of glycogen to glucose
- Promoting gluconeogenesis, conversion of fats and amino acids into glucose

Role of adrenal glands

- Adrenal glands are situated above the kidneys

Composed of two parts:

- Cortex (outer region)
- Medulla (inner region)

Adrenal cortex

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- Adrenal cortex is stimulated to secrete its hormone by adrenocorticotrophic hormone from the anterior pituitary gland
- Hormone secreted is glucocorticoids
- Cortisol regulates carbohydrate metabolism by ensuring enough energy is provided to cells
- This stimulates conversion of glycogen to glucose and increases rate at which amino acids may be converted to glucose by liver if glycogen and fat levels are low

Adrenal medulla

- Adrenal medulla synthesises adrenaline and noradrenaline
 - Noradrenaline produces effects that mimic those brought about by the sympathetic division
1. Increases blood sugar level, adrenaline increases blood sugar levels, counteracting the effect of insulin
 2. Stimulates the production of lactic acid from glycogen in muscle cells and lactic acid can then be used by liver to manufacture glucose.

Gene therapy

- Gene therapy refers to the application of gene technology to correct or replace defective genes
- About two thirds of currently approved gene therapy procedures are targeting cancer, about one quarter aim to treat genetic disorders, such as cystic fibrosis and the remainder are attempting to provide relief for infectious diseases
- Gene therapy involving somatic cells may be therapeutic, but the genetic changes are not inherited

Vectors for gene therapy

- Gene therapy usually requires a vector to introduce the DNA. They include viral and non viral vectors
- The majority of approved clinical gene therapy protocols employ retroviral vectors to deliver the selected gene to the target cells. Other widely used vectors include adenoviral vectors and liposomes. The remaining employ a variety of naked plasmid DNA

Gene delivery systems

- Aerosol
- Hypodermic needle injection
- Ballistic DNA injection
- Extracted cells and cell culture

Using extracted cells

- Gene delivery using extracted cells enable medical researchers to insert a functional gene into a patient's body
- This should make the patient capable of producing the protein encoded in that allele.

Body fluid maintenance

- Human body is made up of approximately 60% water

Type of body fluid	Proportion of total body fluid	Components of the body fluid
Intracellular fluid	2/3 of total body water	Fluid inside the cell, the cytosol
Extracellular fluid	1/3 total body water	Fluid that is outside the cells

Plasma	$\frac{1}{4}$ of extracellular fluid	The fluid part of the blood
intercellular	$\frac{3}{4}$ of extracellular fluid	Lymph, cerebrospinal fluid, synovial fluid in joints, fluids of eyes and ears, fluid in the chest and abdominal cavities and around the heart, fluids of the alimentary canal kidney filtrate

Body fluids

- The different body fluids are not isolated from each other
- There is a continuous exchange of materials between them

Body fluids – plasma

- Is separated from tissue fluid only by thin walls of capillaries
- There is relatively free exchange of materials that occur between the two
- Large, dissolved materials such as proteins, tend to remain within the blood vessels due to their size. Too large to move through the capillary walls.

Body fluid – cytoplasm

- Cytoplasm is separated from the intercellular fluid by the cell membrane
- Cell membrane does not allow large cellular proteins to move through it, therefore the fluid inside the cell has a much higher concentration than either plasma or tissue fluid
- Materials within the fluids of small molecular size can move easily across the cell membrane.

Osmoregulation

- Osmoregulation is the need to regulate a constant solute concentration of body fluids
- Solute, the substance in a solution that is dissolved by the solvent
- Osmotic pressure, the pressure due to osmosis, usually measured as the pressure that would be required to prevent osmosis from occurring.

Isotonic solution

- A solution that has a concentration of solutes equal to that of another solution
- Often used to describe a concentration equal to that of tissue fluid
- E.g. isotonic saline has the same amount of salt concentration as normal tissue fluid

Hypertonic solution

- A solution that has a higher concentration of solutes than another solution
- Often used to describe the concentration of a solution in relation to tissue

Hypotonic solution

- A solution that has a lower concentration of solutes than another solution
- Often used to describe the concentration of a solution in relation to tissue fluid

Need to regulate body fluids

- Composition of intercellular fluid must be constantly regulated to ensure cell survival
- Oxygen and glucose used in cellular respiration must be continually replaced
- Within the cell, chemical wastes produced must be eliminated or the cell may be killed
- The lungs, kidneys, liver, pancreas and pituitary gland help to maintain a constant internal environment in which cells of the body are able to function normally

Excretion

- The continuous exchange of materials between blood and body tissues ensures the internal environment remains constant
- It is the balance between processes that build up materials, anabolic, and processes that break down materials, catabolic that enable this constant internal environment to be maintained
- Both these processes produce by products some useful, others waste
- Most of the waste products are extremely harmful if allowed to accumulate in the body
- All cells produce wastes which must be removed before concentrations reach a harmful level
- Excretion is the removal from the body of waste products of metabolism

Excretory organs

Lungs

- Involved in the excretion of CO₂
- CO₂ and H₂O are by products of cellular respiration
- CO₂ is carried in blood to lungs where it is excreted
- Some H₂O is lost from the lungs as water vapour during exhalation

Sweat glands

- Secretes water containing by products of metabolism such as salts, urea, lactic acid

Alimentary canals

- Passes out bile pigments that have entered the small intestine with the bile
- Pigments are the breakdown products of haemoglobin from red blood cells
- Leave body via faeces

Kidneys

- Principal excretory organ
- Responsible for maintaining a constant concentration of materials in body fluids
- Main waste product to be removed is urea, produced by the liver during breakdown of protein

Regulation of gas concentration

- All cells need a continuous supply of O₂, for respiration
- All cells produce CO₂, as a waste product of respiration
- Respiratory system is responsible for taking in O₂ and releasing CO₂
- The amount of O₂ taken in and the amount of CO₂ excreted

