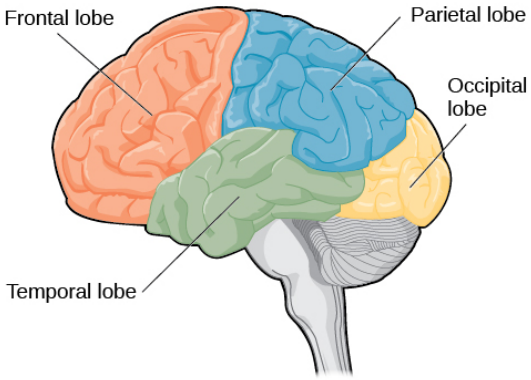
Nervous System

Functions of the parts of the brain and spinal cord summarised

Cerebral Cortex



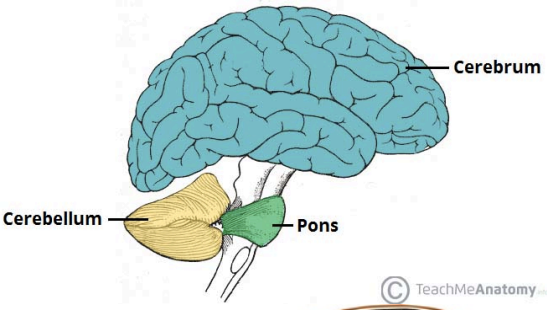
- Higher order functions such as thinking, learning and reasoning
- Intelligence
- Memory
- Perception of the senses
- Sense of responsibility

Medulla Oblongata

- Cardiac centre- rate and force of contraction of the heart
- Vasomotor centre- diameter of blood vessels
- Respiratory centre- rate and depth of breathing
- Involved in some reflexes such as sneezing and coughing

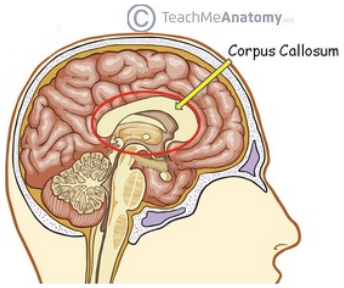
Hypothalamus

- Responsible for maintaining homeostasis
- Controls endocrine function
- Regulates body fluids and body temperature
- Involved in emotional responses
- Waking and sleeping patterns



Cerebellum

- Posture and balance
- Fine coordination of motor movements



Corpus Callosum

- Bridge between left and right hemispheres of brain

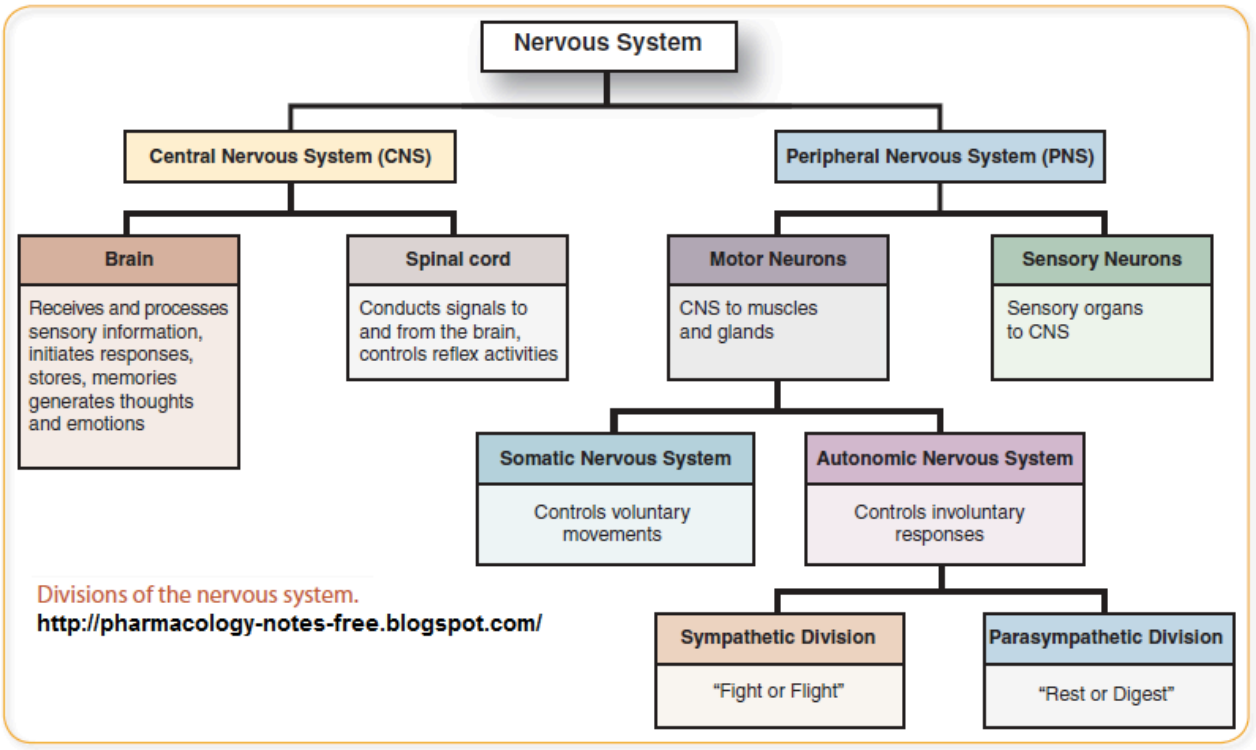
Pons

- Bridge joining brain and brain stem
- Involved in the perception of sight

Spinal Cord

- Control and integration of reflexes
- Relays messages between brain and peripheral nervous system
- White matter inside, Grey matter inside (opposite of brain)

Divisions of the Nervous System



Brain and spinal cord make up the Central Nervous System (CNS)
Nerves that carry messages to and from the Central Nervous System make up the Peripheral Nervous System (PNS)

Protection of the CNS

Bone

- Outer most protective layer is bone.
- The cranium houses and protects the brain
- The vertebral canal (an opening in the vertebrae) protects the spinal cord.

Meninges

- 3 layers of protective tissue forming membranes called the meninges.
- Meninges cover the entire CNS.
- Outer meningeal layer is tough and fibrous; it sticks closely to bones (dura mater – provides resistance to infection)
- Middle meningeal layer is a loose mesh of fibres (vascular arachnoid)
- Inner meningeal layer is extremely delicate and is highly vascularises. It sticks closely to the surface of the brain and spinal cord (pia mater – blood-brain barrier)

Cerebrospinal Fluid (CSF)

- CSF occupies space between the middle and inner meningeal layers, and circulates through cavities in the brain and the central canal of the spinal cord.

- CSF is a clear, watery fluid containing few cells, and some glucose, protein, urea, and salts.
- It acts as a shock absorber to any blows the CNS may sustain and supports the brain (the brain is suspended inside the cranium and floats in the CSF).
- It forms from the blood and circulates around the CNS, eventually re-entering as the blood capillaries. During circulation, it takes nutrients to cells of the brain and spinal cord, and carries away their wastes.
- Thus the CSF has 3 functions; protection, support and transport.

Definitions:

Neurons are the basic structural and functional units of the whole nervous system. All neurons consist of a cell body and 2 different types of extension from the cell (dendrites and axons).
Dendrites are fairly short extensions of the cytoplasm of the cell body. They carry nerve impulses into the cell body.
An axon carries nerve impulses away from the cell body. Most axons are covered with a layer of fatty material called the myelin sheath.
A **nerve fibre** is any long extension of a nerve cell.
Grey matter consists of unmyelinated nerve fibres.
White matter consists of myelinated nerve fibres.
Myelin sheath is formed by Schwann cells which coil around the axon, depositing myelin between the coils. At intervals along the axon are gaps in the myelin sheath called **Nodes of Ranvier**. The myelin sheath acts as an electrical insulator, protects the axon from damage, and increases the speed of nerve impulses along the axon (increases conduction velocity).
Neurilemma is the outer most layer of the Schwann cell that repairs damaged fibres.
Axon terminals are swellings at the ends of axons where neurotransmitters are released to carry the message across a synapse.

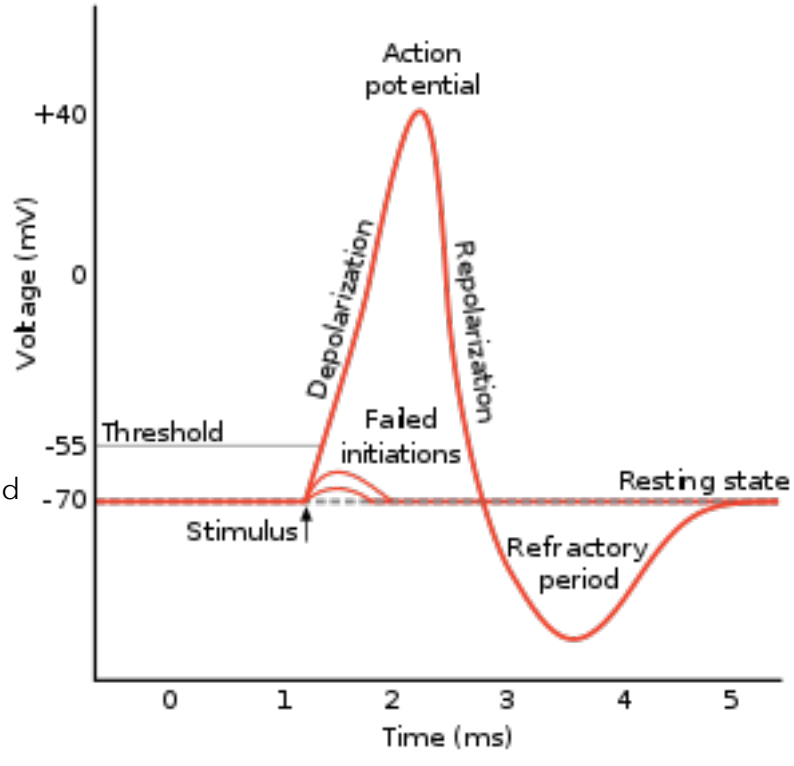
Structural types of neurons:

Sensory Neurons- carry messages to CNS
Motor Neurons- carry messages from CNS
Interneurons- carry messages between sensory and motor neurons

Transmission of Nerve Impulses

Resting membrane potential is -70mV
Negative on the inside, positive on the outside, maintained by:

1. Sodium-Potassium Pump that actively pumps 3 Na+ out and 2K+ in
2. Selective permeability of the cell membrane, high permeability to K+ and Cl-, low permeability to Na+ and impermeable to large organic anions



When stimulus is applies and it is greater than the threshold potential (15mV) an action potential occurs, the nerve impulse is an all or nothing response

First process of the action potential is *depolarisation*
- this is when there is a reversal of charge of the membrane (+in, -out)
- this occurs as stimulus causes Na+ channels to open and and influx of Na+ ions

After this *repolarisation* occurs:
- this is when the membrane charge is returned back to resting state (+out, -in)
- Na+ channels close and become inactivated
- K+ channels open and K+ moves in
- Sodium potassium pump also actively pumps sodium out

After this *hyperpolariation* occurs, then the membrane returns to rest

While the Na+ channels are inactivated (during repolarisation and the short period of time after), the membrane is in a *refractory period*.
- another action potential cannot be generated and inactivated Na+ channels will not open
- this prevents the back flow of nerve impulses

- These changes in the membrane during the action potential causes the adjacent segment of the membrane to depolarise and this repeats itself along the entire fibre
- The speed of nerve impulse depends on if the fibre is myelinated (140m/s) or unmyelinated (2m/s) as well as its diameter (wider=faster), nothing to do with length
- In myelinated fibres, saltatory conduction occurs- where the action potential 'jumps' from one Node of Ranvier to the next

Transmission of Nerve Impulses across a synapse

1. Action potential reaches axon terminal of the presynaptic neuron (also known as the presynaptic knob)
2. This triggers the opening of voltage-gated Ca2+ channels in the presynaptic neuron
3. This influx of Ca2+ stimulates vesicles containing neurotransmitters to undergo exocytosis
4. Neurotransmitters diffuses across the synapse from an area of high concentration to an area of low concentration
5. The neurotransmitters bind to the membrane receptors on the post synaptic neuron
6. This causes Na+ channels to open on the post synaptic neuron causing an influx of Na+ which is the beginning of another action potential

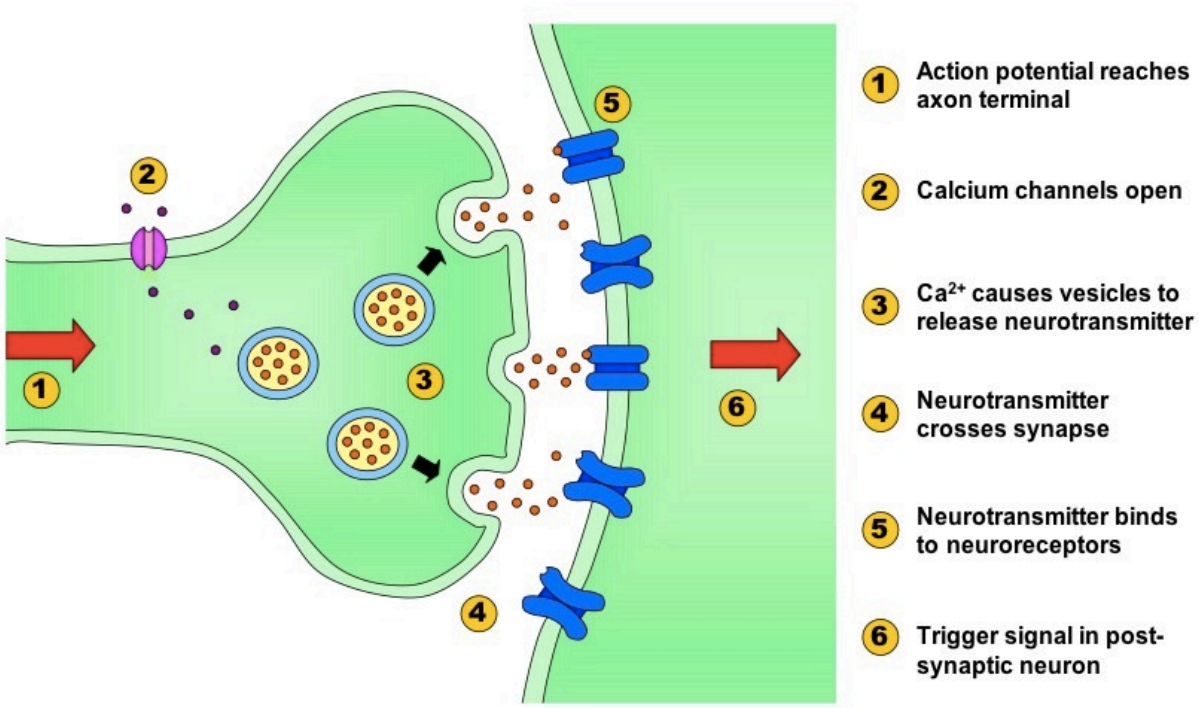
EXAMPLE EXTENDED RESPONSE ANSWER

Process

- impulse passes between 2 neurons at a synapse
- pre synaptic neuron has presynaptic knob
- synaptic knob houses vesicles continuing neurotransmitters (acetylcholine)
- synaptic knob fits into depression on post synaptic neuron
- gap between the neuron called synaptic cleft (synapse)
- when nerve impulses travel down axon to synaptic knob
- it causes an influx of CA 2+
- this trigger vesicles to fuse with pre-synaptic membrane
- and releases neurotransmitter into synaptic cleft/ by exocytosis
- neurotransmitter diffuses to dendrite of post synaptic neurone
- neurotransmitter binds to a specific membrane receptor on dendrite
- Na + gated channels open
- triggering a nerve impulse to be generated causing depolarisation

Effect of neurotoxin

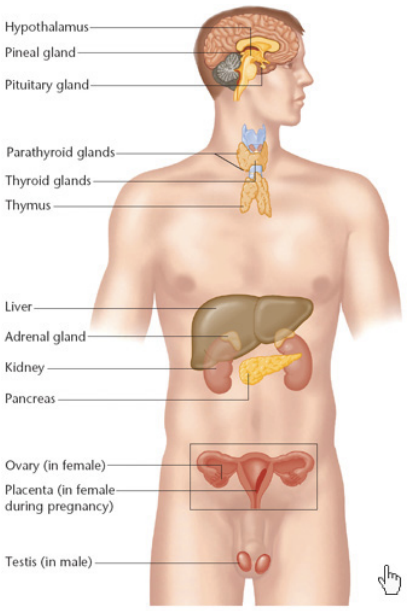
1. neurotoxin blocks receptor on dendrite preventing binding of acetylcholine
2. so no nerve impulse will be able to be generated/ transmitter in post synaptic neutron
3. no muscle contraction stimulated = paralysis/ difficulty controlling muscles



Endocrine System

Exocrine glands- secrete into a duct that carries the secretion to the surface of the body cavities
e.g. sweat glands, mucous glands, salivary glands

Endocrine glands- secrete hormones into the extracellular fluid that surrounds the cells



Functions of the endocrine system

1. maintain homeostasis by ensuring the concentrations of certain substances in body fluids are correct
2. works with the nervous system to help body respond to stress
3. controls the body's rate of growth
4. controls sexual development and reproduction