Control of breathing

- The muscles that control breathing are:
 1. Intercostal muscles
 2. Diaphragm
- The stimulation of these muscles are caused by:
 1. Intercostal nerve, stimulates the intercostal muscle's to contract
 2. Phrenic nerve, stimulates the diaphragm to contract
- Intercostal nerves and phrenic nerves are spinal nerves which have their origins in the spinal cord at the level of the neck and thorax
- Nerve impulses that travel to the diaphragm and intercostal muscles are controlled by respiratory centre in the medulla oblongata
- There are two regions within the respiratory centre

1. Controls inspiration
 2. Control expiration
- To coordinate breathing, messages pass back and forth between neurons in these two regions
 - Both O₂ and CO₂ are carried in the blood and their concentrations affect breathing rate
 - Concentration of CO₂ in blood also affects the concentration of hydrogen ions
 - When CO₂ dissolved in water it forms carbonic acid which breaks down to hydrogen ions and bicarbonate ions
 - Oxygen, carbon dioxide and hydrogen ions all have some effect on the regulation of breathing.

Oxygen concentration

- As O₂ is consumed by the cells, the concentration in the blood decreases
- If the concentration of O₂ falls below normal and other factors are held constant, an increase in breathing rate occurs
- Under normal conditions, O₂ plays little part in the regulation of breathing
- Concentration of O₂ would have to fall to very low levels for it to have a major stimulatory effect on the rate of breathing.

Carbon dioxide concentration

- Concentration of CO₂ in the plasma is a major factor in regulation of breathing rate
- A small increase in CO₂ is enough to cause a marked increase in breathing rate
- The concentration of CO₂ in blood plasma is associated with the concentration of H⁺
- Increase in CO₂ is associated with an increase in H⁺
- An increase in CO₂ and H⁺ in blood plasma stimulates the central and peripheral chemoreceptors
- This transmits nerve impulses to the respiratory centre
- Results in an increase in breathing rate

External defence mechanism

Pathogens

- Bacteria, viruses, fungi and animal parasites are pathogens that can affect the human body
- Viruses and bacteria are the most common forms

Bacteria

- Are essential to life on earth as
 1. They play a role in decomposition of organic material and the cycling of elements
 2. Used in industrial processes such as making yoghurt
- Many are non-pathogenic, meaning they are harmless to humans
- Single celled
- Come in different shapes

Cell membrane, surrounds the cytoplasm of the cell, responsible for the transport of solutes in and out of the cell

Capsule, helps in attachment of the bacterium to other bacteria

Cytoplasm, gel like fluid enclosed within the cell membrane, contains water enzymes

Ribosome, cell structure responsible for protein synthesis

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DNA, a circular DNA molecule which contains the genetic information

Pilli, small Cilia like locomotory organelles

Flagellum, long tail like organelle used for locomotion

Viruses

- An infective agent that typically consists of a nucleic acid molecule
- Is too small to be seen by light microscopy
- Is able to multiply only within the living cells of a host

Fungi

- Microorganisms that can be seen with the naked eye
- Individual cells contain a nucleus, cell wall and other organelles such as mitochondria
- Play a vital role in decomposing dead material and recycling nutrients to make them available for the growth of other plants
- Pathogenic fungi tend to be ones that cause infections to the surface of the skin
- Diseases include athlete's foot, oral and vaginal thrush, ringworm

Animal parasites

- Vary in structure
- Require a host to survive, gains food and shelter from host
- Ectoparasites, fleas and lice
- Endoparasites, worms and protozoa

Transmission of pathogens

- Pathogens enter the body via one of six ways,
 1. Transmission by contact
 - Spread of pathogen is by physical contact
 - May be direct or indirect
 2. Transfer of body fluids
 - From one person to another
 - When blood/body fluids from infected person comes into contact with mucous membrane or bloodstream of unaffected person.
 3. Infection by droplets
 - When tiny droplets of moisture harbouring pathogenic organisms are emitted when breathing, talking, sneezing, coughing
 - Droplets may be breathed in by others
 4. Ingestion
 - Food and drink contaminated with pathogens
 5. Airborne transmission
 - When moisture in exhaled droplets evaporates, many bacteria are killed, but viruses and some bacteria remain viable, causing infection
 6. Transmission by vectors
 - Transfer of pathogens by other animals
 - May be spread directly or indirectly

Defences against disease

- Body is equipped with a number of defences that protect it against the invasion of pathogenic micro organisms
 1. Non specific defences
 - First line of defence
 - Work against all pathogens

2. Specific defences

- Directed to a particular pathogen

Non specific defences, external defences

1. Skin
2. Mucous membrane
3. Hairs
4. Acids
5. Flushing action

Protective reflexes

- Protective reflexes in the body
 1. Sneezing
- Stimulated by irritation of walls of nasal cavity
- Caused by noxious fumes or dust particles which are likely to carry microorganisms
 2. Coughing
- Stimulated by irritation in lower respiratory tract
- Air is forced from lungs to try to remove irritant
- 3. Vomiting
- Physiological stimuli
- Excessive stretching of the stomach and bacterial toxins can all induce vomiting
- Contraction of the muscles of abdomen and diaphragm expel content
- 4. Diarrhoea
- Caused by the irritation of small and large intestines by bacteria, viruses
- Causes the contraction of muscles of walls of intestines to remove irritant quickly

Non-specific defences, internal defences

- If pathogens get passed the external defences, there are internal non-specific defences that can help deal with pathogens
 1. Phagocytes
- Cells that engulf and digest micro organisms and cell debris
- Leucocytes, white blood cells, several types, all play a part in phagocytosis
- Macrophages, large phagocytic cells that develop from some leucocytes, some wander, some are fixed
- 2. Inflammatory response
- Inflammation, response to any damage to the tissues
- Reduce the spread of any pathogens to destroy them and prevent entry of more pathogens
- Remove damaged tissue and cell debris
- Begin the repair of damaged tissue
- Redness, swelling, heat and pain

Inflammatory response

- Once a tissue is damaged, a series of steps in the inflammatory response take place
 1. Mast cells release histamine and heparin into tissue fluid
- Mast cells stimulate and coordinate inflammation by releasing chemicals
- Histamine increases blood flow through the area, causing the walls of the blood capillaries to become more permeable so fluid is filtered from blood
- Increased blood flow causes heat and redness
- Escape of fluid from blood causes swelling

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- Heparin prevents clotting so the release of heparin from the mast cells prevent clotting in immediate area of injury
- Clot of fluid around damaged area forms which slows spread of pathogen to healthy tissues
- Chemicals released by mast cells attract phagocytes
- Macrophages and leucocytes actively consume micro-organisms and debris by phagocytosis
- Dead phagocytes and tissue fluid form yellow liquid called pus

Fever

- Fever is an elevation of body temperature
- Usually experienced during an infection
- Increase in body temperature is due to the hypothalamus resetting the body's thermostat to a higher level
- Pyrogens (help reset thermostat) are released by white blood cells during the inflammatory response to a foreign intruder
- Act directly on the hypothalamus
- When a fever 'breaks' this point is referred to as crisis point
- Person feels hot and appears flushed
- Blood vessels in skin vasodilate
- Profuse sweating occurs

Benefits

- High body temperature is believed to inhibit growth of bacteria and viruses
- Heat speeds rate of chemical reactions which may in turn help body cells repair themselves during disease

Disadvantages of fever

- If body temperature goes too high death will result if body temperature reaches 44.4-45 degrees

The immune system

Lymphatic system

- A transport system that consists of:
- A network of lymph capillaries which join to form larger lymph vessels
- Lymph nodes, which are located along the length of some lymph vessels
- Lymphoid tissue found in organs including the spleen, tonsils, thymus

Main functions:

1. To collect the fluid that escapes from the blood capillaries and return it to the circulatory system
2. Transport lipids and lipid-soluble nutrients absorbed in the small intestine
3. Internal defence against pathogenic organisms

Lymphoid organs

- Contain tissue but are not part of the lymphatic system
- These include the spleen, tonsils, thymus gland and bone marrow
- They contain macrophages that engulf and destroy foreign particles, and lymphocytes
- Lymphoid organs and lymph nodes are part of the immune system

Lymph nodes

- Lymph nodes, also called lymph glands, occur at intervals along lymphatic vessels. They are numerous at the neck, armpit, groin and alimentary canal.
- They are surrounded by a capsule of connective tissue which extends into the node

- They are a store of lymphocytes
- Lymph enters the node at one side, filters through the spaces then leaves the opposite side

Lymph nodes protect the body against infection by:

- Trapping foreign particles and bacteria in their fibrous mesh. Macrophages then engulf and destroy them
- Storing lymphocytes, which are circulated by lymph vessels. Their role is in specific defence
- Site of antibody production

Specific defence

- Defences directed against one particular pathogen
- These specific defences are part of our immune system

Our immune system is composed of:

- Network of lymphatic vessels carrying lymph fluid, lymph nodes and other lymphoid organs such as the tonsils, spleen and thymus
- Specialised white blood cells called lymphocytes
- There are two types of lymphocytes, B cells and T cells

Antigens

- Substances capable of stimulating a specific immune response
- They do so by activating lymphocytes
- Antigens can be protein, carbohydrate, lipid or nucleic molecules found on cell surfaces

Foreign antigens	Self-antigens
Originated from outside of the body. <ul style="list-style-type: none">- Whole pathogen organism such as virus' and bacteria or parts of the pathogen	Originate within the body and are normally recognised by the body as self.

- Foreign antigens are recognised by lymphocytes as being non self-antigens
- On the surface of antigens are regions that fit and bind to receptor molecules on the surface of the lymphocytes
- The binding of the lymphocytes' receptors to the antigens' surface molecules stimulates the lymphocytes to multiply and to initiate an immune response against the antigen

Specific immune response

- The specific immune response is made up of 2 different systems
 1. Cell mediated
 2. Antibody mediated
- There are two types of lymphocytes involved that are both produced in the bone marrow but mature in different location
- B cells mature in the bone marrow and are involved in the antibody mediated response
- T cells mature in the thymus and are involved in the cell mediated response
- After maturation both cells will migrate to lymphoid tissue or circulate in the blood

Antibodies

- specialised proteins belonging to a group called immunoglobins
- 5 classes of these antibodies which vary in structure
- Antigens have specific active sites complementary to specific antibodies

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- This is how the antibodies bind to antigens.

Antibody mediated (humoral) response

- Provides resistance against viruses, bacteria and bacterial toxins before they enter the body's cells
- Involves B cells that produce antibodies that inactivate antigens
- For a B cell to initiate an antibody mediated response it must be activated by an antigen or helper T cell

Antibody mediated (how it works)

1. When activated by a helper T cell or antigen the B cell enlarges
2. It then divides into a group of cells forming a clone
3. Some of these cells develop into memory B cells
4. The rest develop into plasma cells
5. The plasma cells secrete antibodies into the blood, lymph or tissue fluid
6. The antibodies then attach to the active site on a specific antigen to form an antigen-antibody complex

Primary response

- Takes time for B cells to multiply and develop into plasma cells
- Response is fairly slow, taking several days to build up antibodies
- Response leaves memory cells to that antigen for future exposures
- Individual tends to get sick during this time as no immunity

Secondary response

- Response is much faster due to activity of memory cells
- Plasma cells form quickly, with antibody levels rising rapidly
- Usually so quick that no illness results to individual as they are immune

Cell mediated response

- Provides resistance to intracellular viruses and bacteria
- Provides resistance to fungi and parasites
- Involved in the rejection of transplants of foreign tissues and also appears to help fight cancer cells
- Involves T cells that attack foreign organisms directly
- For a t cell to initiate a cell mediated response it must be present with an antigen. This is achieved by antigen presenting cells

cell mediated response (how it works)