Hypothalamus:

- located at the base of the brain and links endocrine and nervous systems
- regulates body functions such as water balances and heart rate
- produces releasing and inhibiting factors

Pituitary gland

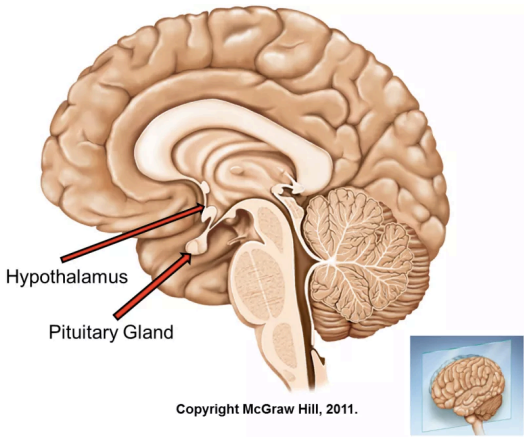
- lies under the hypothalamus by a stalk called the infundibulum

Anterior lobe:

- front lobe, largest
- connected to the hypothalamus by a complex network of blood vessels, no nerves

Posterior lobe:

- back lobe, smallest
- joined to the hypothalamus by nerve fibres that come from nerve cell bodies in the hypothalamus.
- these fibres pass through the infundibulum
- not a true gland as it the hormones it secretes are produced in the hypothalamus



Pineal gland

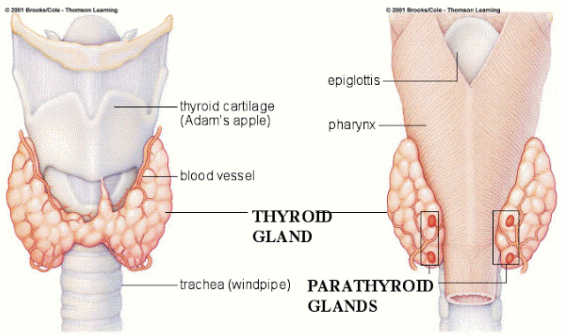
- pea-sized gland in children and shrinks from age 7 to become a lump of fibrous tissue in adulthood

Thyroid gland

- just below larynx, two lobes surrounding the trachea

Parathyroid glands

- four pea-sized glands embedded at the back of the two lobes of the thyroid



Thymus

- located just above the heart, behind the sternum
- decreases in size after puberty

Adrenal glands

- two glands, just above each kidney

adrenal medulla

- inner portion of adrenal gland

adrenal cortex

- outer portion of adrenal gland
- hormones produced here called corticosteroids
-

Pancreas

- just below stomach, alongside duodenum
- both an endocrine and exocrine gland
- clusters of special cells called the *Islets of Langerhans* are the endocrine part
- the Islets contain two types of cells- *alpha* and *beta* cells

GLAND	HORMONE	TARGET CELLS	MAIN EFFECTS
Hypothalamus	Gonadotropin releasing hormone (GnRH)	Anterior pituitary	stimulates the release of gonadotropins (hormones which affect gonads) - FSH and LH
Hypothalamus	Corticotropin releasing factor (CRF)	Anterior pituitary	stimulates the release of adrenocorticotrophic hormone (ACTH)
Hypothalamus	Thyroid stimulating hormone releasing factor	Anterior pituitary	stimulates the release of thyroid stimulating hormone (TSH)
Hypothalamus	Prolactin releasing factor	Anterior pituitary	stimulates the release of prolactin
Hypothalamus	Growth hormone releasing hormone (GHRH)	Anterior pituitary	stimulates the release of growth hormone (GH)
Anterior lobe of pituitary	Follicle Stimulating Hormone (FSH)	Ovaries (female) Testes (male)	stimulates the development of follicles containing ova production and maturation of sperm
Anterior lobe of pituitary	Luteinising Hormone (LH)	Ovaries (female) Testes (male)	ovulating and maintenance of corpus luteum secretion of testosterone
Anterior lobe of pituitary	Adrenocorticotrophic Hormone (ACTH)	adrenal cortex	controls the production and release of hormones from the adrenal cortex

Anterior lobe of pituitary	Thyroid Stimulating Hormone (TSH)	thyroid gland	stimulates the production and release of hormones from the thyroid gland
Anterior lobe of pituitary	Prolactin	mammary glands	initiate and maintain milk production in females (while breastfeeding)
Anterior lobe of pituitary	Growth Hormone (GH)	All cells	stimulates body growth, particularly skeletal growth increases rate of protein synthesis maintains size of organs when person is mature
Posterior lobe of pituitary	Antidiuretic Hormone (ADH)	kidneys	increases permeability of nephrite tubules in kidneys causing more water to be reabsorbed back into the blood and hence helps to retain fluid within the body
Posterior lobe of pituitary	Oxytocin	uterus mammary glands	stimulates contraction of muscles during labour stimulates the release of milk while breastfeeding
Pineal gland	Melatonin		involved in the regulation of sleeping patterns
Thyroid gland	Thyroxine	most cells	controls body metabolism brings about the release of energy and maintains body temperature
Parathyroid glands	Parathyroid hormone (PTH)	bones kidneys	controls the levels of calcium and phosphate in the blood
Thymus	Thymosins	T-lymphocytes	a group of hormones that influence the maturation of T-lymphocytes (disease-fighting cells)
Adrenal medulla	Adrenaline	most tissues	helps body prepare for a threatening situation (e.g. fight-or-flight response)
Adrenal medulla	Noradrenaline	most tissues	similar effects to adrenaline however it particularly increases the rate and force of the heartbeat

Adrenal cortex	Aldosterone	kidneys	reduce the amount of sodium and increase the amount of potassium in urine
Adrenal cortex	Cortisol	most cells	promote normal metabolism helps the body withstand stress helps to repair damaged tissues
Pancreas	Insulin (beta cells)	most cells	increases blood glucose levels
Pancreas	Glucagon (alpha cells)	liver and fat storage tissues	decreases blood glucose levels

Other endocrine tissues include:

The stomach and small intestine

- secrete hormones that coordinate exocrine glands of the digestive system

Kidneys

- secrete hormones including erythropoietin (EPO)
- this stimulates the production of red blood cells by the bone marrow

Heart

- secretes a hormone which helps to reduce blood pressure

Placenta

- secretes a number of hormones during pregnancy that help to maintain pregnancy, stimulate development of the foetus, and stimulate the mothers mammary glands.

What is a hormone?

- secretion of an endocrine gland
- secreted only by specialised cells
- transported through the body by the bloodstream
- may affect all the cells of the body or only a particular group of cells (traget cells)
- a hormone is any substance manufactured in one part of the body in response to a stimulus and transmitted to another part of the body where it produces a response
- are **potent,** that is they can stimulate a large number of tissue responses throughout the body

How do the nervous and endocrine systems work together to maintain homeostasis?

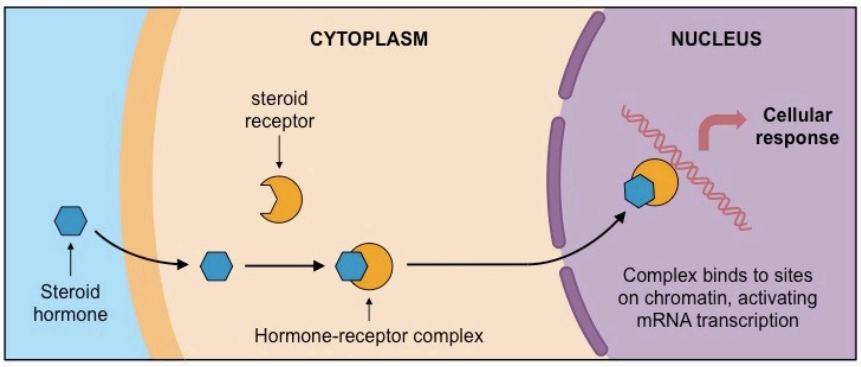
nervous –> exerts control by transmutation of nerve impulses to and from various tissues
endocrine –> influences activities of cells by release of chemical messengers (hormones)

What are paracrines?

Any chemical secreted by all cells in a particular ties and diffuses to and affects adjacent cells, also known as *local hormones*

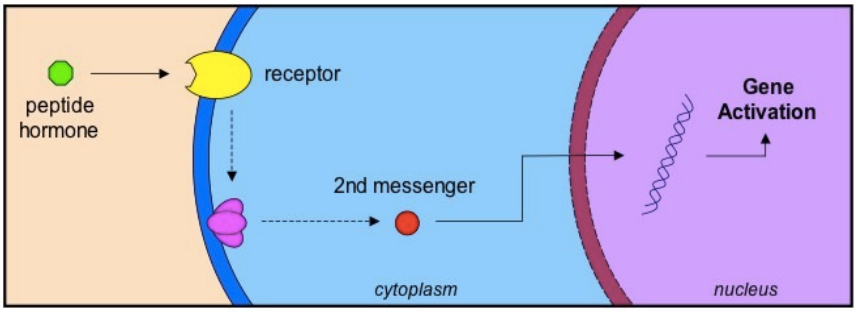
There are two types of hormones- steroid hormones and amine hormones

Steroid Hormones



- lipids (made from cholesterol)
- small in size
- slow acting (cortisol) (hours or days)
- as they are lipid soluble they pass easily through the cell membrane
- they diffuse from blood and enter target cells where they combine with a receptor protein inside the cell
- receptor may be on the mitochondria, other organelles or in the nucleus
- the hormone-receptor complex activates gene controlling formation of particular proteins

Amine or protein Hormones



- made of amino acids, from 2 to 190 amino acids thus they vary in size
- fast acting (thyroxine, GH)
- hormone NEVER enters the cell (seconds or minutes)
- they are water soluble and bind to receptor proteins on the cell membrane of target cell
- hormone-receptor complex causes a secondary messenger to diffuse through the cell and activate particular enzymes in the cytoplasm

Receptor proteins are **specific**. Each type of receptor protein will bind with only one specific molecules

Saturation can occur as there is limited number of receptor proteins in the membrane of each cell and therefore when each receptor is bound to a hormone molecule, there can be no further increase in the rate of the cell's activities

Different cells have different types and numbers of receptor proteins and this is why there is variation in the sensitive of cells to hormone and other substances

Hormones can…

- change the functioning of cells by changing type, actives or quantity of proteins produced
- are not enzymes, but can change the concentration or activity of enzymes
- may activate certain genes in the nucleus so that a particular enzyme or structural protein is produced
- change the shape or structure of enzyme so that it is turned "on" or "off"
- change the rate of production of an enzymes of structural protein by changing the rate of transcription or translation during protein production

Enzyme amplification

- one hormone molecule can cause the manufacture or activation of thousands of enzymes

- triggers a cascading effect in which t rhumba of reacting molecules involved is increased by hundreds or thousand for each step along the metabolic pathway
- thus a very small stimulus can produce a very large effect

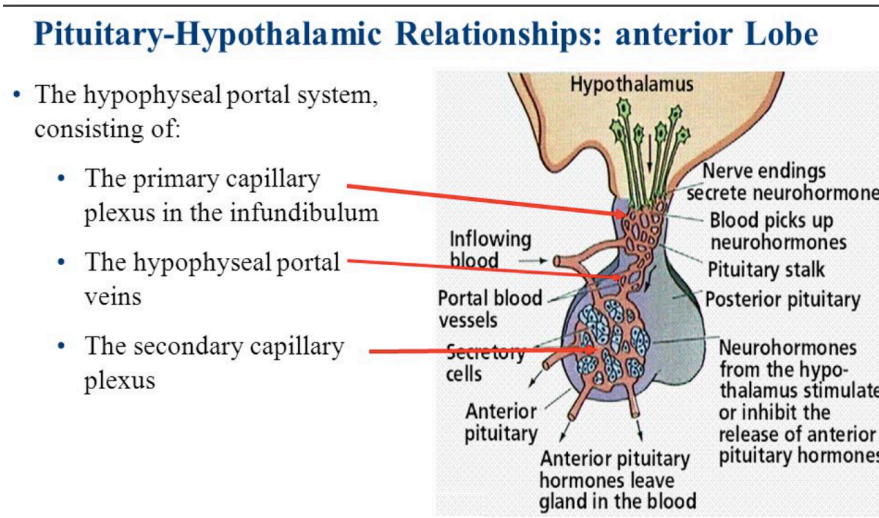
Hormone clearance
- hormones turned off by the breaking down of hormone molecules
- some broken down in target cells
- most broken down in liver and kidney which is then excreted in bile or urine

Path of releasing/inhibiting factors to the anterior pituitary gland

1. Stimulus within the nervous system either increase or decrease the secretion of releasing or inhibiting hormones from the neurons of the hypothalamus

2. The releasing or inhibiting hormones are produced by specialised neurons of the hypothalamus called neurosecretory cells

3. Releasing or inhibiting hormones pass through the hypophyseal portal system (complex network of blood vessels)



4. They are released into a capillary network (primary plexus) and transported through veins (hypophyseal portal veins) to a second capillary network (secondary plexus) which supplies the anterior pituitary

5. The primary plexus and the hypophyseal portal veins are in the infundibulum and the secondary plexus is in the anterior pituitary

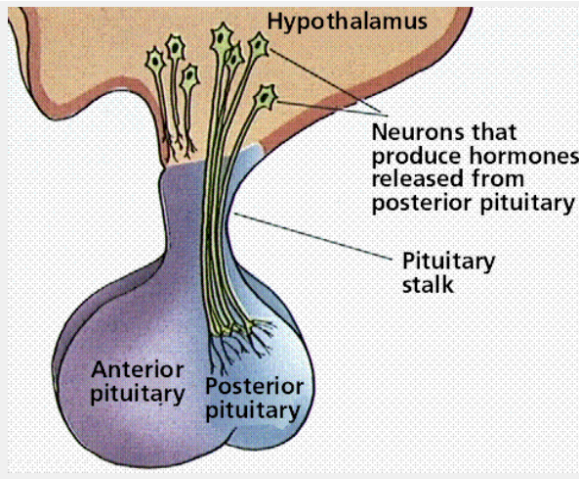
6. Releasing or inhibiting hormones bind to membrane bound receptors and stimulate or inhibit the release of hormones from the anterior pituitary gland

7. Anterior pituitary hormones are now carried in the blood to target tissues

How does the hypothalamus control the posterior pituitary gland?

1. Communication between the hypothalamus and posterior pituitary occurs through the neurosecretory cells that span the short distance between the hypothalamus and the posterior pituitary gland (through the infundibulum)

2. Hormones produced by the cell bodies of the



neurosecretory cells (in the hypothalamus) are packaged in vesicles and through the axon (nerve cell) it is transported. It is then stored in the axon terminals that lie in the posterior pituitary gland

3. When the neurosecretory cells (in the hypothalamus) are stimulated, the nerve impulse triggers the release of these stored hormones from the axon terminals to the capillary network within the posterior pituitary gland

Recombinant DNA technology

1. The gene/ segment of DNA is isolated at a specific *recognition site* (sequence of bases) and cut by a *restriction enzyme*
2. The enzyme cuts either side of the gene resulting in a *staggered cut*, one which unpaired nucleotides overhang at the break. These are called *sticky* ends
3. A plasmid (a circular strand of DNA) is removed from a bacterium and this is cute with eh same type of restriction enzyme to create sticky ends as well
4. The sticky ends of the isolated gene and plasmid ate joined together by *DNA ligase*
5. The combined gene and plasmid are inserted into the bacterial cell
6. This bacterial cell is then cloned and large amounts of the gene of its product is made
7. It is then cultured or grown in vats before the product can be harvested

- the nervous and endocrine systems work together to co-ordinate functions of all body systems, but differ in terms of:
  - speed of action
  - duration of action
  - nature and transmission of the message
  - specificity of message

Nervous and Endocrine System compare and contrast

Similarities
- work together to maintain homeostasis by coordinating and regulating the activities of other cells, tissues, organs and systems

	ENDOCRINE	NERVOUS
Speed of Action	Response is fast acting	Response is slow acting
Duration of Action	Long duration time	Short duration time
Nature and Transmission of Message	Hormones are transported chemically through the bloodstream	Nerve impulses are transported electrochemically through nerve fibres
Specificity of Message	Affect different organs of the body and has a widespread effect	Impulses target specific sites/ particular parts of the body (localised effect)

EXAMPLE EXTENDED RESPONSE ANSWER

Differences between their actions include:
- Nervous responses are more rapid than hormonal ones as nerve impulses travel rapidly along nerve fibres, whilst hormones are transported by the blood stream.
- When a stimulus ceases, the nervous system stops generating nerve impulses and the response ceases almost immediately, whiles hormones are typically slower acting, and responses can last a considerable amount of time after a stimulus ceases.
- Nervous messages= electrochemical changes travelling along the neuron membrane. Endocrine messages= chemicals transported by the blood.
- Nerve impulses travel along a nerve fibre to a specific part of the body, and often influence one effector; hormones travel to all parts of the body and often affect multiple organs.

Important similarities include:
- Some substances function as hormones and as neurotransmitters e.g. noradrenaline.
- Some hormones are secreted by neurons into the extracellular fluid e.g. oxytocin and adrenaline.