1. Macrophages phagocytose the pathogen, then present the antigen on their cell surface
2. They then travel to the nearest lymph node and present the antigen to helper T cells
3. They specifically programmed T cell for that antigen becomes activated or sensitised
4. Sensitised T cells enlarge and divide, each giving rise to a clone of identical T cells
5. Most clone cells develop into other T cell types, migrate to infection site and fight infection
6. A small number develop into memory T cells and remain in lymphoid tissue for future infection by same antigen

Helper T cells

- Secrete substances that result in lymphocytes becoming sensitised and intensifying the response

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- Activated B cells to release antibodies
- Attract more macrophages to site of infection
- Release substances that intensifies phagocytic action of macrophages

Killer T cells

- Migrate to site of infection to destroy cells infected by pathogens
- They attach to the cells and secrete a substance to destroy the antigen

Suppressor T cells

- Act when immune activity is excessive, or infection has been dealt with successfully
- They release substances to inhibit the secretion of substances produced by the killer T cells and the development of the B cells and antibodies
- They are the 'off' switch of the immune system

Memory T cells

- Programmed to recognise the invading antigen and will recognise the antigen should it re-enter the body, bringing about a much faster and more intense response than during the first invasion
- They result in an individual only getting sick with different diseases once as they eliminate the pathogen before you exhibit any symptoms of the disease on subsequent exposures

Types of immunity

- We are said to have acquired immunity to a disease when we have made a supply of antibodies for that antigen and have a bank of memory cells
- Memory cells can be activated when we are re-exposed to the antigen, making our symptoms far less and recovery time much quicker

Immunity can be:

Natural immunity - due to exposure to an antigen without human intervention

Artificial immunity - due to being given an antigen to trigger an immune response, or by receiving antibodies for an antigen

Active immunity – where we manufacture our own antibodies due to presence of memory cells

Passive immunity – where we are given antibodies made by someone else

Artificial active immunity occurs when we are given a measured dose of an antigen via a vaccine and we make our own antibodies. The antigen could be dead or weakened

Natural active immunity occurs when we suffer the disease by the antigen entering the body naturally. We can make our own antibodies as a result.

Artificial passive immunity occurs when we are given a dose of antibodies into the bloodstream through an injection

Natural passive immunity occurs when antibodies cross the placenta or through breast milk to a baby

- When we are exposed to an antigen, we make antibodies. Each successive time we are exposed to the antigen we have a larger and quicker response.

Vaccination

- Vaccinations prime the immune system so it will respond more rapidly

- This priming is called immunisation
- Vaccines provide active artificial immunity
- It introduces the antigen into the body to trigger an immune response

An effective vaccine must:

- Cause large numbers of memory cells to form from immune response
- Not make the individual sick

Types of vaccines

1. Attenuated vaccines: they use a weakened form of the living pathogen. Its antigen is intact but its ability to cause disease has been reduced
 2. Dead form: has an intact surface antigen such as whooping cough. Immunity in this way is not prolonged
 3. An inactivated form of a toxin, called a toxoid for example diphtheria and tetanus
 4. Sub-unit vaccine: a fragment of the pathogen containing the antigen used
- Recent trends in vaccine development involve manipulating the pathogens DNA
 - E.g. recombinant DNA achieved by either removing genes which code for the antigen of a pathogen into harmless bacteria or virus

Developing vaccination programmes

- A successful programme will provide long term and wide-spread protection against disease
- The following need to be considered when developing a successful programme
- Ideally herd immunity is developed: this requires a large percentage of the population to be immunised so that there are fewer hosts to transmit the disease/pathogen. This then protects those who are not vaccinated
- Its important to vaccinate children at an early age as they are more vulnerable to infection due to an immature immune system

Antiviral drugs

Viral replication

- A virus cannot replicate on its own
- It must attach to and enter a host cell
- It then uses the host cell's energy to synthesize protein, DNA and RNA

Viruses are difficult to kill because they live inside the cells, any drug that kills a virus may also kill cells

- Viruses have no cell wall and made up of nucleic acid components
- Viruses containing envelope, antigenic nature
- Viruses are obligate intracellular parasite
- They do not have a metabolic machinery of their own, uses host enzymes
- Certain viruses multiply in the cytoplasm but others do in the nucleus
- Most multiplication take place before diagnosis is made

Characteristics of antiviral drugs

- Able to enter the cells infected with virus
- Interfere with viral nucleic acid synthesis
- Some drugs interfere with ability of virus to bind to cells
- Some drugs stimulate the body's immune system
- Best responses to antiviral drugs are in patients with competent immune systems
- A healthy immune system works synergistically with the drug to eliminate or suppress viral activity

Antiviral drugs

- Used to treat infection caused by viruses other than HIV

Antiretroviral drugs

- Used to treat infection caused by HIV, the virus that causes AIDS

Mutations

- A new variation, resembling neither parent, that occurs quite suddenly and purely by chance
- A permanent structural alteration in the DNA
- They occur through changes to genes or chromosomes
- In most cases, changes to the DNA have little effect or cause no harm
- Occasionally a mutation can improve an organism's chance of surviving
- Mutant, an organism with a characteristic resulting from a mutation

mutations can be classified as either:

1. Gene mutations, changes in a single gene
2. Chromosomal mutations, all or part of a chromosome is affected

Mutagens/mutagenic agents

- Any agent that increases the rate at which mutations occur
- Examples include X-rays, mustard gas, UV radiation, cosmic rays, radiation from radioactive waste

Somatic mutations

- Mutations that occur in body/somatic cells
- Only the individual with the somatic mutation is affected
- Involved in many cancerous growths resulting from a mutagenic agent

Germline mutations

- Mutations that occur in the reproductive cells/gametes
- Individuals is not usually affected
- May be passed on to the next generation and subsequent generations

Effects of mutations

Gene mutations

- A change in just one base is known as a point mutation

Point mutations can form

1. Substitution of a base for another base
2. Insertion of a base
3. Deletion of a base

Effects of insertion/deletion

- Inserting or deleting one or more nucleotides changes the reading frame like changing a sentence
- Proteins built incorrectly, huge impact

Effects of point mutations

- No effect on protein, abnormal protein, may be non-functional or missing protein
- Proteins include enzymes, antibodies, structural proteins, membrane transport channels
- Just one missing or abnormal protein can have an enormous effect on the entire body
- The same symptoms may be caused by different mutations
- Understanding the molecular cause of a disease may assist in diagnosis and treatment

Lethal recessives

- Some recessive mutations are lethal if they are not masked by a dominant normal allele

- These lethal recessives cause the death of the embryo or foetus or the early death of the child

Changes to allele frequencies in gene pools

1. Mutation

- Mutations introduce new and different alleles into the gene pool
- If new allele helps the individual to survive, allele composition of the gene pool may change

2. Natural selection

- Process by which a species becomes better adapted to its environment
- Those individuals with favourable characteristics have a survival advantage and so pass those characteristics on to subsequent generations
- Natural selection is not a random process
- Major cause of changes in allele frequency

3. Random genetic drift

- Random, non-directional variation in allele frequencies
- Occurs in small populations

Dunker population

- Dunkers live in Pennsylvania but originally came from Germany
- Their religion does not allow them to marry outside their group and thus they constitute an isolated breeding population within the total population of the US.
- For most of the traits studied, dunkers varied in allele frequency from the present day Hesse population and also from the surrounding American population

Founder effect

- Type of genetic drift that occurs when a small group moves away from its homeland to new location and establishes a community
- Migrant group is not representative of the original homeland population
- Therefore new population formed not typical of original homeland population
- Small sample size can cause marked deviations in allele frequencies

Barriers to gene flow

- Barriers to gene flow affect the allele frequency of a population
- Populations are kept apart by barriers that inhibit the amount of interbreeding between them
- As no two environments are exactly the same, environmental pressures on one population will be different from the pressures on the other.
- This results in slightly different characteristics being favoured in one population compared to the other
- Over time, allele frequencies of each gene pool will change depending on which characteristics are favoured for survival
- These changes in each population over many generations result in populations becoming less alike as they develop characteristics better suited in the development of separate gene pools

Natural selection

Darwin's theory of natural selection

Evolution, gradual change in the characteristics of a species

Darwin's theory of natural selection was based on three observations:

1. Variation
- All members of a species vary

- Variations are passed on from one generation to the next
 2. Birth rate
- All living organisms reproduce at a far greater rate than that at which the available food supply and their resources increase
 3. Nature's balance
- Although the birth rate of organisms was very high, each species tended to maintain its numbers at a relatively constant level

From these observations, Darwin concluded:

1. Excessive birth rate and limited resources meant that there must be a struggle for existence
2. Range of variations in any species meant that those with characteristics best suited to their environment were the ones that were more likely to survive -> survival of the fittest

Survival of the fittest is possible because:

1. There is a variation within any species
2. Members of a species differ from one another in their physical characteristics, body functioning and behaviour
3. Many of these variations are inherited but Darwin was unable to explain the origin of the variations he observed in a species, much of this variation is due to the effects of meiosis and fertilisation

Principles of evolution through natural selection summarised

1. There is variation of characteristics within a species
2. More offspring of a species are produced than can possibly survive to maturity
3. Due to excessive birth rate and limited resources, there is a struggle for existence, competition for survival
4. Individuals with characteristics best suited to the environment have more chance of surviving and reproducing, survival of the fittest
5. Favourable characteristics are passed onto the next generation
6. In the gene pool, the proportion of alleles that produce favourable characteristics gradually increases

Examples of natural selection in humans

1. Body stature
 - Body stature can be correlated with resistance to cold and heat
 - Initially human gene pool would have contained alleles for whole range of statures from short bodied, long limbed physique of present-day African's, to the long bodies, short limbed stature of the Inuit today.
2. Sickle cell anaemia
 - Anopheles mosquito transmits the malaria parasite
 - Requires quiet, stagnant pools of water for breeding sites, which is more often found in open areas
 - Not normally found in tropical forests for agriculture, the environment changed which created a breeding area for the mosquitoes
 - The increased food supply from agricultural production allowed human population to increase, providing more bodies for mosquitoes to feed on
3. Malaria and sickle cell
 - **Homozygous dominant** -> normal blood cells individuals can reproduce and pass their alleles onto subsequent generations

- **Homozygous recessive** -> suffer from sickle cell anaemia fatal, individuals usually die before reproducing
- Sickle cell allele tends to be higher in regions where risk of malaria is high
- Individuals with one sickle cell allele are more resistant to malaria than those with normal haemoglobin in their red blood cells.
- Sickle cell example shows how natural selection occurs in human populations
- A favourable mutation established a new allele in the population
- Having one of these alleles gave individuals living in malaria-prone areas a survival advantage
- Presence of malaria acted as a selective agent for the sickle cell allele
- **Heterozygous** -> sickle cell trait individuals can reproduce and pass their alleles onto subsequent generations

Speciation

- Process of producing two new species from a common ancestor
 1. Variation in a population
 2. Isolated population
 3. Reproduce more than will survive
 4. Struggle for existence
 5. Reproduction by survivors
 6. Next generation has more survivor genes
 7. Allele frequency becomes significantly different to adjoining population
 8. Interbreeding no longer able to occur between overlapping/adjoining populations
 9. Speciation has occurred

DNA profiling and DNA fingerprinting

DNA sequencing -> PCR -> Sequencing reaction -> Gel electrophoresis

DNA profiling -> PCR -> electrophoresis -> DNA profiling/fingerprinting

- DNA sequencing attempts to determine the nucleotide sequence in DNA sample
- DNA profiling attempts to identify who a DNA sample belongs to and does not need to determine the whole nucleotide sequence
- Within the same species, most individuals DNA is identical
- Remaining 0.1% varies between individuals
- DNA fingerprinting/profiling has many purposes in identifying variations such as forensic investigation and paternity testing