- Some hormones and neurotransmitters have the same effect on the same target cells e.g. noradrenaline and glucagon act on liver cells to cause glycogen to be broken down into glucose.

HOMEOSTASIS

Definition: The maintenance of a constant internal environment despite fluctuations in the external environment
Tolerance limits: upper and lower limits to a range of factors, if the tolerance limits are exceeded dysfunctions will occur.

Feedback Systems

circular situation in which the body response to a change
Stimulus- change in the environment that causes system to operate
Receptor- detects the change
Modulator- control centre responsible for processing information received from the receptor and for sending information to the effector
Effector- carries out a response
Response- either counteracts or reinforces the effect of the stimulus
Feedback- original stimulus is changed by response

Negative Feedback- when the response has the effect of reducing or eliminating the stimulus that caused it

Dynamic equilibrium- stable, balanced ,unchanging system which allows levels to fluctuate slightly

Positive Feedback- response to a stimulus which reinforces and intensifies the stimulus and this results in an even greater response, and so on
e.g. blood clotting
e.g. childbirth

1. Head of foetus pushes against cervix
2. Nerve impulses from cervix transmitted to brain
3. Brain stimulates posterior pituitary gland to secrete oxytocin
4. Oxytocin is carried in bloodstream to uterus
5. Oxytocin stimulates uterine contractions and pushes foetus towards cervix

Receptors

Chemoreceptors

- Respond to changes in concentration of chemicals
- H+ and CO2
- Peripheral chemoreceptors- Aortic and carotid bodies
- Central chemoreceptors- Medulla oblongata

Osmoreceptors

- Changes in osmotic pressure
- Tendency of a cell to draw water into itself
- Hypothalamus

Nociceptors

- respond to pressure/heat/abnormal situations in the environment to produce the sensation of pain
- found everywhere all over the body –> widespread

Touch receptors

- found in skin (upper layer)
- respond to pressure, vibration and movement

Thermoreceptors

- respond in changes in temperature of internal or external environment
- central thermoreceptors- hypothalamus and other central locations
- peripheral thermoreceptors- heat and cold thermoreceptors located in the skin and mucous membranes

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Temperature Regulation

The maintenance of a balance between heat production and heat loss
The chemical reaction occurring within the cells are heat sensitive
Temperature of 37°C is optimum for cellular reactions (thermoneutral zone)
Heat produced in metabolic reactions help to maintain this higher level

How is heat produced in the body?

Metabolic rate- rate at which energy is released by the breakdown of food
Exercise, stress and body temperature affect metabolic rate
A 1°C increase in temperature results in a 10% increase in the rate of biochemical reactions

Hypothermia- Less than 36°C
Heat Exhaustion- Normal body temperature but sweating in a humid environment

- do not have a cooling effect as the water doesn't evaporate from the skin
- high water content in external environment
- high water loss –> decreased blood pressure
- drink more water to reduce symptoms

Heat stroke

- fatal
- high body temperature leads of the denaturing of enzymes
- decreased metabolism
- ice bath or other mechanisms to cool the body

Fever

- Infection –> mast cells release cytokines and chemokines (some of which are pyrogens)
- Pyrogens alter the thermostat in the hypothalamus to adjust the set point to a higher level

Stimulus- Increase in body temperature or increase in the temperature of the external environment

Receptor- thermoreceptors send a message via nerve impulses

- peripheral thermoreceptors- in the skin and mucous membranes
- central thermoreceptors- hypothalamus

note: heat receptors

Modulator- hypothalamus activates mechanisms to decrease heat production and increase heat loss

Effector-

1. Sweat glands
2. Smooth muscles walls of blood vessels in the skin
3. Thyroid gland
4. Cerebrum

Response-

1. Sweating
    - The active secretion of fluid (containing salts, water and some wastes) by the sweat glands
    - This is done by the periodic constriction of cells surrounding ducts to pump sweat to the skins surface
    - It helps the body lose heat through evaporative cooling
    - Cooling of skin results in cooling of blood flowing through it
    - Evaporation- change in state from liquid to gas which brings a great cooling effect
    - This only cools being if the environment is fairly dry, will not work in humid environments
    - Above 28°C sweating mechanism takes place , above 37°C , only avenue of heat loss
    - Evaporation of H2O from the skin has a cooling effect as energy is required from the body for water to evaporate

2. Vasodilation-
    - An increase in diameter of blood capillaries which increases the blood flow through the skin thereby increases heat loss by convection, conduction and radiation
    - Skin becomes reddish in colour and surface temperature rises
    - Heat is lost through mainly through radiation and convection
    - Convection- the process of air or water flowing by the skin and carrying away body heat
    - Radiation- heat generated within the body is given off to the surroundings
    - Conduction- transfer of heat between two objects that are in contact with each other, it will flow from an area of high temperature to an area of low temperature

3. Decrease in thyroxine
    - This causes a decrease in basal metabolic rate
    - Decrease in heat production
    - Due to seasonal changes

4. Behavioural Responses
    - decrease heat conservation
    - increase heat loss

- Turning on fan or aircon
- Removing external clothing
- Reducing physical activity
- Cold drink

Feedback- decrease in body temperature

Stimulus- decrease in body temperature

Receptor- thermoreceptors send a message via nerve impulses

- peripheral thermoreceptors- in the skin and mucous membranes
- central thermoreceptors- hypothalamus

note: cold receptors

Modulator- hypothalamus activates mechanisms to increase heat production and decrease heat loss

Effector-

1. Sweat Glands
2. Skeletal muscles
3. Smooth muscle walls in the blood vessels in the skin
4. Thyroid gland
5. Adrenal Medulla
6. Hair Follicle
7. Cerebrum

Response-

1. Decrease in sweating
2. Shivering
    - Hypothalamus send stimuli to parts of the brain that increase skeletal muscle tone
    - An increase in muscle tone leads to oscillating, rhythmic muscle tremors occurring at a rate of about 10 to 20 per second purely dedicated to decreasing heat production
    - More heat is produced by increased cellular respiration and so the metabolic rate increase generates more internal heat.
    - Under primary control of the hypothalamus, but conscious input from cerebral cortex can suppress this urge

3. Vasoconstriction-
    - An decrease in diameter of blood capillaries which decreases the blood flow through the skin
    - This is stimulated by the sympathetic nerves
    - Skin becomes warmer due to less warm blood flowing through it
    - Less heat will be lost from body surface by convection, conduction and radiation

4. Increase in thyroxine
    - increase in basal metabolic rate, increase in heat production
    - For seasonal changes, slow acting and long term

5. Secretion of adrenaline and noradrenaline
    - Stimulated by sympathetic nerves
    - Increase in cellular metabolism that leads to an increase in heat production thereby increasing body temperature
    - Helps maintain body temperature in conditions where there is rapid heat loss

6. Piloerection
    - Hair follicles stand up and trap a layer of air above the skin
    - This acts as an insulator to decrease heat loss
    - Not as effective in humans due to humans having less hair than animals

7. Behavioural Responses
    - Curl up
    - Putting on more clothing
    - Turning on heater

Feedback- increase in body temperature

Role of skin in thermoregulation

Subcutaneous fat layer (fat under the surface of the skin)

- Acts as an insulator therefore decreasing heat loss

Blood Glucose

Hyperglycaemia- an abnormally high level of sugar in the blood, frequently found in people with diabetes mellitus

Hypoglycaemia- an abnormally low level of sugar in the blood

Glycogen- a polysaccharide made up of thousands of glucose molecules bonded together in branching chains, functions as a store of glucose molecules in the muscles and liver cells

**Portal vein carries glucose to liver, where:

1. Glucose may be removed from the blood by the liver to provide energy for liver functioning
2. It may be removed by the liver and/or muscles and converted in glycogen for storage
3. It may continue to circulate in the blood, available for body cells to absorb and use as a source of energy
4. Excess glucose which is required to maintain both normal blood level and tissue glycogen level is converted into fat for long-term storage.

Stimulus- decrease in blood glucose levels

Receptor- chemoreceptors in the pancreas

Modulator- alpha cells in the Islets of Langerhans of the pancreas release glucagon

Effector- Liver and body cells

Response

- **Glycogenlysis-** formation of glucose from stored glycogen in the liver
- **Gluconeogenesis-** formation of glucose from amino acids, fats and glycerol
- Stimulating effects on protein breakdown in some cells

Feedback- increase in blood glucose levels

Stimulus- increase in blood glucose levels

Receptor- chemoreceptors in the pancreas

Modulator- beta cells in the Islets of Langerhans of the pancreas release insulin

Effector- Liver and body cells

Response

- **glycogenesis-** process whereby glucose molecules are chemically combined in long chains to form glycogen molecules (glucose –> glycogen)
- Stimulates conversion of glucose into adipose (fat storage tissue)

- Causes an increase in protein synthesis in some cells
- Accelerating transport of glucose from blood into cells, especially those of the skeletal muscles

Feedback- decrease in blood glucose levels

Adrenal Medulla (inner region)

It secretes the hormones adrenaline and noradrenaline

Effect:

- Increases blood glucose levels as adrenaline counteracts the effects of insulin
- It stimulates the production of lactic acid from glycogen in the muscle cells, and the lactic acid can then be used by the liver to manufacture glucose
- Both adrenaline and noradrenaline assist in the conversion of stored glycogen to glucose

Adrenal Cortex (outer region)

It is stimulated to secrete its hormones by the adrenocorticotrophic hormone from the anterior lobe of the pituitary gland

It secretes glucocorticoids such as cortisol

Function of cortisol: regulates carbohydrate metabolism by making sure enough energy is provided to the cells by:

1. Increasing the rate of which amino acids are removed from muscle cells and transported to the liver (muscle –> amino acids –> glucose)
2. Stimulating the conversation of stored glycogen into glucose in the liver

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Osmoregulation

The need to regulate constant solute concentration of body fluids i.e. maintaining a constant solute concentration

Osmotic pressure: pressure due to osmosis, usually measured as the pressure that would be required to prevent osmosis

Isotonic solution:

- A solution that has 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 had 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 fluid
- e.g. hypertonic saline has a higher concentration of salt than that of normal tissue fluid

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

- e.g. hypotonic saline has a lower concentration of salt than that of normal tissue fluid

Excretion- removal of waste products of metabolism from the body

Lungs

- excretion of CO_2 when it is breathed out
- some water lost too in the form of water vapour

Sweat Glands

- secrete water containing salts, lactic acid and urea

Alimentary Canal

- passes out bile pigments (which are the breakdown of haemoglobin from the red blood cells) in the faeces

Kidneys

- responsible for maintaining a constant concentration of body fluids, important waste removed is urea

Regulating Water Intake

Water is continually lost from the body in sweat, urine, exhaled breath and faeces
As water is lost, the plasma becomes more concentrated, has a lower water content and hence a higher osmotic pressure
This results in water moving from the intercellular fluid into the plasma by osmosis
Now the intercellular fluid is more concentrated and water diffuses out of the cells, so that the cells start to shrink from dehydration.

Stimulus- decreased amount of water in the blood –> concentration of water in blood plasma decreases –> osmotic pressure of blood increases
Receptor- osmoreceptors in the hypothalamus detect raised osmotic pressure
Modulator- hypothalamus produces ADH (anti-diuretic hormone) in the cell bodies of specialises neurons (neurosecretory cells) which is then transported down the cell extensions to the posterior lobe of the pituitary gland where ADH is stored. Nerve impulses then stimulate the release of ADH
Effector- The walls of the distal convoluted tubule and the collecting ducts in the nephrons of the kidneys
Response- Increased permeability of the walls thereby increasing the active reabsorption of water from the tubules into the capillary network surrounding nephrons (peritubular capillaries)
Feedback- Increased water content in blood –> osmotic pressure of the blood decreases

Stimulus- decreased amount of water in the blood –> concentration of water in blood plasma decreases –> osmotic pressure of blood increases.
Receptors- osmoreceptors in the thirst centre of the hypothalamus are stimulated
Modulator- thirst centre of the hypothalamus is stimulated

Effector- cerebrum
Response- brings about conscious awareness of thirst (dry mouth and throat) stimulating the person to drink water and the water is then absorbed from the intestines into the blood stream
Feedback- osmotic pressure decreases

Stimulus- decrease in blood volume, which causes a decrease in blood pressure
Receptors- baroreceptors (blood pressure receptors) in renal artery
Modulator- adrenal cortex release aldosterone
Effector- sodium pumps in Loop of Henle and distal convoluted tubule
Response- more sodium reabsorbed
Feedback- increase in osmotic pressure (higher concentration of water)

Aldosterone increases the reabsorption of sodium ions into tissue fluid, this in turn increases osmotic pressure which is the stimulus for the reabsorption of water
Dehydration- water loss exceeds water intake

- Symptoms become noticeable when the person has lost 2% or more of their normal body water
- Loss may be through sweating, vomiting and diarrhoea
- Thirst reflex becomes less effective as we grow older
- Symptoms of dehydration include: severe thirst, low blood pressure, dizziness, headache
- If condition becomes untreated, patient becomes delirious , loses consciousness and dies
- Occurs when not enough water is taken in during physical activity

Water Intoxication- too much water in the body also known as water poisoning

- occurs when body fluids become diluted and cells take in extra water by osmosis
- may happen is a person loses a lot of water and salts through sweating and replaces the loss through only plain water, they should replace it with water containing electrolytes
- in such cases the water should contain dissolved substances to replace the salts lost as well as the water
- Symptoms- first sign is usually light-headedness, headache, vomiting and collapse may follow

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Regulation of Gas Concentrations

Under normal conditions, oxygen plays little part in the regulation of breathing (i.e. a large decrease in oxygen would stimulate a negative feedback loop)
Oxygen, carbon dioxide and hydrogen ion concentration interact with each other to regulate breathing rate

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

carbon dioxide + water — *carbonic acid* — *bicarbonate + hydrogen ion*

Stimulus-

1. High carbon dioxide concentration
2. Decrease in pH caused by an increase in hydrogen ion concentration

Receptor-

1. Central chemoreceptors
    - medulla oblongata
    - these are responsible for 70-80% of the increase in breathing rate
    - increased CO2 stimulates these
2. Peripheral chemoreceptors
    - aortic bodies- a group of cells within the walls of the aortic arch
    - carotid bodies- a group of cells within the walls of the carotid arteries
    - these are responsible for the immediate increase in breathing rate
    - increased H+ stimulates these

**chemoreceptors more sensitive to carbon dioxide than oxygen

Modulator- Respiratory centre in the medulla oblongata

Effector- Diaphragm and intercostal muscles (in between ribs)

*diaphragm is stimulated by impulses from the phrenic nerves

*intercostal is stimulated by impulses from the intercostal nerves

Response- Increase in activity of diaphragm and intercostal muscles –> increases rate and depth of breathing

Feedback-

1. decrease in levels of carbon dioxide
2. decrease in hydrogen ion concentration –> increase in pH
3. increase in concentration of oxygen gas

Voluntary control of breathing

- Voluntary control occurs via connections from the cerebral cortex to descending tracts in the spinal cord
- Voluntary control bypasses the respiratory centre in the medulla oblongata
- This is a protective mechanism to prevent irritating gases and water from entering into the lungs
- However the build up of carbon dioxide in the plasma stimulates the inspiratory centre to send impulses to the inspiratory muscles
- Thus the individual is forced to take a breath.

Hyperventilation

- *Rapid, deep* breathing in which more oxygen is taken in than what is necessary
- It can occur voluntarily or be stimulated by physical stress such as severe pain or emotional stress such as extreme anxiety

- It usually corrects itself because the reduction in carbon dioxide concentration means that the chemoreceptors are not stimulated and there is no urge to breath until carbon dioxide levels return to normal

Why is dangerous to hyperventilate before swimming?