Two methods to produce a DNA fingerprint/profile include the use of:

1. Southern blotting technique
2. Short tandem repeats

Southern blotting

- Technique is used to simultaneously detect lots of minisatellites in non coding regions of DNA
- Radioactive DNA probes are used to identify these variations in a certain number of genes at a time

Process:

1. DNA is extracted and isolated from a sample
2. Restriction enzymes cut DNA into smaller fragments of different lengths
3. Gel electrophoresis is used to separate DNA fragments by size
4. Nitrocellulose/nylon membrane is placed on top of agarose gel
5. Radioactively labelled DNA probes used to identify and tag/attach to particular genes

6. X-ray film is placed over nylon membrane to visually expose genes tagged by radioactive probes

DNA profiling using STRs

- Modern day profiling techniques utilize short tandem repeats
- STRs are polymorphic between individuals
- Each individual inherits a unique combination of polymorphisms from both of their biological parents

Short tandem repeats

- STRs are short sequences of nucleotides that are repeated consecutively many times
- Found in non coding regions of DNA
- Usually 2-10 base pairs long
- Number of repeats/length of STRs differ between individuals, useful for identification
- There are two alleles for each gene, if both alleles same length then homozygous, if both alleles are different then heterozygous

DNA profiling using STRs process

1. DNA is extracted and isolated from a sample
2. PCR is used to amplify extracted DNA, fluorescent tags are added to DNA primers during PCR
3. Capillary or column electrophoresis used to separate fragments
4. Results are generated onto an electropherogram

Evidence for evolution

- Evolutionary theory is now supported by a wealth of observations and experiments
- Although biologists do not always agree on the mechanisms by which populations evolve, the fact that evolution has taken place is well documented

Evidence for evolution comes from many sources

1. Palaeontology, the identification, interpretation and dating of fossils gives us some of the most direct evidence of evolution
2. Embryology and evolutionary developmental biology, the study of embryonic development in different organisms and its genetic control
3. Comparative anatomy, the study of the morphology of different species
4. Biogeography, the study of geographic distributions can indicate where species may have originally arisen
5. Artificial selection, selective breeding of plants and animals has shown that the phenotypic characteristics of species can change over generations as particular traits are selected in offspring
6. Biochemistry, similarities and differences in the biomechanical make-up of organisms can closely parallel similarities and differences in appearance
7. Molecular genetics, sequencing of DNA and proteins indicates the degree of relatedness between organisms

Comparative DNA

- Chemical compound making up genes that determine the proteins a cell makes
- Complete set of DNA in each cell referred to as the genome
- Has been found that all living organisms use the same DNA code
- However, the code in DNA sequence varies between different species
- Studying the relatedness of DNA sequence helps determine how closely related different species are

- Recent advanced techniques have enabled the sequence of DNA in different species to be determined
- Species though to be closely related on the basis of other evidence were found to have a greater percentage of DNA sequences in common

DNA hybridization

- One way to reconstruct the evolutionary history of a species is using DNA hybridization
- In this technique, the DNA from different species is 'unzipped' and recombined to form hybrid DNA
- Heat can be used to separate the hybridized strands. The amount of heat required to do this is a measure of how similar the two DNA strands are

DNA hybridization method

- DNA is isolated from blood samples from each species
- The greater the similarity in the DNA base sequence, the stronger the attraction between the two strands and the harder it is to separate them again
- A crude measure of DNA relatedness can be achieved by measuring how hard it is to separate the hybrid DNA
- This is done by finding the temperature at which it unzips into single strands again

Junk DNA

- Non-coding sequences also found in DNA
- Sometimes referred to as junk DNA
- Comparisons between junk DNA help determine relatedness between species on the basis of the common ancestor hypothesis
- More closely related species have more junk DNA sequences in common
- E.g. endogenous retrovirus
- ERVs has genetic information stored as RNA and upon entering an organism copies its genetic information into the organism's DNA
- ERVs only become endogenous if copied into the gametes
- Offspring will then inherit the ERVs in the same location on the same chromosome in every cell
- Comparison of the location of ERVs in different species help determine their relatedness

Comparative mitochondrial DNA

- Mitochondrial DNA form of DNA in mitochondria organelles
- Found as small circular molecules and made up of 37 genes
- 24 genes code for the synthesis of transfer RNA
- 13 genes code for enzymes needed during cellular respiration
- Easier to extract DNA from mitochondria than the nucleus, due to large number of mitochondria present
- Unlike nuclear DNA which is inherited from both parents, mtDNA is only inherited from the mother
- mtDNA has higher mutation rate than nuclear DNA
- this means that human mtDNA slowly diverging from common ancestors mtDNA
- amount of mutations approximately proportional to amount of time that has passed from common ancestor
- comparing similarities in mtDNA between individuals indicates how closely related they are

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- if mtDNA more closely related between individuals indicates that a common maternal ancestor lived more recently
- if mtDNA less closely related, indicates common maternal ancestor is further in the past
- comparing mtDNA very valuable for closely related individuals
- e.g. used to trace migration of ancient peoples

comparative amino acid sequencing

- amino acids are sequenced together to form large range of proteins in an organism
- the ordering of amino acids produces a particular protein living things contain thousands of proteins produced from just 20 amino acids
- certain proteins are found in all living organisms from bacteria to animals known as ubiquitous proteins

comparative amino acid sequencing

- sequences of amino acids in certain proteins have revealed great similarities and specific differences between species
- closely related species have proteins with similar amino acid sequences
- amino acid sequences are determined by inherited genes and differences are due to mutations
- the degree of similarity of these proteins is determined by the number of mutations that have occurred
- distantly related species have had more time for differences to accumulate

example cytochrome C

- this ubiquitous protein has important role in production of cellular energy
- human cytochrome C, 104 amino acids
- 37 of these amino acids are in the same location regardless of species tested which suggest a common ancestor
- Chimpanzee and gorilla cytochrome C, 104 amino acids identical to humans, suggesting closely related species have diverged from a more recent common ancestor

Fossils

A fossil is an impression, cast, original material or track of any animal or plant that is preserved in rock after the original organic material is transformed or removed

Prime conditions for fossilization:

- Hard body parts such as skeletal bones or exoskeletons
- Rapid burial and/or lack of oxygen

Types of fossils:

Body fossils – actual parts of an organism, unaltered or altered bones, shells, leaf imprints

Trace fossils – evidence of life that is not a body fossil. Tracks, burrows.

Modes of fossils

Unaltered

Original material – original, unaltered material from the living organism unaltered bone or shell

Encrustations or entombments – material is trapped inside coating such as amber

Mummification – quickly dried material

Refrigeration – material is trapped inside ice and tissue is preserved

Altered

Permineralization – pores in tissue are filled by minerals

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Replacement – replacement of tissue with minerals

Carbonization – tissue material is decomposed or reduced to a film of carbon

Trace fossils

Mold – reproduction of the inside or outside surface of a living thing

Cast – duplicate of the original organism, usually formed by replacement of inside of living thing

Burrows or borings – spaces dug out by living things and preserved as is or filled in

Gastroliths – smooth stones from abdominal cavity of dinosaurs

Coprolites – fossilized excrement, usually preserved by replacement

Tracks – impressions of passage of living things

Fossil dating

Scientists use 2 methods to determine the age of fossils:

1. Relative dating
2. Absolute dating

Relative dating

- Shows the order in which fossils occurred
- Shows what organisms lived together
- Scientists look at where fossils are located within the rock column
- Use the law of superposition

Law of superposition

- Sedimentary layers are deposited in a time sequence
- Oldest rock on the bottom, youngest at the top

Absolute dating

- Determines the specific age of a fossil
- Looks at chemical properties

2 types:

- Carbon 14
- Potassium argon

Carbon 14 dating

- Also known as radiocarbon dating
- Used to date organic substances
- Scientists measure the radiocarbon in the fossil to determine its age
- Can only date specimens up to about 60000-70000 years old
- Half-life 5730 years old
- Cannot date rocks
- Only organic

Potassium argon dating

- Scientists determine the age of the rock surrounding the fossil to determine the fossil's age
- Used only for inorganic substances
- Scientists measure the amount of argon in the rock to determine its age
- Dates rock 60,000 years old and older but can only get a figure between 100k and 200k years old
- Half life 1.3 billion years

Relative dating

Three techniques include

1. Stratigraphy (law of superposition, correlation of rock strata)
2. Index fossils
3. Fluorine dating

Stratigraphy

- Stratigraphy is the study of layers usually in sedimentary rock samples

Two methods of stratigraphy used for fossil dating

- Law of superposition
- Correlation of rock strata

Law of superposition

- Bottom layers in sedimentary rock formations are older
- Top layers are younger
- Fossils found in top layers of the rocks will be younger than those found in layers lower down

Correlation of rock strata

- The matching and comparing of rock layers from different areas
- Done by examining rocks themselves
- Can be done by directly studying the fossils in the rocks
- Fossils that are widely distributed geographically and has a rapid evolutionary trend
- Makes correlation of rock strata more precise

Fluorine dating

- A measure of the amount of fluorine absorbed in bones to determine their relative dating
- Fluoride ions present in the water located in soil
- These ions replace some of the ions in bone bones located in the same deposit or strata will contain similar amounts of fluoride ions
- Specimen containing more fluoride ions will have been buried in soil for longer indicating it is older
- Cannot be used to absolutely date fossils as fluoride ion concentrations differ between location

Characteristics of primates

Evolutionary trends within primates

- Limbs of primates, unspecialized in structure -> allows great diversity in their use

Digits are:

1. Pentadactyl – contain 5 digits
 2. Highly mobile – can be related to arboreal way of life of primate ancestors
 3. Opposable – first digit can touch each of the other digits, degree of opposability varies from species to species and depends on relative length of first digit compared to other 4 digits
 4. Contain nails – instead of claws on fingers and toes, claws limit grasping, preventing opposable surfaces from coming together
 5. Friction ridges – ends of digits have sense receptors so that the digits can grip and manipulate objects
 6. Precision grip – hallmarks of being human, amount of contact between the index finger and thumb, enables humans to handle small or delicate objects effectively, requires a truly opposable thumb
- Increasing ability to move digits independently of one another, most highly developed digits in this respect are the thumb and big toe

- Big toe, lost opposability in humans
- Thumb, became more opposable in humans
- Nails evolved from claws
- Human hand, short and broad, short, straight fingers, long strong thumb, gives thumb great degree of freedom

Evolutionary trends – dentition

- Evolutionary changes have taken place in the number and structure of teeth of primates
- Primitive mammals have a dental formula of 3:1:4:3
- Lower front incisors are slanted forward with the crowns narrow and closely spaced
- Used in the grooming of fur and only rarely used for feeding
- Canines are large and sharply pointed in the OWM and apes, projecting beyond the level of the other teeth
- Modification have been made to adjacent teeth to allow the mouth to close
- Most primates with large canines have a diastema, gap between the upper 2nd incisor and upper canines to accommodate lower large canine
- Crown of the first premolar is slanted back and has a sharp edge
- Larger canines are important in predator defence and social displays