- It allows the person to stay underwater for longer, but this is not because of the extra oxygen in the blood, it is due to the loss of carbon dioxide (i.e. stimulus to breath is delayed)
- The breath-holding ability could be increased to such an extent that the individual loses consciousness from lack of oxygen to the brain before feeling the urge to breath
- Many drowning deaths in Australia have been the direct result of hyperventilation

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Gene Therapy

Gene therapy refers to the application of gene technology to correct or replace defective genes. It targets:

- cancer
- genetic disorders (e.g. cystic fibrosis)
- infectious diseases
- other autoimmune diseases (e.g. type 1 diabetes)
- Effective for single gene disorders***

Types:

1. **Somatic-** transfer of DNA section to cell not producing sperm or eggs, thus the effect will not be passed onto the patients children
2. **Germline-** transfer of DNA cell that is producing sperm/eggs, the effect will be passes onto the patient's children

Use of gene therapy

- restore a function of gene that has been lost as a result of mutation
- replace missing genes/ modify faulty genes (i.e. treat genetic diseases)
- Render healthy cells resistant to toxic drugs used in medical treatment of genes and kill abnormal cells (i.e. treat cancer)
- Inhibit reproduction of infectious agents (i.e. treat infectious diseases)

Vectors for gene therapy

1. Retrovirus vectors
   - Advantages: integrate genes into chromosomes of human host cells, offer a change for long-term stability
   - Disadvantages: infect only dividing cells, genes integrate randomly into chromosomes, so might disrupt useful genes in host cells. May have a reaction to the vector (e.g. for a virus)

2. Adenoviral vectors
   - Advantages: infect human cells and express normal genes, do not cause disease, have a large capacity to carry foreign genes
   - Disadvantages: may have poor survival due to attack by host's immune system, genes function only sporadically because they aren't integrates into host cell's chromosomes
3. Liposomes
   - Advantages: seek out target cells using sugars in their membranes that are recognised by cell receptors, have no viral genes that may cause disease
   - Disadvantages: less efficient as viruses at transferring genes into cells (recent work = improved success rate)
4. Naked DNA
   - Advantages: no viral genes that may cause disease, expect to be useful for vaccination
   - Disadvantages: unstable in most tissues of body, inefficient at gene transfer

Gene delivery system

The way the gene is transferred into a patient's cells

1. Aerosols and nebulisers
   - offer an effective spread and effect delivery of the vector to the site of target cells especially in respiratory tract
2. Hypodermic needle injection
   - injection of vectors directly into the bloodstream or other organs by a hypodermic needle
3. Extracted cells and cell culture
   - target cells are isolated from the tissue
   - non-specific gene delivery to total cell population
   - cells that have taken up normal allele are cultured outside the body and reinfected into patient
4. Ballistic DNA injection
   - plasmid DNA encoding genes of interest are coated into microbes and fired at target cells, allows delivery of precise DNA dosages

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Homeostatic Dysfunction

Diabetes mellitus

When an individual has an abnormally high level of glucose in the blood - hyperglycaemia
Large quantities of glucose are excreted in the urine
Occurs when an individual either does not produce any/enough insulin or their cells are resistant to the effects of insulin

Type One Diabetes (insulin dependent diabetes)

- Begins in early childhood (10-15% of patients in Australia)

- Caused by a fault in the immune system
- Beta cells in Islets of Langerhans are destroyed (i.e. individual can no longer produce insulin)
- Other body cells are usually still receptive to the hormone, so it can be manages by providing regular injection of insulin
- Insulin cannot be taken in tablet form because it is digested in the alimentary canal
- No cure currently
- Even with treatment, sufferers are still at high risk for
    - kidney failure
    - heart attack
    - stroke
    - amputations
    - blindness
    - nerve damage

Type Two Diabetes (non insulin dependent diabetes)

- Begins in adulthood, usually over the age of 45
- Caused by cells becoming non responsive to insulin
- Type 2 diabetes can still produce insulin
- Common in unhealthy, overweight individuals and risk factors include:
    - lack of physical activity
    - being overweight or obese
    - high fat, sugar, sodium and low fibre diet
    - high blood pressure
    - high cholesterol
    - smoking
- No cure, however early diagnosis is important to manage it:
    - management to keep blood glucose within an normal range
    - strict and careful diet
    - regular exercise
    - maintaining a healthy weight
    - monitoring of blood glucose
    - sometimes medications as a final measure
- Even with treatment, sufferers are still at high risk for
    - kidney failure
    - heart complications
    - eye problems
    - nerve damage
    - skin and foot problems (e.g. gangrene)

Thyroid Dysfunction

The over or under secretion of thyroid hormones
Thyroid gland secrete thyroxine and this hormone affects nearly every tissue in the body
This is important in maintain basal metabolic rate and long term metabolism such as from summer to winter
It is also important in the homeostatic of body temperature
Over or under active thyroids are often linked with an imbalanced in thyroid stimulating hormone

Hyperthyroidism (Grave's Disease)
Excess of thyroxine and enlargement of thyroid

- Causes
  - immune response
  - genetic predisposition
- Symptoms
  - Weight loss
  - Rapid heart beat
  - Fatigue
  - Sweating
  - Anxiety
  - Increased appetite
  - Protruding eyeballs (exophthalmia)
- Treatments
  - surgery to remove a part of the gland
  - drugs to block iodine use
  - radioactive iodine to kill thyroid cells

Hypothyroidism
Deficiency of thyroxine, more common of hyperthyroidism

- Causes
  - lack of iodine
  - autoimmune ideas (Hashimoto's disease)
  - issues with the pituitary gland or hypothalamus, which regulate thyroid function
- Symptoms
  - Slow heart rate
  - Unexpected weight gain
  - Fatigue
  - Intolerance to cold
  - Swelling of the face and goitre (enlarged thyroid)
- Treatments
  - Iodine supplements

    - Thyroid stimulating hormone tablets
    - Removal of part of the enlarged gland

- Hypothyroidism in infants
    - Iodine deficiencies in a pregnant mother's diet can affect the development of the infant
    - Causes cretinism, the retardation of mental and physical growth, with impaired movement or hearing

Growth retardation or dwarfism

- Can be caused by lack of human growth hormone from the anterior pituitary gland
- Severe cases of growth retardation in children can be treated with injections of the hormone
- Used to be make by extracted the hormone from pituitary glands of deceased individuals
- Now made by genetical engineers E. coli using recombinant DNA

Behavioural Disruptions to Homeostasis

Drugs:

- Abuse of medication or non-medicinal drugs may disrupt homeostasis
- Drug molecules may be similar to some neurotransmitters and bind to receptors and other cells, blocking or slowing down certain nerve transmissions

Excessive Activity:

- Extreme consumption of energy with insufficient replacement
- Causes damages to bones, cartilage, muscles, joint etc.
- In extreme cases, the body may begin to break down muscle cells for energy, causing muscle to degrade and lose mass.

Eating habits and disorders:

- Inadequate levels of certain nutrients, vitamins and minerals
- Anaemia
    - Caused in inadequate iron in diet
    - Causes a deficiency in haemoglobin, the oxygen carrying protein in red blood cells
    - Slows the supply of oxygen to cells, and thus slowing cellular respiration and edgy production
    - Causes fatigue, shortness of breath and high heart rate
    - Pernicious anaemia caused by lack of vitamin B12

The Immune System

Communicable/ infectious disease- A disease based from one person to another by infection with micro-organisms

Pathogen- A disease causing organism

Bacteria

There are many healthy bacteria that live on the skin, alimentary canal and other parts of the body and they have no ill effect on our health

Structure of bacteria

- consist of a single cell and can only be seen with a microscope
- cell shape is used to classify bacteria
- reproduce asexually by binary fission

Diseases caused by bacteria

- Whooping cough
- Tetanus
- Chloera
- Tuberculosis
- Scarlet fever
- Chlamydia

Viruses

Structure of viruses

- contain genetic material either DNA or RNA not both
- surrounded by a coat of protein
- no cell wall, lipid membrane

How do viruses reproduce?

- the DNA or RNA induces the cell to manufacture more virus particles
- the new virus particles are then able to leave the host cell to infect others
- viruses that multiply in bacterial cells, causing the death of bacterium are called *bacteriophages*

How can viruses be useful to humans?

They can be used to insert new genes into other organism such as genetically modified bacteria which are used to produce insulin

Diseases caused by viruses

- HIV/ AIDS
- Ebola
- Rubella
- Influenza
- Chicken pox
- Colds
- Measles
- Birdflu
- Smallpox

Fungi

Structure of fungi

- no chlorophyll
- most are multicellular
- have a cell wall
- varies by type of fungi
- cause of skin diseases
- reproduce asexually by fragmentation budding or producing spores

Diseases caused by fungi

- Ringworm
- Thrush
- Athletes foot (tinea)

Parasites

Organisms that live on or in another living thing, gaining food and shelter from it

Reproduce in host cells

Ectoparasites- live on the surface (e.g. fleas, lice)

Endoparasites- live inside the body (e.g. tapeworms, protozoa)

Transmission of pathogens

1. Transmission by contact

- Spread of pathogen by actual physical contact
- *Direct contact:* touching an infected person
- *Indirect contact:* touching an object touched by an infected person
- e.g. skin infections, STIs

2. Transfer of body fluids

- From one person to another
- When blood or other body fluids of an infected person come into contact with mucous membranes or bloodstream of unaffected individuals
- e.g. HIV, hepatitis B and C

3. Infection by droplets

- Tiny droplets of moisture, harbouring pathogenic organisms are emitted when breathing, sneezing, coughing or talking
- May be breathed in or ingested with food
- e.g. colds and influenza

4. Ingestion

- Of food and drink contaminated by pathogens may result in disease
- e.g. salmonella food poisoning, dysentry, typhoid

5. Airborne transmission

- When moisture in exhaled droplets evaporates, many bacteria are killed but many bacteria and viruses remain viable and can cause infection when inhaled

6. Transmission by vector
- Transfer of pathogen by animals (e.g. insects, mites)
- Some vectors transfer pathogen directly, some spread pathogen to food and water
- Many vector-borne diseases are spread by a specific vector
- e.g. dengue fever

Specific defences- directed at a particular pathogen
Non-specific defences- work against all pathogens, body's first line of defence

External Defences

Skin
- Impervious barrier
- Good at preventing micro-organism from entering if no cuts or abrasions
- Opening in the skin such as mouth, eyes, anus get special protection
    - Bacteria live on skin, occupy area, pathogens find it hard to establish themselves
- Sebum- oily secretion produced by oil glands in skin, it contains substances which kill pathogenic bacteria
- Sweat- acidic, contains salts and fatty acids, prevents growth of microorganisms

Mucous membrane
- Secrete mucus which inhibits entry of micro-organisms to the body
- Examples: digestive, urinary and reproductive tracts (places where the body opens to the exterior)

Hairs
- Found in nasal cavity and ears
- Nose- hairs and mucus layer trap up to 90% of particles inhaled while breathing

Cilia
- Tiny hair-like projections which are capable of a beating motion
- Beating motion moves mucus, containing trapped particles and micro-organisms to the throat to be coughed up or swallowed
- Examples: nose cavity, trachea, bronchi and other air passages

Acids
- Acid kills off bacteria taken in with food or contained in mucus swallowed from nose and windpipe
- Acid secretions reduce growth of micro-organisms

- Examples: stomach juices, sweat and vagina

Flushing Action

- Lysozyme- an enzyme which kills bacteria (found mainly in tears)
  - Also found in sweat, saliva, nose and tissue fluid
- Cerumen- protects outer ear from infection by some bacteria
  - Slightly acidic
  - Contains lysozyme
  - Also known as ear wax
- Flushing action in body fluids- prevent bacterial growth
  - Helps to stop bacteria reaching bladder and kidneys
  - Urethra, which empties the bladder to the outside
  - Women are more prone to urinary tract infections as they have a shorter urethra

Protective reflexes

A reflex is an automatic, involuntary response to a stimulus.
Protective reflexes help to protect the body from injury.

Sneezing

Stimulus- Irritation of walls of nasal cavity, caused by noxious fumes or dust particles likely to be carrying pathogenic micro-organisms
Forceful expulsion of air from lungs carries mucus
Foreign particles and irritating gases out through mouth and nose

Coughing

Stimulus- Irritation of lower respiratory tract – bronchi and bronchioles
Air forced from lungs in an attempt to remove the irritant
Air drives mucus and foreign matter up the trachea towards throat and mouth

Vomiting

Stimulus- Psychological stimuli, excessive stretching of the stomach and bacterial toxins
Contraction of muscles of abdomen and diaphragm expel stomach's contents

Diarrhoea

Stimulus- Irritation of small and large intestines by bacteria, viruses and protozoans
Causes increased contractions in muscles in walls of intestines to expel irritants
Material doesn't stay in large intestines for long enough resulting in watery faeces

Internal non-specific defences

Lymphatic System

Phagocytes

- Cells that can engulf and digest micro-organisms and cell debris

- Attack organism which penetrate our external defence

Leucocytes

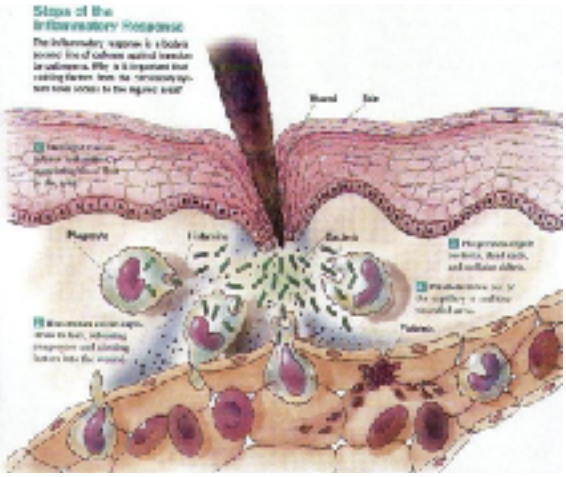
- White blood cells, play a part in phagocytosis
- Leave blood capillaries and migrate through the tissues to places of infection and injury
- Secrete substances that destroy bacteria before engulfing them or they engulf live bacteria and digest them

Macrophages

- Large phagocytic cell that develop from some leucocytes
- Some are wandering cells that move through tissue looking for pathogens and destroying them
- Some are fixed in one place and only deal with pathogens near them
- They either engulf and digest micro-organism or release substances that destroy them or eliminate many pathogens before an infection has a chance to take hold

<u>Inflammatory Response</u>

Inflammation- a response to any damage to the tissues



Purpose of Inflammation

- reduce the spread of pathogens, destroying them and preventing additional pathogens from entering
- remove damaged tissues and cell debris
- begin repairing damaged tissue

Signs of inflammation

- redness, swelling, heat and pain

How does the inflammatory response occur?

1. When stimulated by mechanical damage or local chemical changes, mast cells release histamine, heparin and other substances into tissue fluid. Mast cells are special cells present in most tissues which stimulate and coordinate inflammation
2. Histamine increases blood flow through the area and causes the walls of the blood capillaries to become more permeable so that fluid is filtered from the blood begins to leak out. It is the *<u>increased blood flow</u>* that causes heat and redness associated with inflammation, and *<u>the escape of fluid from the capillaries</u>* causes swelling
3. Heparin prevents clotting, so the release of heparin from mast cells prevents clotting in the immediate area of injury. A clot of fluid around the damaged area does form and this slows the speed of pathogen into healthy tissues
4. The chemicals releases by mast cells attract phagocytes. Macrophages and leucocytes actively consume micro-organisms and cell debris by phagocytosis
5. The *<u>abnormal conditions in the tissue stimulate pain receptors</u>*, and so the person feel pain in the inflamed area
6. The phagocytes, filled with bacteria, debris and dead cells, begin to die. The dead phagocytes and tissue fluid form a yellow liquid called pus

7. New cells are produced by mitosis and repair of damaged tissue takes place

Fever

- An elevation of body temperature usually experience during the course of an infection
- This change of body temperature is due to a resetting of the body's thermostat by the hypothalamus to a higher level
- When the body's thermostat rises suddenly the person feels cold and the body attempts to conserve heat (vasoconstriction, shivering etc.) and drives body temperature up rapidly
- After a period of time, the fever breaks and when this happens it is as though the body's thermostat has been reset to normal. The person appears hot and flushed (vasodialation, profuse sweating)
- High body temperature is believe to inhibit bacterial and viral growth. Heat speeds up chemical reactions and may help body cells repair themselves more quickly during a disease.
- A fever is harmful is the temperature goes to high. It is fatal at 44.4 - 45.5 C
- The resetting of the body's thermostat is due to substances called *pyrogens*. These are related by white blood cells during the inflammatory response to a foreign intruder and they act directly on the hypothalamus

Lymphatic System

A transport system that consists of

1. A network of lymph capillaries which join to form larger lymph vessels
2. Lymph nodes (glands), which are located along the length of some lymph vessels
3. Lymphoid tissue found in organs including the spleen, tonsils, thymus

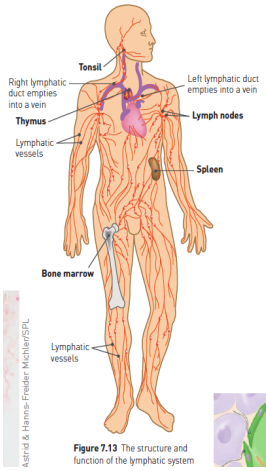


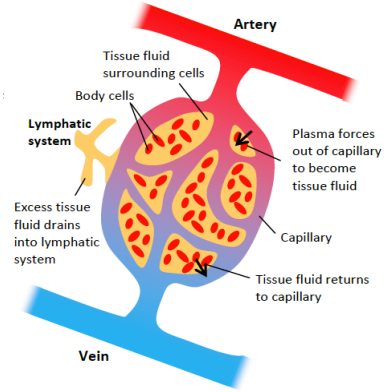
Figure 7.13 The structure and function of the lymphatic system

Functions:

1. To collect the fluid that escaped 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

How it works

1. At the arteriole end of the blood capillaries blood is under high pressure
2. This pushes fluid out of the gaps in the capillary walls into the surrounding tissues
3. This fluid contains plasma, dissolved nutrients and oxygen. It is called tissue fluid (intercellular fluid)
4. Some of this tissue fluid will return to the blood in the capillaries at the venous end, which is under low pressure
5. The excess tissue fluid then drains into lymphatic vessels and is called



lymph

6. This lymph passes through lymph nodes and is later returned to the blood via subclavian ducts of the lymphatic system

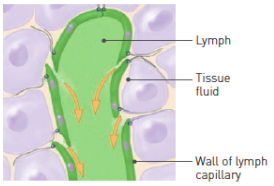


Figure 7.13d Lymph capillaries have blind ends.

Lymph vessels

- Lymph capillaries originate as blind-ended tubes
- Lymph capillaries are larger than blood capillaries and are more permeable
- Lymph capillaries drain into larger lymph vessels
- Pathogens in the tissue fluid (intercellular fluid) can pass into the lymph capillaries and be carries along in the lymph
- Movement of lymph is slow in the lymphatic system as it does not have a pump like a circulatory system
- Lymph is under low pressure and is pushed by action of skeletal muscles
- Lymph vessels contain valves to prevent back flow

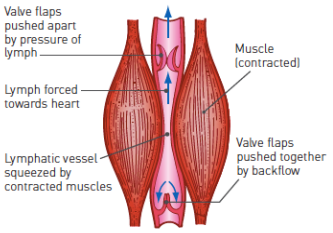


Figure 7.13a Lymph is pushed along the lymph vessels by the squeezing action of skeletal muscles.

Lymphoid organs

- Contain lymphoid tissue but are <u>not</u> part of the lymphatic system
- Examples: spleen, tonsils, thymus gland and bone marrow
- They contain lymphocytes and macrophages that engulf and destroy foreign particles

Lymph nodes

- Also called lymph glands
- Occur at intervals along lymphatic vessels.
- At the neck, armpit, groin and alimentary canal
- Surrounded by a capsule of connective tissue which extends into the node
- Are a store of lymphocytes (type of white blood cell)
- Lymph enters the node at one side, filters through the spaces, then leaves the opposite side
- They protect the body against infection by
  - trapping foreign particles and bacteria in their fibrous mesh (spaces criss-crossed by fibres)
  - macrophages then engulf and destroy them
  - storing lymphocytes (B and T cells) , which are circulated by lymph vessels, their role is in specific defence
  - site of antibody production (specific response by B cells)

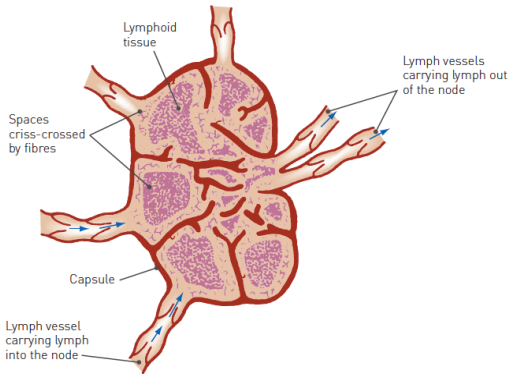


Figure 7.14 A section through a lymph node; the arrows indicate the direction of lymph flow

Antibodies

- Specialised protein that is produced in response to an non-self antigen
- Specialised proteins belonging to a group called immunoglobulins (Ig)

- 5 classes of Ig antibodies which vary in structure
- Antigens have specific **active sites** complementary to specific antibodies and when they combine they form the **antigen-antibody complex**
- This is how the antibodies bind to antigens (similar to the lock and key principle of enzymes)

Antigens

- A substance capable of stimulating a specific immune response, by activating lymphocytes and causing the body to produce specific antibodies
- They can be protein/ carbohydrate/lipid or nucleic molecules found on cell surfaces
- Antigens are large molecules which may be a virus particle, whole micro-organism or part of bacterium

Foreign (non-self) antigens- originate from outside the body

Examples: whole pathogen organism (virus/bacteria) or parts of the pathogen (flagella/ cell wall)
substances made by pathogens e.g. toxins
components of red blood cells from other people

Self-antigens- originates within the body and are normally recognised by the body as self

On the surface of antigens are regions that fit and bind to receptor molecules on the surface of the lymphocytes.
The binding of lymphocytes' receptors to the antigens' surface molecules stimulates the lymphocytes to multiply and to initiate an immune response against the antigen
When lymphocytes attack self-antigens, this can produce an autoimmune disease such as rheumatoid arthritis or allergies

Types of lymphocytes

1. B-cells
   - produced in the bone marrow
   - mature in the bone marrow
   - involved in antibody mediated response
2. T-cells
   - produced in the bone marrow
   - mature in the thymus
   - involved in cell-mediated response

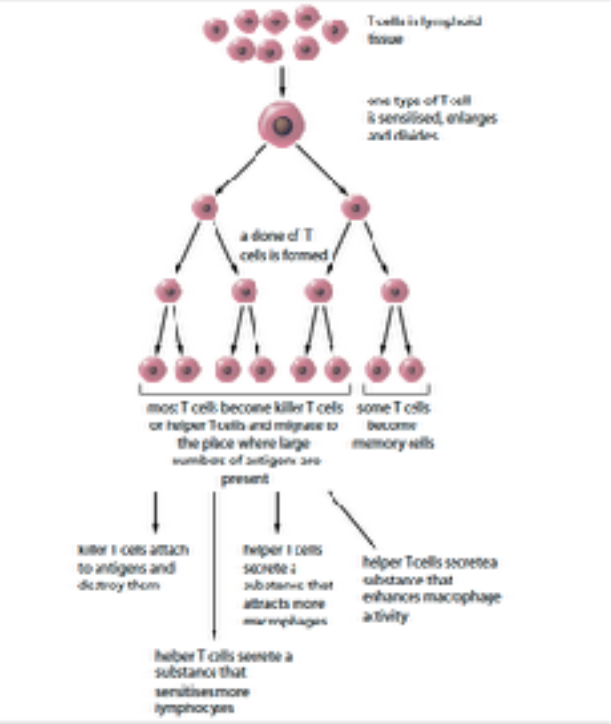
After maturation both cells will migrate to lymphoid tissue or circulate in the blood

Specific Immune Response

Immune response is a homeostatic mechanism. It helps to deal with invading micro-organisms or foreign substances and restores the internal environment to its normal conditions

- T-cells and B-cells work simultaneously

- The T-cells work on cells infected with the pathogen and the B-cells work on the pathogen existing outside the body's cells



Cell-mediated response

provides resistance to intracellular (host cell) 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' and each T-cell responds to a specific antigen

How it works

When a foreign antigen enters the body the following occurs:

1. A macrophage or B-cell engulfs the pathogen (antigen presenting cells)
2. It then displays antigen fragments on its cell surface and travels to the nearest lymph node to present the antigen to a helper T-cell
3. The helper T-cell then sensitises or activates the specifically programmed T-cell for that antigen
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, such as killer T-cells and migrate to the site of infection to fight it
6. A small number develop into memory T-cells and remain in the lymphoid tissue in case of future infections by the same antigen
7. Suppressor T-cells help to stop the immune response

Types of T-cells

1. Helper T-cell (important to both cellular and antibody response)
   - secrete substances that result in lymphocytes becoming sensitised and intensifying the response
   - activates B cells to release antibodies
   - attract more macrophages to site of infection
   - release substances that intensifies phagocytic action of macrophages

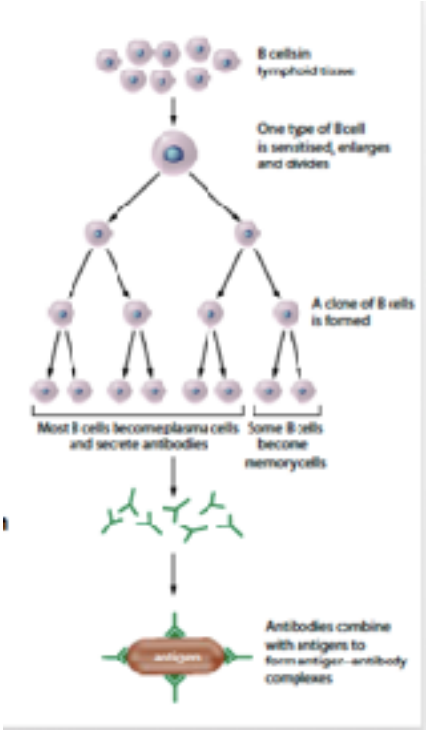
2. Killer T-cells
   - migrate to the site of infection to destroy cells infected by pathogens (viruses and sometimes bacteria)
   - they attach to the cells and secrete a substance to destroy the antigen

3. 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

4. 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 disease once they eliminate the pathogen before you exhibit any symptoms of the disease on subsequent exposures

Antibody mediated response (humoral response)

provides resistance against viruses, bacteria and bacterial toxins before they enters the body's cells (extracellular defence)
involves B-cells that produce antibodies (proteins) that inactivate antigens, each specific to a particular non-self antigen



How it works:

1. When activated by a helper T-cell or antigen the B-cell is sensitised and enlarges
2. It then divides into a group of cells forming a clone (a group of cells with the same genetic characteristics)
3. Some of these cells develop into memory B-cells (a type of cell which recognises an antigen to which the body has previously been exposed to)
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

The antibodies help fight infection by either:

1. Binding to surface antigens on bacteria, coating them, making it easier for macrophages to phagocytose them
2. Binding to surface antigens on viruses preventing them from invading cells
3. Agglutinate particles (cause particles to clump) making them less mobile meaning phagocytes can engulf them easier
4. Make soluble particles insoluble so they are easily consumed by phagocytes

5. Combining with foreign enzymes or toxins to inactivate them by inhibiting reactions with other cells
6. Dissolve organisms

Table 11.1 Summary of immune responses

Antibody-mediated immunity (humoral immunity)	Cell-mediated immunity (cellular immunity)
Works against bacteria, toxins and viruses before they enter the body's cells; also against red blood cells of a different blood group than the person.	*Works against transplanted tissues and organs, cancer cells and cells that have been infected by viruses or bacteria; also provides resistance to fungi and parasites.*
1 Foreign antigen reaches lymphoid tissue. **2** Certain B-lymphocytes are stimulated to undergo rapid cell division. **3** Most new B-cells develop into plasma cells, which produce antibodies and release them into blood and lymph. **4** Antibodies combine with the specific antigen and inactivate or destroy it. **5** Some of the new B-cells form memory cells.	**1** Foreign antigen reaches lymphoid tissue. **2** Certain T-lymphocytes are stimulated to undergo rapid cell division. **3** Most new T-cells develop into killer T-cells or helper T-cells, which migrate to the site of the infection. **4** Killer T-cells destroy the antigen, while helper T-cells promote phagocytosis by macrophages. **5** Some sensitised T-cells form memory cells.

Primary response

The immune reaction for the first exposure to an antigen

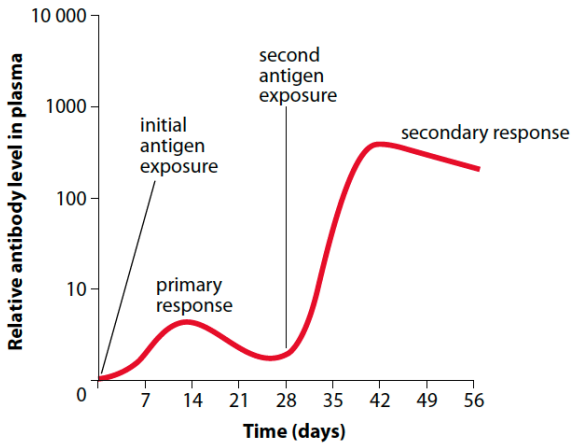
- takes time for B-cells to multiply and develop into plasma cels
- response is fairly **slow** and takes several days to build up antibodies
- response leaves memory cells to that antigen for future exposures
- individual tends to get sick during them time as they have no immunity against this disease

Secondary response

The immune reaction for the second and subsequent exposure to an antigen

- response is **much faster** due to the activity of memory cells
- plasma cells form quickly, with antibody levels rising rapidly
- usually so quickly that no illness results to the individual as they are immune

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



Types of immunity

Immunity

Immunity is resistance to infection by invading micro-organisms

The body has the ability to respond quickly enough to deal

with any invasion by pathogenic organisms before symptoms of the disease appear.

- 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

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 (vaccines)
Active Immunity- where we manufacture our own antibodies due to the presence of memory cells **(make antibodies)**
Passive Immunity- where we are given antibodies made by someone else **(given antibodies)**

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 (attenuated)
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.

Vaccines
Immunisation- programming of the immune system so that the body can respond rapidly to infecting micro-organisms either naturally or artificially.
People who have had chickenpox or measles once in their life are now immune of the rest of their lives due to natural active immunity
Vaccination- artificial introduction of antigen of pathogenic organisms so that the ability to produce the appropriate antibodies is acquired without the person having to suffer the disease
Vaccine- antigen preparation used in artificial immunisation.

The immunised individual does not contract the disease but the vaccine trigger the immune response thereby manufactures antibodies (memory cells) against the antigen

Types of Vaccines
Attenuated vaccines- they use a weakened form of the living pathogen, microorganism with reduced ability to produce disease symptoms (microorganism with reduced virulence). Its antigen is intact but its ability to cause disease has been reduced.
e.g. MMR vaccine (measles, mumps and rubella), polio, tuberculosis, yellow fever

A dead form of the pathogen- with an intact surface antigen. Immunity in this way is not as prolonged
e.g. whooping cough, typhoid, cholera

Inactivated form of a toxin **(toxoid)-** for pathogens that cause disease by producing toxins
e.g. diphtheria and tetanus

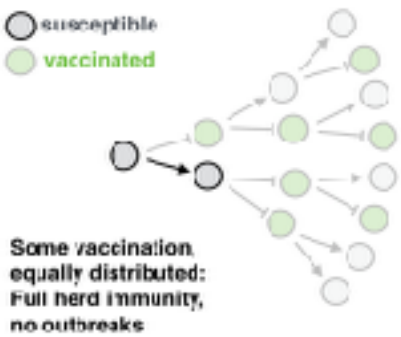
Sub-unit vaccine- a fragment of the pathogen containing the antigen is used to provoke the immune response.
e.g. hepatitis B and HPV

How are vaccines manufactured?
Recent trends in vaccine development involve manipulating the pathogens DNA
For example recombinant DNA
- removing genes which code for toxin production
- modifying the characteristics of the pathogen by slightly changing the DNA in the micro-organisms so that the pathogen is less virulent (disease-causing)
- inserting certain DNA sequences from the pathogen into harmless bacterial cells. The chosen DNA sequences causes the production of antigen that are characteristic of the pathogen. Vaccination with the harmless bacterium results in immunity against the pathogen

How are vaccines delivered into the body?
- injected using a syringe (most common)
- fine spray into the nostrils
- skin patches
- including vaccines in food (ingesting)

Problems with vaccines
- risk of side effects and serious adverse allergic reactions
- some older vaccines give good protection against the disease but are only effective for a short period of time

Herd Immunity
- A type of group immunity that occurs when such a high proportion of people in a population are immunised that it protects those who are not immune.
- When there are a large number of immune individuals in a population, there is less chance of the disease being transmitted between them.
- Herd immunity not only reduces the chance of disease but also



increases the overall immunity of the population.
- It is crucial in protecting people who cannot be vaccinated such as newborn babies under 2 months old, those with immune system problems and those too ill or old to receive vaccines
- Herd immunity does not protect against all vaccine-preventable diseases and it only works for diseases that are spread directly between people (i.e. they are contagious) and doesn't protect against infectious diseases. For example tetanus
- Herd immunity and vaccines had helped to eradicate one human disease, smallpox. It was caused by the variola virus and it was eradicated in 1980 after enough people were vaccinated that it could no longer spread.

Vaccination Programs

A successful programme will provide long term and wide-spread protection against disease

- Ideally herd immunity is developed, 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
- It is important to *vaccinate children at an early age* as they are more vulnerable to infection due to an immature immune system
- However, it has to be done one they are unlikely to have natural passive immunity in the form of antibodies from the mother in the placenta and breast milk as the antibodies would recognise the antigen in the vaccination as a foreign material and destroy is without evoking an immune response
- *Booster shots* may be required to ensure that enough memory cells are created for long lasting immunity
- The timing of the booster shot has to be considered to ensure there are no remaining antibodies present from the first vaccination
- Vaccinations need to be *derived in a manner that is safe, hygienic and cost effective*
  - Needles/ Injections are the most effective method but pose issues in less developed countries
  - Other methods being developed include
    - Syrup (polio)
    - Nasal sprays
    - Skin patches
    - Non-plant foods (ingested)

Australia has a vaccination schedule that aims to have children fully vaccinated against common diseases by the age of 4

- Hepatitis B
- Diphtheria
- Tetanus
- Mumps
- Measles
- Polio and Rubella
- Rotavirus
- Chicken pox
- Meningococcal C

For some disease a vaccination is required/recommended every year. E.g. influenza
This is due to the high mutation rate in the virus that causes the antigen to constantly change. This means that memory cells gained from one infection wouldn't recognise the antigen for subsequent infections as the antigen shape changes.