Evolutionary trends within primates – Vision

- An arboreal lifestyle requires an increasing emphasis on vision and decreasing reliance on the sense of smell
- Flattening of the face and forward facing eyes are an important evolutionary trend
- Allows for stereoscopic vision
- Primates have developed eye sockets that face forward, enables field of vision of each eye to overlap so that distances can be judged accurately
- Forward facing eyes create a narrower field of view than if the eyes were facing sideways
- This has been compensated by primates evolving a highly mobile head and neck
- Most primates have rods and cones in the retina of their eyes
- Rods, important for vision in dim light
- Cones, concerned with fine visual discrimination and colour vision
- Bone eye socket was developed to protect forward facing eyes
- Region of the brain associated with interpretation of visual information has increased in size, the area concerned with olfaction has decreased

Evolutionary trends within primates – relative size of the cerebral cortex

- Cerebrum in particular, the cerebral cortex, has increased in size
 - Brains of apes and humans have strong pattern of convolutions, enable the surface of the brain, hence the cerebral cortex to be greatly increased
 - Increase in brain size, enables primates to move about, locate food and develop special skills
1. Tool making
 - Most highly developed in humans, but is also seen in chimpanzees
 - Involves a predetermined image of what the completed tool should look like
 2. Greater variety of behavioural responses to meet a wide array of environmental problems
 - Daily life involved numerous interactions with relatives, allies and adversaries

- Threats, sometimes followed by fighting, to maintain the hierarchy of dominance that pervades many primate troops

Evolutionary trends with primates – gestation and parental care

- Most species are not restricted to limited reproductive seasons and show rhythmical sexual cycles
- Most primates have only one offspring at a time
- There is a long period of growth and maturation during which there is a marked degree of parental care
- Apes and humans have a more efficient placenta that allows a closer contact between blood supplies of mother and developing offspring
- Time between conception and birth
- Along with the trend in the lengthening of the period of growth and development is an associated delay in maturation, sexual maturity is attained much later in apes and humans
- Period of learning is greatly extended, important facet of primates life as it enables ideas and techniques to be passed on from one generation to the next.

Evolutionary trends within hominids

Adaptions of an erect posture

1. Position of an erect posture

- Foramen magnum, hole at the base of the skull where spinal cord joins brain
- In humans its located centrally beneath the skull which allows skull to balance on top of vertebral column
- In quadrupeds, foramen magnum is towards the back of the skull, require large neck muscles to hold head in position

2. Curvature of spinal cord

- Double curve
- S shaped

3. Jaw

- Apes have a protruding jaw, humans facial profile is much flatter
- Size of jaw has greatly reduced, allows skull to balance on top of spine so weight in front of foramen magnum is equal to weight behind
- Balance is achieved with minimal muscular effort

4. Pelvis

- Broader and bowl shaped in humans
- Narrower in gorillas
- Carrying angle created by pelvis results in hip joint being directly under the trunk and head
- Allows the weight of the body to be transferred from pelvis to legs
- Head of femur is large and fits into the acetabulum
- Neck of femur is short and angled superiorly and medially from the shaft, allowing femur to articulate with side of pelvis
- This arrangement forms an angle to the vertical, carrying angle
- Carrying angle ensures the weight distribution remains close to the central axis of the body whilst walking
- Also allows for greater stability when walking. Enables the body to be rotated about the lower leg and foot

5. Knee

- Weight of the body is transmitted down the outside of the femur to the knee
- Knee joint is a two part hinge joint with one hinge on either side of the ligaments in the middle joint
- Weight of the body transmitted to the outer hinge, thus it is large and stronger than the inner one
- Centre of gravity of the body tends to fall through a line just in front of the knee, resulting in a force that tries to bend knee backward but is resisted by the ligaments that make up the knee joint
- This natural resistance produces a joint that requires no energy to support the body in a standing position

6. **Foot**

- From the knee joint, most of the weight of the body is transmitted through the tibia to the ankle
- Tibia is stronger and larger of the two lower leg bones
- At ankle bodyweight is transmitted through the talus that articulates with the tibia and fibula then to metatarsals and phalanges via the arches of the foot
- Bones of foot between the toes and metatarsals are shaped to form two arches, longitudinal, running from front to back and transverse, running side to side
- Transverse arch is unique to humans and together the two arches enable humans to perfect bipedal locomotion

7. **Centre of gravity**

- Humans legs are longer than their arms
- Relatively long legs
- Increase the length of the stride when walking
- Lower the centre of gravity of the body, point at which all the weight of the body appears to be concentrated
- Centre of gravity for humans is at the level of the pelvis, in apes it is at chest level
- Lower centre of gravity in humans contribute to stability when moving bipedally or when standing erect

Stance and locomotion

Striding gait

- Walking in such a way that the hip and knee are fully extended

In the striding gait

1. Foot hits ground
 2. Weight is transmitted from heel along the outside of the foot as far as the ball
 3. Crosses the ball of the foot, via the transverse arch
 4. Finally borne by the big toe
- When walking the trunk rotates about the pelvis. The forward swinging of the arms compensates for this natural rotation of the body
 - Swinging of the arms tends to keep the shoulders at right angles to the direction of travel and reduces the amount of energy expended

Relative size of cerebral cortex

- Humans have relatively large brains, which contrasts markedly with the apes
- Most of the difference in brain size is associated with the cerebrum
- Cortex shows the greatest degree of development
- Surface area is greatly increased by convolutions

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- Frontal lobe has the greatest enlargement in surface area. This is where higher functions such as reasoning, thinking, planning and processing takes place
- Large brain requires large cranium, in humans more of the skull is used to house the brain as compared with apes
- As a consequence, brow tends to vertical and lacks the prominent brow ridges possessed by apes
- These features together with a shortening of the snout have given humans a flat face, although the bones of the nose still protrude. Thus humans have a far more prominent nose than any other primate
- Gradual increase in the size of the cranium to house a larger and more complex brain is an evolutionary trend in hominins
- Brain size can be determined by measuring the volume inside the cranium, cranial capacity
- Fossil evidence confirms a gradual increase in cranial capacity as the hominin species evolved towards modern humans

Prognathism and dentition

- Canines progressively got shorter and smaller
- Molars became 4 cloved instead of 3
- Jaw shape became broader and shorter, prognathism