Booster shots

- When an individual is vaccinated, their immune system will activate a certain number of B-cells. These cells will multiply and some produce antibodies and others will become memory cells. These can last for decades and are able to produce the necessary antibody when exposed to the antigen again
- In most cases, the first dose of a vaccine does not enable enough B-cells to become activated and booster shots are required to activate more B-cells thus producing more antibodies
- This in turn results in greater protection from the disease-causing micro-organism that the person was vaccinated against
- The timing of the booster shot is also important. If it is given too soon, the antibodies present in the blood will eliminate the material in the vaccine before more B-cells can be activated.
- Usually a period of 2 months waiting time

Antibiotics

Definition: Drugs that are used to fight infections of pathogenic bacteria. They are selective and will attack bacterial cells but not our own

Types of antibiotics

Bactericidal antibiotics- kill bacteria by changing the structure of the cell wall or cell membrane or by disrupting the action of essential enzymes
Bacteriostatic antibiotics- stop bacteria from reproducing by disrupting protein synthesis

Broad spectrum antibiotics- affect a wide range of different types of bacteria
Narrow spectrum antibiotics- only effective agains specific types of bacteria

Antibiotic resistance

Using antibiotics when it is not necessary or not finishing the prescribed dose of antibiotics may mean that they will not work in the future for the individual.
Occurs due to overuse and misuse of antibiotics

Antibiotics do not work on viral infections. Viruses are difficult to kill as they live and replicate inside host cells, so it is hard to differentiate them from host cells. Viruses and bacteria have different structures and ways to reproduce, such as viruses not having cell walls.

Antiviral Drugs

Drugs that are used to fight off viral infections by interfering with a virus's ability to enter a host cells and replicate itself with a host cells DNA.

Antivirals work in two main ways

1. affecting DNA/RNA of viruses or the protein coat
2. inhibiting viruses life-cycle and their ability to invade and affect body cells.

Gene Pools Notes

Gene Pools

Population- a group of organisms of the same species living together at a particular place at a particular time

- When studying populations, geneticists prefer to consider the characteristics of the population as a whole rather than those of individuals that make up the populations, pooling the genotypes of all the individuals capable of reproducing

Gene Pool- sum of all alleles in a given population

Allele Frequencies- how often each allele of a gene occurs in the gene pool for that population

- Population that differ in characteristics they possess can be due to differing frequencies of various alleles of a gene in their respective gene pools.
- Thus, any two populations having differing characteristics are likely to have different gene pools

Over time, the frequency of particular alleles in a population may change. Such changes may be due to:

I. *chance events* –e.g a mutation that alters the expression of a gene

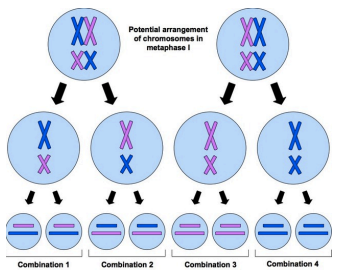
II. *natural means* – changes in the environment which may result in variation of allele frequencies

Changes to the frequency of alleles in a gene pool allow populations to be compared at different times or in different locations

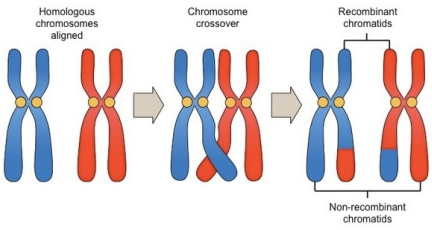
Evolutionary Mechanisms

Variations that exist between individuals within a species are due to:

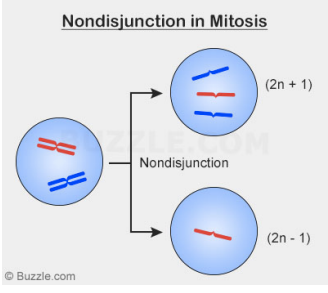
1. **Random Assortment**
   - Random assortment of chromosomes during meiosis results in gametes that have a huge number of possible chromosome arrangements that originally came from the male parent and the female parent



2. **Crossing Over**
   - Crossing over of the chromosomes during meiosis may results in pieces of chromatid being broken off and attaching to a different chromatid.
   - This results in a changed sequence, or recombination, of the alleles along the resulting chromosomes



3. **Non-disjunction**
   - Where one of more members of a chromosome pair fail to seperate during meiosis, This results in gametes that have more or less than the



correct number of chromosomes
- If such gametes are involved in fertilisation, the resulting embryo will have the incorrect number of chromosomes

4. Random Fertilisation
- Each person will produce a huge number of different sperm or eggs in regards to the alleles they contain
- Any sperm can fertilise any egg and thus there is an almost infinite number of possible combinations of alleles in the offspring

5. Mutations
- Permanent changes in the DNA of a chromosomes
- May result in totally new characteristics in an individual
- If a mutation is beneficial and occurs in the gametes, it can be passed on from generation to generation

Changes to allele frequencies in gene pools

1. Mutations
- Introduce new and different alleles into the gene pool
- If the 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 onto subsequent generations
- Survival of the fittest
- Selection of favourable alleles

3. Random Genetic Drift
- Random, non-directional variation in allele frequencies
- Occurs only in small populations
- The occurrence of characteristics as a result of chance, rather than natural selection

Example 1- Dunker Population
- Dunkers live in Pennsylvania, but originally came from Hesse in Germany
- They descend from Old German Baptist Brethren who came to the US in the early 18th century
- Their religion does not allow them to marry outside their group and thus they constitute of an isolated breeding population within the total population of the US

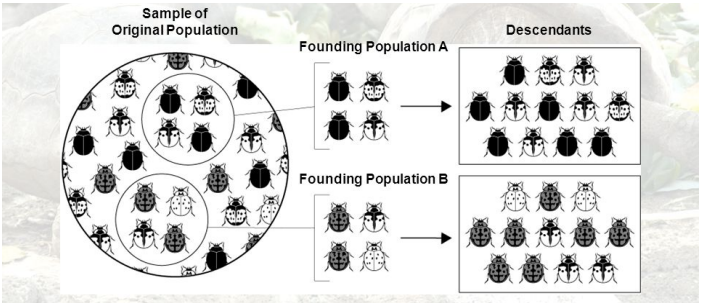
- Studies investigated a number of easily measured physical traits such as frequency of ABO, Rh and MN blood groups, mid-digital hair, left or right handedness, attached or free earlobes
- For most of the traits, Dunker's varied in allele frequency from the present day population in Germany and also from the surrounding American population
- Environment for both the Dunkers and the surrounding American population is essentially the same so natural selection would not account for the differences in allele frequencies
- Random genetic drift accounts for these differences

Example 2- Isolated population of Australian Aborigines

- Isolated population of the islands of Bentinck and Mornington in the Gulf of Carpentaria
- Originally, these islands were part of the mainland. Rising sea levels cut them off and populations they contained became isolated
- Mornington Islanders maintained some contact with the mainland by using smaller islands to "hop" from island to mainland
- Blood group frequencies of the islanders have been studied and compared with those of the population occupying Bayley Point on the mainland
- Occupants of Bentinck Island show allele frequencies for blood groups that fall outside the range for Aborigines in the rest of Australia
- There is a high proportion of I^B and a complete absence of I^A unlike the mainland which has a high proportion of I^A and low proportion of I^B

Founder Effect

- Type of genetic drift that occurs when a new population is formed by a small number of individuals
- Small sample size can cause marked deviations in allele frequencies from the original population



Example 1- Pitcairn Island

- A small island in the Pacific was inhabited in 1790 by the descendants of nine mutineers together with 6 men and 12 women Polynesians from Tahiti
- Due to their isolation, there has been very few newcomers to the population and so few alleles have been introduced from outside
- Descendants from the original Pitcairn Island show less genetic diversity than the original parent population because they all descended from the small number of original settlers

Example 2- Finland

- Finland's current population is believed to have come from a small group of individuals who settled in the south-western part of the country approximately 2000 years ago
- Since the initial migration, the population has remained relatively isolated with little immigration
- Gene pool of the Finn's is quite different from gene pools in neighbouring European nations

Example 3- Pingelap

- In 1755 a typhoon reduced the population of the tiny island in Micronesia to 20 people, forming the founding population for the current inhabitants
- Some of the survivors were heterozygous for achromotopsia (total colour blindness)
- Incidence of achromotopsia is 5% in Pingelap, but in the world it is 0.0033%
- 30% of the population of Pingelap are carriers

Example 4- Tristan De Cunha

- Isolated group of islands in the South Atlantic Ocean between South Africa and South America
- Current population can be traced back to 15 British immigrants who formed the first permanent settlement in 1816
- There have been few migrations
- There are only seven surnames on these island which has about 250 inhabitants
- The small founding population and subsequent isolation has produced a gene pool that is quite different from the British population today

4. Migration

- Gene flow from one population to another
- Immigrants to a certain country can bring alleles that may not already be present in that population, resulting in allele frequencies of that gene to be altered

Example 1- China

- In the past, Chinese population consisted of only Rh+ blood group
- When European countries began trading with China in the 16th Century, European immigrants and sailors introduced Rh- allele in the Chinese population
- Frequency of this allele is still relatively low in China compared to other countries

Example 2- Arrival of Europeans in Australia

- Prior to colonisation by the British in 1788, Indigenous population of Australia has no contact with European disease and very little genetic resistance that Europeans had developed over time

- Chickenpox, smallpox, influenza and measles spread throughout the Aboriginal population
- Approximately 90% of the decline in Aboriginal population was a result of disease
- Allele frequency of the surviving population changed and survivors were more likely to have some genetic resistance
- Thus, natural selection was occurring, but at the same time interbreeding between Aboriginal people and colonists would have introduced new alleles into the Aboriginal population

5. 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 results in population becoming less alike as they develop characteristics better suited in the development of seperate gene pools
- For early human populations, most common barriers to interbreeding were geographical barriers (oceans, rivers, mountain ranges, large lake systems, deserts, ice sheets)
- Today these barriers are sociocultural barriers (economic status, educational background, social position, religious group, language, other social and cultural factors)

6. Genetic Diseases

- An allele causing an inherited, fatal disease would be expected to gradually be eliminated from a population because people with the allele would die and not pass it on to the next generation
- However, sometimes alleles that cause serious disease do persist in certain populations

Example 1 – Tay-Saches Disease

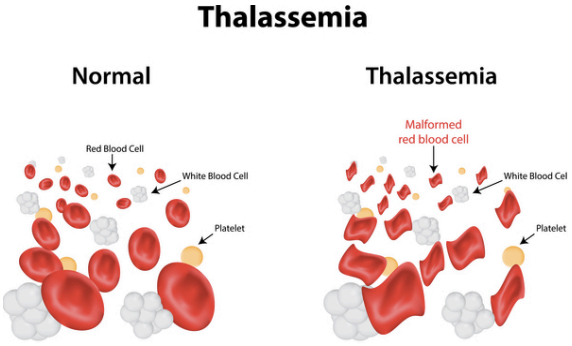
- Hereditary disorder of lipid metabolism
- Caused by a missing enzyme that results in the accumulation of a fatty substance in the nervous system
- Death usually occurs by age 4/5
- Populations affected include

A. French Canadians of Quebec

B. Cajuns of Louisiana, USA – ethnic groups who have been reproductively isolated for several hundred years because of language differences, mutations may have entered the Cajun population when a Jewish family assimilated into the Cajun society
C. Ashkenazi Jews around the world – Jewish descent from Eastern Europe (non-random mating)

- Frequency worldwide is very low, approximately 1 in 500,000 births, however for Ashkenazi Jews, incidence is much higher 1 in 2,500
- Speculation of cause – high frequency of the allele in this population
  - Genetic drift- Jewish populations have tended to be small and isolated, factors that increase the chance of genetic drift
  - Individuals who are heterozygous (have 1 allele for Tay-Saches) appear to have an increased advantage in situations where Tuberculosis (TB) is prevalent.
  - Individuals with 2 normal alleles would be more susceptible to TB and possibly die, individuals with 2 Tay-Saches alleles would die early in life
  - Therefore, heterozygotes would have a survival advantage and would be more likely to reproduce and pass on their alleles to the next generation
  - Due to discrimination, the Ashkenazi Jews often found themselves isolated in crowded ghettos under conditions that would increase the threat of TB, leading to the frequency of allele for Tay-Saches to be maintained in the population

Example 2 – Thalassemia

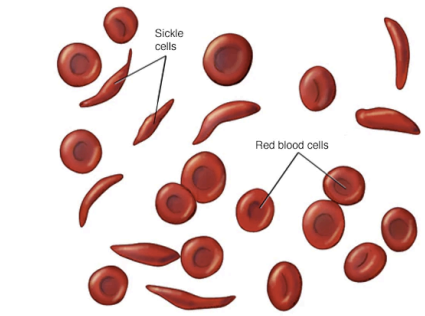


- Marriage between cousins was once common among people inhabiting countries around the Mediterranean
- In these populations, thalassemia, recessive disease in which anaemia results from defects in the formation of haemoglobin, is relatively high
- In Australia, thalassemia occurs in people of Mediterranean origin, especially migrants from Italy and Greece and their children
- People with thalassemia require frequent blood transfusions throughout their life and special medications to remove excess iron that tends to build up in their body

Example 3 – Sickle Cell Anaemia

- Occurs mainly in black Africans or in people of black African ancestry
- In the tropical zone of Africa, up to 40% of some populations carry the allele for sickle-cell anaemia
- Disease occurs when a person inherits the allele from both parents
- It results in the red blood cells being crescent shaped (or sickle shaped)
- Disease is usually fatal, as the sickle shaped cells do not carry as much oxygen as normal red blood cells and they stick together, thereby blocking small blood vessels

- Individuals with one allele for sickle-shaped cells show no ill effects unless oxygen is in short supply. When this occurs, their red blood cells show mild sickling
- These individuals suffer from **sickle-cell trait**
- Sickle-cell trait provides certain advantages for those who have it
- It provides a degree of immunity to malaria, a disease prevalent in parts of the world where sickle-cell allele is found
- For this reason, the allele is maintained in areas where malaria is present



Example 4 – Amish populations

- Isolated populations such as the Amish of USAs have a much higher incidence of genetic disorders than the wider US population

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 characteristics being displayed by the parents being passed on to their offspring

2. **Birth Rate**
   - All living organisms reproduce at a far greater rate than that at which the available food supply and other resources increase and this would result in overcrowding

3. **Nature's Balance**
   - Although 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 who were more likely to survive= *survival of the fittest*

Survival of the fittest is possible because…

1. There is variation within a 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

Today…

- Natural selection is viewed as *"the selection of those alleles in a population that give an organism a greater survival advantage"*
- Organisms that survive will pass on favourable alleles to their offspring
- Gradually over a period of time, the characteristics of a population changes so that it becomes better suited to its environment
- Where the environment is gradually changing, characteristics that enhance survival will enable succeeding generations to gradually adapt to it
- ***Individual organisms do not adapt, the species adapts to its environment by natural selection and the process of its adaption takes many generations***

The process of natural selection can now be looked at in terms of the frequencies of the allele in the gene pool of a population
If the environment tends to favour a particular characteristic, more of the alleles for that trait will be passed on to the next generation, resulting in a change in the frequency of that allele in the gene pool resulting, over time, in that characteristics being becoming more frequent in the population

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 survival 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

Example 1- Body Stature

- Body stature can be correlated with resistance to cold and heat
- Initially human gene pool would have contained alleles for a whole range of statures from the short-bodied, long-limbed physique of present day Africans, to the long-bodies, short-limbed stature of the Inuit of today

Hot Climate

- Individuals who have short bodies and long limbs have a larger surface area to body volume
- Lose more heat – survival advantage in hot climates

Cold Climate

- Individuals who have long bodies and short limbs have a smaller surface area to body volume
- Lose less heat – survival advantage in cold climates

Example 2- Sickle Cell Anaemia

- formed by a mutation of the gene responsible of the production of normal haemoglobin
- substitution of valine for glutamic acid during the formation of the haemoglobin protein
- mutation affects only one of the 287 amino acids of the haemoglobin molecule
- The affected haemoglobin is referred to as haemoglobin S

Speciation

Process of producing two new species

1. Variation in a population
2. Isolated population – no gene flow
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 –> speciation has occurred

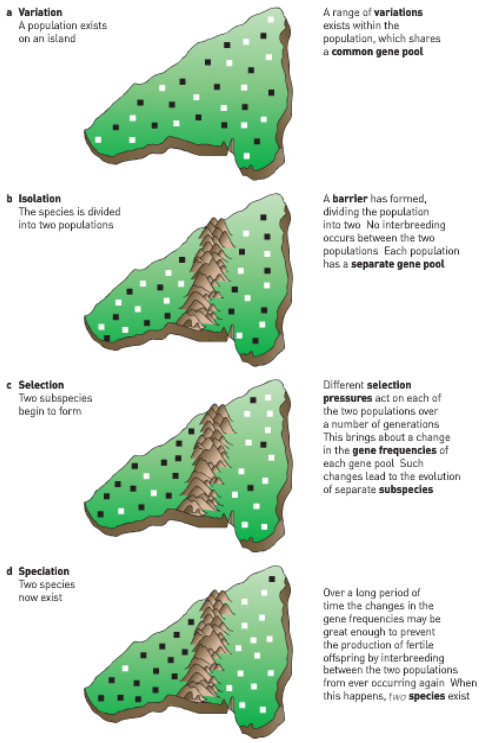


Figure 14.14 A diagrammatic representation of variation, isolation, selection and speciation

Mutations Notes

Mutations are permanent structural alterations in DNA.

- They occur through changes to genes or chromosomes.
- In most cases, DNA changes either have little effect or cause no harm
- Occasionally a mutation can improve an organism's chance of surviving and passing the beneficial change to its descendants

Mutation- a change in a gene or chromosome leading to new characteristics
Mutant- an organism with a characteristics resulting from a mutation

Types of Mutations

1. *Gene Mutations-* changes in a single gene so that the traits normally produced by that gene are changed or destroyed
2. *Chromosomal Mutations-* all or part of a chromosome is affected

Mutagens increase the rate at which mutations can occur
Examples of mutagens include mustard gas, formaldehyde, sulfur dioxide, some antibiotics, UV light, X-rays, cosmic rays, radiation from radioactive waste

Somatic Mutations

- affects body cells
- the individual is affected as each time mutant body cell divides it is passed onto the daughter cells
- the mutation is not passed on and once the individual dies the mutation is lost
- somatic mutations are involved in many cancerous growth that may be a result of a mutagenic agent

Germline Mutations

- affects reproductive cells (sperm or egg)
- the individual is unaffected
- the individual produced gametes with changed DNA and diseases can be passed onto the offspring
- however, if conception occurs using the affected gametes, the embryo is often actually aborted early in the pregnancy
- for example PKU (phenylketonuria) arises throughout a mutation during the formation of gametes, involves a missing enzyme

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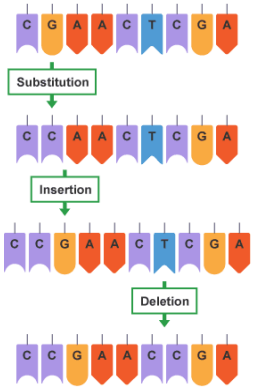
Gene Mutations



Genetic information is contained in the sequence of bases in DNA.

Point mutations- a change in just one base

Gene mutations are a change in a single gene so that the amino acid produced changes and thus so does the protein produced. This alters the traits expressed by the gene.

Types of Gene Mutations

Substitutions- Substitution of one base for another

1. Silent- no effect on the amino acid and protein produced, thus no effect
2. Nonsense- produces the stop codon (UAG, UAA, UGA)
3. Missense- produces the wrong amino acid thus the wrong protein

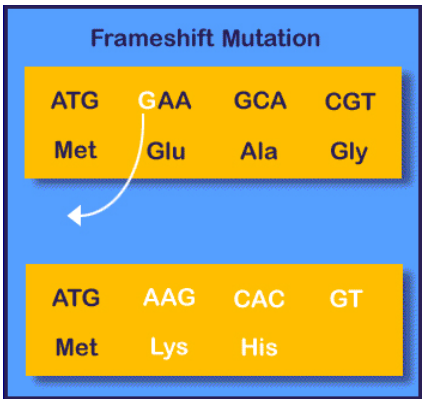
	No mutation	Point mutations		
		Silent	Nonsense	Missense
DNA level	TTC	TTT	ATC	TCC
mRNA level	AAG	AAA	UAG	AGG
protein level	Lys	Lys	STOP	Arg

Insertion- new bases inserted

Deletion- certain bases deleted

Frameshift- changes in the way the bases are read

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



Effect of point (gene) mutations

Can be

1. no effect on protein
2. abnormal protein (non-functional)
3. missing protein

- Proteins include enzymes, antibodies, structural proteins, membrane transport channels etc
- 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 e.g. protein injected, gene therapy

Lethal recessives

Recessive alleles that if inherited in the homozygous condition result in the death of the embryo, foetus or child

For example: Tay-Saches disease

- A disorder of lipid metabolism that is inherited in an autosomal recessive pattern
- It occurs most frequently in individuals of Jewish descent from eastern Europe

- the missing enzyme results in the accumulation of a fatty substance in the nervous system
- a baby with two recessive alleles for TSD develops normally for the first few months and then deteriorations causing metal and physical disabilities begins and death usually occurs in early childhood

Examples of gene mutations

Albinism

- result of one missing protein, tyrosine (the enzyme which codes for melanin production)
- absence of pigment from the hair, skin and eyes
- prone to skin cancers

Duchenne muscular dystrophy

This condition affects boys due to:

- germline mutation in the mother, which can then be inherited by her sons
- or germline mutation in a male zygote so that the child develops the disease

- It is the wasting away of the leg muscles and then later the arms, shoulder and chest
- It becomes apparent around the age of 3 to 5 years.
- As the boy gets older muscle tissue if replaced with fat and death occurs due to the failure of respiratory muscles (at about 20-25 years)

Sickle Cell Anaemia

- The sickle cell mutation involves the substitution of one base for another in the HBB gene, causing a single amino acid to be altered
- Haemoglobin clusters together to form fibre, which deforms the red blood cells into sickle shape
- it is usually fatal as the sickle shaped cells do not carry as much oxygen as normal red blood cells. they also stick together and block small blood vessels

Cystic Fibrosis

- Autosomal recessive condition
- Mutation on chromosome 7
- Over 500 different recessive mutations of the CFTR gene have been identified including deletions, missense, nonsense, terminator codon
- The gene has the code for 1480 amino acids that make up a protein that regulates the passage of chloride ions across the cell membrane
- It is common in Caucasians as 1 in 26 are carriers
- Without the correct protein the affected person suffers from a variety of symptoms (respiratory, digestive, reproductive, excretory)
- Defective chloride transport affects osmosis –> thick secretions –> blockages –> inflammation and infection

Huntington's Disease (or Huntington's chorea)

- Autosomal dominant mutation of the HD gene which is caused by an increase in length of a CAG repeat region
- Mutation is on chromosome 4
- Mutant gene forms defective protein, Huntingtin
- Progressive selective nerve cell death associated with chorea (jerky ,involuntary movements), psychiatric disorders

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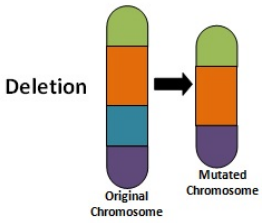
Chromosomal Mutations

Involve all of part of a chromosome and therefore affect a number of genes

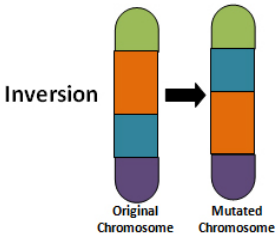
Occurs due to errors during cell division especially egg and sperm cells therefore the offspring are affected

Types of chromosomal mutations



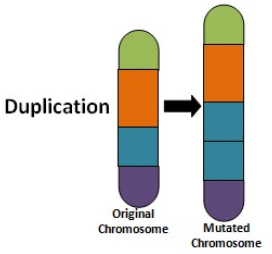
Deletions

- part of a chromosome is lost due to breakage



Inversion

- breaks occur in a chromosome and the broken piece joins back in the wrong way around, changes the order of genes on the chromosomes and disrupts the pairing of homologous chromosome in meiosis

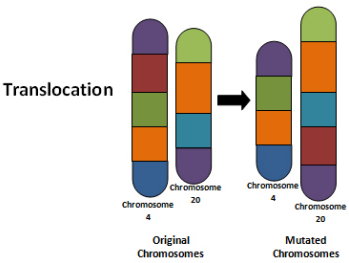


Duplication

- occurs when a gene sequence is repeated
- a section of a chromosome occurs twice, this may happen in part of a chromatid breaks off and joins onto the wrong chromatid, extra DNA

Translocation

- involves two chromosomes that are not homologous
- part of one chromosome is transferred to another chromosome
- part of a chromosome breaks off and is rejoined to the wrong chromosome



Effects of deletions, inversions, duplication and translocation

- Depend on their locus (genes involved)
- *Deletions*
  - Gametes missing genes are often inviable (can't survive) or result in miscarriage early in the pregnancy.
  - Known to cause Wolf-Hirschorn syndrome, Jacobsen syndrome

- *Inversions*
  - All genes are still present therefore offspring is unaffected
  - However, unusual order causes difficulties in crossing over during meiosis (inversion loop)
  - Leads to infertility
- *Duplication-*
  - Extra DNA can cause symptoms
  - Known conditions include Charcos Marie tooth disease type 1A
- *Translocation-*
  - All DNA is still present so the organism has no symptoms
  - However, gametes will receive chromosomes with extra or missing DNA
  - Leads to infertility

Nondisjunction

- During meiosis chromosomes fail to seperate
- This causes gamete to have too many or too few chromosomes
- The result is that one daughter cell has an extra chromosome and one daughter cell has one less chromosome

Aneuploidy

- A change in the chromosome number (may involve autosomes or sex chromosomes)

Disomy

- Two copies of each chromosome, normal for human somatic cells

Trisomy

- Three copies of a chromosome

Monosomy

- One copy of a chromosome

One extra (trisomy) or one missing (monosomy) chromosome has major consequences as there are many extra genes are therefore extra proteins being produced. It is usually fatal and results in a miscarriage. They result in a number of syndromes

Why are they called syndromes?

- When a disease causes multiple effects it is called a syndrome
- Virtually all chromosome abnormalities are in this category

Maternal Age Effect

Many aneuplodies show a maternal age effect, where incidence increases with the age of the mother

Maternal age effect most probably arises because

- All eggs are present at birth but are suspense in their development in early prophase until puberty

- A woman on average will produce about 400 eggs in her lifetime (12 per year)
- Therefore by the end of her reproductive life, the egg cells that remain are old and there is a greater chance that errors in meiosis will occur

A similar, though less marked effect is exerted by the age of the father, linked to smoking and chemical exposure in the father

Examples of chromosomal mutations

Trisomy 16

- The most common trisomy in humans, occurring in more than 1% of pregnancies
- This conditions also usually results in spontaneous miscarriage in there first three months of pregnancy

Partial monosomy 5- Cri du Chat

- A rare genetic disorder due to a missing protein of chromosome 5
- The infant's cry sounds like a meowing kitten, due to problems with the larynx and nervous system

Trisomy 13- Patau Syndrome

- Occurs in about 1 out of every 5000 live births
- However, more than 80% of children with trisomy 13 die within a month of birth
- Individuals with mental retardation, a small head, an extra finger on each hand, a cleft palate and/or cleft lip and malformations of the ears and eyes
- The extra chromosome 13 can come from either the mother's egg cell or the fathers sperm cells
- Result in an extra chromosome 13 in each of the body's cells

Trisomy 18- Edward Syndrome

- Second most common trisomy after Down Syndrome but much more severe
- Occurs in about 1 in 6000 live births
- Females are affected more than males (ratio of 1:2 of males : females)
- It is commonly a result of non-disjunction in meiosis I or II, more rarely translocation

Phenotype:

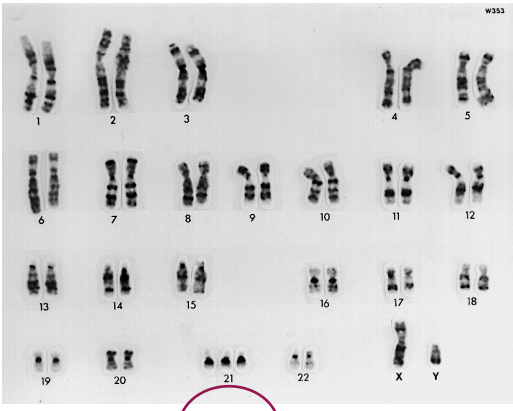
- Ear deformities
- Heart defects
- Spasticity and other defects
- About 30% of babies with this condition die in the first month. fewer than 10 % survive the first year
- Mosaicism (only some cells affected) probably accounts for most of the survivors

Trisomy 21- Down Syndrome

- Three of chromosome 21, instead of the normal two
- Most common form of aneuploidy in human newborns that remain viable at birth
- Incidence rate is 1 in 800 births in woman giving birth at 30 to 31 years of age
- Relatively frequent in children of older mothers
- Also occurs for partial trisomy

Causes of Down Syndrome:

1. In 95% of all cases, it is a result of non-disjunction of chromosome 21 during meiosis (see karyotype on the right)
2. 3-4% result from translocation of chromosome 21 (usually on to chromosome 14)
3. 1-2% arise from a failure during mitosis (non-disjunction of chromosome 21) in a cell of a very early embryo. The resulting individual is a 'mosaic' of normal and Down Syndrome cells



Klinefelter Syndrome

- Either an extra X or Y chromosome
- XXY, XYY
- Individuals with trisomy XXY are normal as boys but develop Klinefelter's syndrome as adults
- They have small testes that do not produce sperm, the breasts are enlarged and the body hair is sparse
- Occasionally, the individual is mentally retarded

Turner's Syndrome- monosomy X (XO)

- Lack of secondary sexual characteristics as the sex organs don't mature at adolescence
- Infertile

XYY

- Normal male traits
- More acne
- Lower than average IQ
- Often tall and thin
- Associated with antisocial and behavioural problems

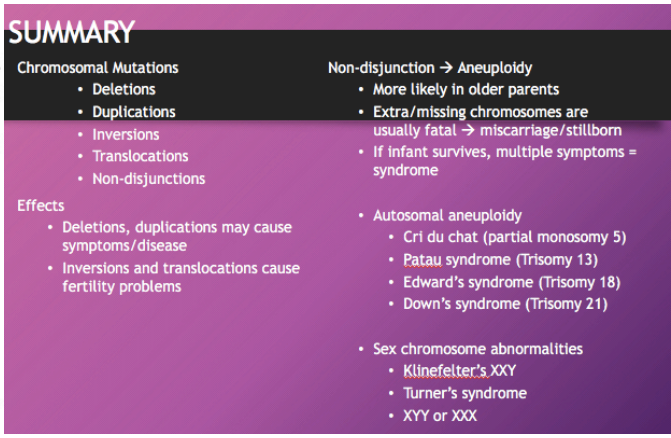
XXX- Trisomy X

- Female
- Little or no visible differences
- Tall stature
- Learning disablities

- Limited fertility

Sex Chromosome Disorders

Abnormal Chromosome Combination	Medical Name	Characteristics of Individual
XXY	Klinefelter syndrome	Male genitals, but with female secondary sex characteristics. Penis, scrotum, and testes are small; enlarges breasts. Sometimes timid and withdrawn; possible learning disabilities; sterile.
XO (no Y present; only one X)	Turner syndrome	Female external genitals; ovaries lacking; lack of menstruation, pubic hair and breast development. Stunted growth, with several body abnormalities. Sense of direction and spatial relationships may be abnormal; may be mentally retarded.
XO/XY	Mixed gonadal dysgenesis	May have female or male genitals, or a combination of the two. Usually no other bodily abnormalities, except may not mature sexually without treatment, and tend toward short body stature.
XYY	Supernumerary Y syndrome	Appearance of normal male. Tend to be tall in stature. May show some lack of control over impulsive behaviors. Usually average intelligence levels.
XXX	Triple-X syndrome	Appearance of normal female. Sometimes infertile. Occasional impairment of intelligence.
XX/XY	May be a true hermaphrodite	Variable. Have some combination of both ovarian and testicular tissues. Usually have uterus. External genitals may be distinctly masculine or feminine, or may be an ambiguous combination of both. At puberty, most experience breast enlargement, and the majority menstruate.



Heterozygote advantage

A heterozygote has the sickle cell trait, a condition that is not fatal but the red blood cells become sickle shaped when oxygen concentration is low. They are more resistant to malaria than those individuals with normal red blood cells

- Homozygous recessive –> sickle-cell anaemia
- Homozygous dominant –> normal haemoglobin –> more susceptible to malaria –> often die
- Heterozygote –> sickle cell trait –> survival advantage in high-risk malarial areas

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With respect to evolution, or gradual change of a species characteristic, mutations are the most common source of variation in individuals

Gene pool- the sum of all the alleles carried by members of a population

Allele Frequency- how often each allele of a gene occurs in the population

What does mutations do to gene pools and how does this cause a gene pool to change?

Mutations changes the allele frequency of a specific allele and if they are advantageous they stay and other alleles die out.

In summary, it adds variation into a gene pool.

For example variation in human skin pigmentation

- Skin colour is determined by number and size of melanocytes (melanin producing cells) as well as how active they are.

- Melanocytes have photosensitive receptors that detect ultraviolet radio from the sun and other sources, they produce melanin within a few hours of exposure

- There are two types of melanin
    1. Eumelanin- dark brown to black
    2. Pheomelanin- red to yellow in colour

- UV radiation is more intense at locations closer to the equator as there is more sun overhead. UV high energy light damages and destroys the molecules that skin is made of.

- Melanin acts as a protective biological shield against ultraviolet radiation.
    - By doing this it helps to prevent sunburn damage that could result in DNA changes and subsequently several kinds of malignant skin cancers
    - They also are less likely to experience heat exhaustion and heat stroke.
    - For example, melanoma in particular is a serious threat to life
    - Dark skin in areas near the equator, and light skin and other areas

- The skin's ability to tan in the summertime is an acclimatisation to the seasonal change of more UV in the summer and less UV in the winter
- Tanning is an increase in number and size of melanin particles due to the stimulation of UV radiation

- However it would be harmful if melanin acted as a complete shield.
    - A certain amount of shortwave ultraviolet radiation (UVB) must penetrate the skin layer in order for the body to produce vitamin D
    - Approximately 90% of this vitamin is normally synthesised in the skin

- Too much UV radiation penetrating the skin may cause the breakdown of folate in our body which can cause anaemia
    - Folate is also needed for DNA replication in dividing cells, its absence can have an effect on many body processes, including the production of sperm cells.

- People who live in far northern latitudes, where solar radiation is relatively weak most of the year, have an advantage if their skin has little shielding pigmentation.
    - Nature selects for less melanin when UV radiation is weak
- In such an environment, very dark skin is a disadvantage because it can prevent people from producing enough vitamin D, potentially resulting in rickets disease in children and osteoporosis in adults.

- Another example where it may be disadvantageous is:

- The highest skin cancer rates in the world are suffered by people of European origin who currently live in equatorial places such as Australia.

SKIN COLOUR ADAPTATION

- Genes can influence skin colour
- Skin colour is due to the presence of melanin
- Melanin is located in the epidermis and is produced by melanocytes
- Melanocytes contain photosensitive receptors that detect UV radiation– responds by producing melanin– resulting in a tan
- Exposure to UV radiation induces greater melanin production
- Genetic changes can alter the development and migration of melanocytes, regulation and expression of genes that generate melanin or chemical steps in the synthesis of the pigments
- Level of skin pigmentation shows a close correlation with latitude
- People living near the equator tend to have dark skin, while light-skinned people live nearer the poles
- Skin pigmentation correlated with altitude because it serves as a dense against UV radiation
- UV is more intense at lower latitudes where sun is more often directly overhead
- High energy UV light damages and destroys the molecules that ski is made of
- UV radiation can cause severe burns and leave skin unable to maintain its normal protective cooling functions, can also cause long-term damage to DNA of skin cells leading to skin cancer
- Dark skin reduces the incidence of skin cancer and sunburn
- Melanin acts as a protective shield against UV radiation –> helps o prevent sunburn damage
- UV radiation is necessary in the metabolism of Vitamin D
- People who live in far northern latitudes where solar radiation is relatively weak, have an advantage if their skin has little shielding pigmentation
- Nature selects for less melanin when UV radiation is very weak
- In such an environment, very dark skin is a disadvantage because it can prevent people from producing Vitamin D potentially resulting in rickets and osteoporosis.

Evidence for Evolution

Polymerase Chain Reaction

- A technique used to amplify a piece of DNA
- It is a chain reaction of DNA replication events
- At each cycle of synthesis, the number of DNA copies doubles

The process

PCR mixture contains

1. A sample of DNA which acts as a template
2. A source of the four nucleotides (A,T, C,G)
3. Taq polymerase, a heat resistant enzyme
4. Single-stranded DNA primers, which are synthetic short pieces of DNA complementary to the sequences of bases that flanks the DNA being amplified

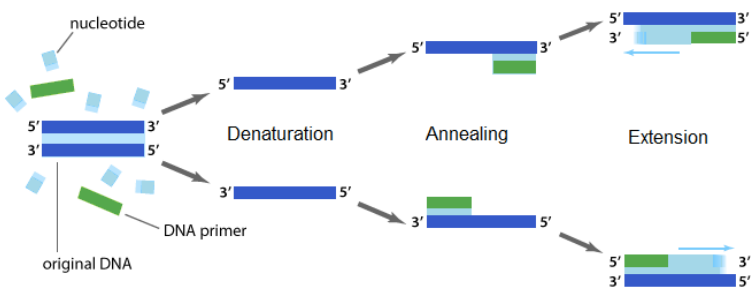
These are all placed together in a plastic test-tube and into a DNA thermocycler

Denaturing

- 95°C
- Hydrogen bonds between the two strands are broken

Annealing

- 50-60°C
- primers attach to the two strands and begin the process of replication



Elongation

- 72°C, optimum temperature of Taq polymerase
- Taq polymerase begins to move along the template DNA starting from the primer and adding nucleotides in the 5′ to 3′ direction

DNA sequencing

- Determines nucleotide sequence of DNA
- Allows human genome to be sequenced
- Mutations can be detected by comparing a sample with normal DNA

The process

1. DNA amplified by PCR
2. Heat added to seperate the two strands to single-strands
3. Temperature lowered and DNA polymerase, DNA nucleotides and DNA template strands, DNA primers and dideoxynucleotides (ordinary DNA nucleotides except that one OH- group has been chemically changed to a H+, usually dyed with a fluorescent dye)

4. Primers bind to the DNA and polymerase begins to add nucleotides in the 5′ to 3′ direction. The original DNA serves as a template and the new DNA is made by complementary base pairing
5. Chain elongation continues normally until by chance a dideoxynucleotide is added in place of a normal DNA molecule
6. The new DNA chains ending with dideoxynucleotides of varying lengths are separated by their size through gel electrophoresis

Gel Electrophoresis

- A technique for separating fragments of DNA
- also used to seperate proteins of different charge, size and shape
- different sized molecules will migrate through the gels at different rates when driven by a drop in electric voltage

The process

1. DNA test sample is cut into fragment by restriction enzymes, the size of the fragments will depend on the bases sequence of that particular DNA
2. DNA sample is placed in a well in a gel, Other test samples and molecular weight standards, which are DNA segments of known length can be added to the other wells for comparison. The gel is an agarose gel
3. Gel is placed in a buffer solution in an electrophoresis bath. This buffer solution is a controlled pH solution
4. Power source is attached and switched on, the DNA is negatively charged and so it moves through the gel towards the positive terminal
5. The gel is like a molecular sieve, the smaller the DNA fragments the faster they move through the gel.
6. When the power is switched off the DNA in the gel can be observed in a UV light box
7. The size of the bands (DNA profile of various samples can be determined by comparing them against molecular weight standards

Importance of Biotechnology

PCR –> enables the amplification of minute pieces of DNA
Gel electrophoresis and DNA sequencing –> establish a DNA profile, tracing ancestry and relationships between individuals and groups
Restriction enzymes –> necessary to slice the DNA molecule at precisely located sites so that a small set of homologous fragments are produced

Evolution- the gradual change in characteristics of a species over time
There is a hypothesis that all living things are related to each other and have evolved from a **common ancestor**

DNA

- chemical compound that makes up genes and determines the types of proteins a cell can produce
- a sequence of three bases code for on particular amino acid in a protein
- when speciation occurs, new species would have similar DNA, however as the new species gradually change they accumulate more differences in their DNA
- distantly related= more differences, closely related= more similarities

DNA-DNA hybridisation

- determines the similarity of DNA from different species –> indicate their genetic relationship
- single strands of DNA from two different species are mixed together and hybrid double stands are able to form as the base pairs match up
- hybrid strands are heated up to break H-bonds formed the higher the temp the more energy needed –> greater extent of complementary base sequences (gene similarity) thus the more closely related to two species are
- shows that humans and chimpanzees DNA 98% similar

Endogenous Retroviruses

- more closely related species have more "junk" non-coding DNA in common
- retroviruses store their genetic information of RNA not DNA and upon entering a cell it copies its RNA genome into DNA, a process called *reverse transcription*
- becomes endogenous when it inserts into a cell whose chromosomes will be inherited by the next generation (ovum or sperm cell)
- ERV: a viral sequence that has become part of an organisms genome
- 16 instances of humans and chimpanzees ERV matching exactly

Mitochondrial DNA

- small circular molecules, inherited only from mother
- 37 genes, 24 code for tRNA molecules and 13 for cellular respiration enzymes
- inherited only from mother
- higher rate of mutation than nuclear DNA, amount of mutation is roughly proportional to amount of time passed
- last common maternal ancestor for modern humans and neantherthals 600,000 years ago

Protein Sequences

- longer the period of time from common ancestor, greater number of amino acids different

Ubiquitous proteins

- found in all organism from bacteria to humans
- carry out the same function no matter where it is found

- e.g. Cytochrome C which performs an essential step in the production of cellular energy. This has changed very little over million years of evolution. Of the 104 amino acids found in humans, 37 are found at the exact same position in every cytochrome C molecule
- this originated from a primitive microbe 2 billion years ago

Bioinformatics
- the use of computers to describe the molecular components of living things

Comparative studies in anatomy
- involves comparing the structural features of related animals to ascertain the degree of similarity between them

Comparative studies in embryology
- involves comparing the early stages of development in organisms
- embryonic gill punches and arches present in all
- they all also have an absence of paired appendages, presence of a well-developed ftail, two-chambered heart, similar brain development
- implies common ancestry with later evolution along different pathways

Homologous structures
- organs with similar structure but with different function
- e.g. pentadactyl limb (five fingered limb) and forelimb of vertebrae

Vestigial organs
- organs that may once have been important but have since lost or changed their function
- these remanants are not harmful in any way thus they have not been completely eliminated

Nictitating Membrane- transparent third eyelid, now seen as humans by a pinkish membrane at the inner corner of each eye
Muscle to move the ears
Wisdom Teeth- third molars, erupt abnormally and cannot be used in mastication
Pyramidalis Muscles- muscles that lie about the pubic bone
Coccyx- vertebrae for a tail that fused to form the tail bone, tail was once there for mobility and balance
Appendix- remains of original human caecum (start of large intestine), no longer needed human diet is not primarily plant based anymore

Fossils
Definition- evidence of, or remains of, an organism that lived long ago, usually bones, teeth or footprints

Artefacts are objects deliberately made by humans

What conditions favour fossilisation?

1. Hard body parts
2. Soils that are neutral/slightly alkaline with high oxygen content- acid wears away bones and dissolves the mineral within it
3. Rapid burial- conditions not suited for activity of decay organism and decomposition is slowed or prevented
4. Long period of stability- the organism needs to be left undisturbed for a long period of time

What occurs during the process of fossilisation?

- mineral replacement- alkali salts replace the protein framework and then substitute molecule by molecule the minerals in the bone
- new mineral often lime or iron oxide are deposited in the pores of the bones, replacing the organic matter
- bone becomes petrified (turned into rock) but details of structure are preserved)

Dating of Fossils

Absolute dating

These techniques provide the actual age of the specimen

Carbon-14 Dating

1. C-14 produced in upper atmosphere by the action of cosmic radiation on nitrogen
2. When plants take in atmospheric CO2 they take in C-14, animals who then eat this plant gets C-14 in their tissues
3. When the animal dies, their intake of C-14 ceases and the C-14 already present begins to decay at a constant rate into N-14, half life of C-14 is 5730 years
4. By measuring the ratio of C-14 to C-12 the age of a sample can be determined

Limitations

1. can only date specimens up to 60,000 years old
2. only date organic matter (containing C), thus cannot date rocks

Potassium Argon Dating

1. This technique is based on the decay of radioactive K-40 to Ar-40 at a constant rate
2. The half life of K-40 is 1.25 billion years and by determining the amounts of K-40 and Ar-40 in a sample the age can be determined
3. This technique is used to date volcanic and igneous rock

Limitations

1. not suitable for all rock types (not sedimentary and metamorphic rock)
2. can only date rocks older than 100,000 to 200,000 years old

3. to date a fossil, a rock of similar age must be used/be available

Dating of Fossils

Absolute dating

These techniques can only tell if one sample is older or younger than the other

Stratigraphy- the study of layers or strata

Principle of stratigraphy

- Assumes that layers of sedimentary rock, the layers at the top are younger than the ones beneath them
- Thus any fossils or other material found in top layers will be younger than those below them

Limitations

1. distortions of the Earth's crust may occur and the sequence of rock layers will be turned upside down
2. it is possible for fossils or artefacts to be buried by animals or early humans some time after the deposition of sediment

Correlation of rock strata

- Involves matching of rock layer from different areas
- Can be done by examining the rock itself, or the fossil is contains, rocks containing the same fossils= same age

Index Fossils

- Are widely distributed and were present on earth for only a limited period of time, making relative dating of strata more precise
- Can be used to correlate strata from different localities, often hundreds or thousands of kilometres apart

Fluorine Dating

1. When a bone is left in soil, fluoride ions, which are present in the groundwater in the soil, replace some of the ions in the bone itself
2. All the fossil bones in a particular deposit should contain the same amount of F
3. The older the fossil, the more F it should contain allowing relative ages to be established

Limitations

1. Only compares fossils in same locality
2. The concentration of fluoride in groundwater varies from place to place and time to time

Adaptions to bipedalism

Position of the foramen magnum

- The hole in the skull where the brain joins the spinal cord is called the foramen magnum.
- Located centrally in humans but posteriorly (back) in apes
- During evolution the foramen magnum has gradually moved forward until the skull is able to balance on top of the vertebral column.
- Thus humans do not need the large neck muscles seen in apes.

Curvature of the Spinal Column

- Humans have a double curvature (S-shaped curve), which contributes to upright stance. Apes, however, have a C-shaped curve
- Vertebrae in the lower (lumbar) region are wedge-shaped from front to back, thus forming a forward jutting curve.
- Lumbar curve of vertebral column improves body balance in the upright position.
- Enables head to balance on top of neck.
- Cervical curve in neck brings the vertebral column directly under the centre of gravity of the skull.

The Jaw

- Apes have a protruding jaw (prognathic) whereas in humans the facial profile is much flatter.
- Humans have an orognathic jaw, as seen through the presence of a chin
- During evolution, the size and protrusion of the human jaw and gradually been reduced.
- Change has been important in allowing the skull to balance on top of the spine because the weight in front of the foramen magnum is approximately equal to the weight behind.
- This allows balance to be achieved with a minimum muscular effort.

The Pelvis

- *Short, wide, bowl-shaped*
- Apes have a long and narrow pelvis
- Vertebral column articulates with the pelvis.
- Human pelvis is broader and shorter from top to bottom
- Bowl shape –> supports abdominal organs when standing erect and the developing foetus during pregnancy.
- Broad hip bones (ilia crest is flared) provide an attachment point for the large gluteus muscles, which move the legs and keep the upper body erect.

Carrying Angle

- Shape and orientation of the pelvis results in the hip joint being directly under the trunk and head.
- Allows weight of body to be transferred from pelvis to the legs.
- Head of the femur is large and fits into the hip sockets.
- Because pelvis is broad, hip sockets are wide apart, but the femurs tend to converge at the knees.
- Arrangement of the femurs forms an angle to the vertical called the carrying angle, which ensures weight distribution remains close to the central axis of the body when walking.

- Also allows for greater stability when walking as it enables the body to be rotates about the lower leg and foot, and each footstep to follow more or less in a straight line.
- Enables for striding gait locomotion
- Weight transmission falls through the outside of the femur.

The 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 either side of ligaments in the middle of the joint.
- Weight is transmitted to the outer hinge, it is larger and stronger than the inner one.
- Weight of body is transmitted down the outside of each leg, but centre of gravity tends to fall through a line just in front of the knees. This results in a force that tries to bend the knees backwards but is resisted by the ligaments, thus allowing for more energy efficient bipedalism

The Foot

- Weight of body transmitted through tibia to the ankle, then transmitted to the metatarsals and phalanges via the arches of the foot.
- Human foot one of the most distinctive adaptions for bipedal locomotion.
- The foot has lost grasping ability (prehensility).
- This change is most noticeable in the big toe (not opposable, parallel to other toes, robust)
- Bones of the foot between the toes and the ankle (the metatarsals) are shaped in such a way that they form a longitudinal arch and a transverse arch.
- Transverse arch is unique to humans
- Humans have a large/robust calcaneus (heel bone) as the heel bears the weight of the body for a second while in striding gait locomotion

Centre of Gravity

- Humans have legs longer than the arms.
- Increases the length of the stride when walking.
- Also serves to lower the centre of gravity of the body.
- Lower centre of gravity (at the pelvis in humans, chest in apes) contributes to stability when moving bipedally or when standing erect.
- Centre of gravity falls in front of the body in apes but in humans the centre of gravity is centrally in the body

Stance and Locomotion

- One of the essential elements for maintaining an upright stance is muscle tone (partial contraction of skeletal muscles).
- Sustained muscle tone is evident in those muscles that support the body in an upright position. In humans, the muscles that do are those that bring about movement of the spine, hip, knee and ankle, and abdominal muscles.
- Walking upright in such a way that the hip and knee are fully straightened is the striding gait.

Relative size of the Cerebral Cortex

- Compared with apes, frontal lobe has the greatest enlargement of surface area. The frontal lobe is responsible for higher order functions such as thinking and reasoning
- A large brain requires a larger cranium. Gradual increase in cranium size to house a larger and more complex brain is an evolutionary trend.

- Humans have a higher number of cerebral convolutions and larger cerebrum compared with apes
- Gradual enlargement of the cranial portion of the skull to accommodate the increasing size of the frontal region of the brain also led to a more distinct forehead and a reduction in the size of the brow ridge.
- Apes and early hominins have a distinct brow ridge, the bony ridge located above the eye sockets (very evident in gorillas).
- Humans cranial capacity = 1350 cc, Apes cranial capacity= 500 cc

Prognathism and Dentition

- In humans, canine teeth do not project, beyond the level of other teeth, they interlock.
- Human canines look more like incisors.
- Humans also have smaller molars and premolars
- Small canine teeth and relatively small incisors take up less room in the jaw. As a consequence, the dental arcade has evolved to be more parabolic in shape as opposed to U-shaped like in apes
- Accompanying the gradual reduction in tooth size was a flattening of the face, development of a chin and a prominent nose.
- Apes have a distinct forward-jutting jaw (prognathism) and a diastema (gap between upper canine and upper second incisor to accomodate for a large lower canine)
- Humans also do not have a nuchal or sagittal crest which act as attachment point for muscle that functions to keep the head upright in humans. The front and back of skull is well balanced