14.1 Homeostasis in Mammals

Homeostasis

Explain what is meant by the term homeostasis.

- Maintaining a constant internal environment in the body.

Outline how a negative feedback mechanism works // Explain what is meant by negative feedback.

- Change in parameter occurs away from the norm / set-point.
- This change is detected / sensed by a receptor.
- Coordination: Hormone is released or nerve impulse is sent.
- Hormone / impulse reaches target organ / effector.
- Effector performs corrective action.
- The parameter returns to norm / set-point.

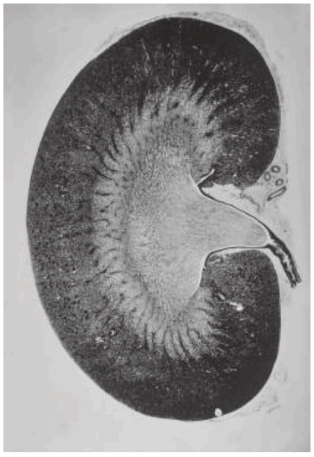
Production of Urea

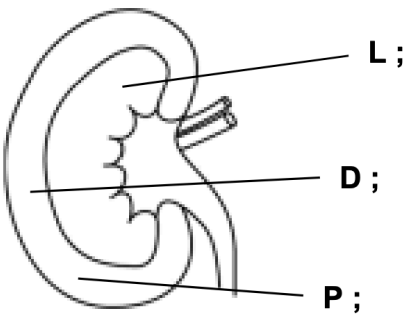
Outline the formation of urea from excess amino acids by liver cells.

- Deamination: amine group (--NH2) is removed from amino acid in liver cells.
- Ammonia / NH3 is formed.
- Ammonia is combined with carbon dioxide.
- Through a series of reactions called the urea cycle, urea is produced.

Structure of the Human Kidney

photograph of a section through a kidney:





L	Medulla
D & P	Cortex

Photomicrograph of kidney cortex:

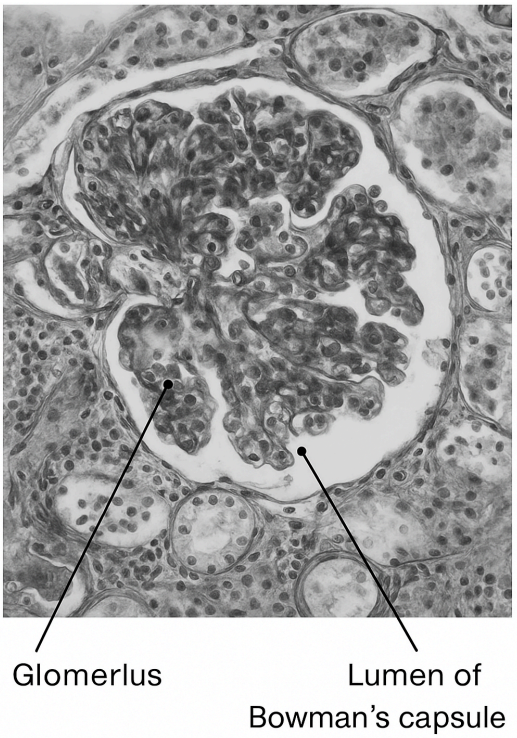
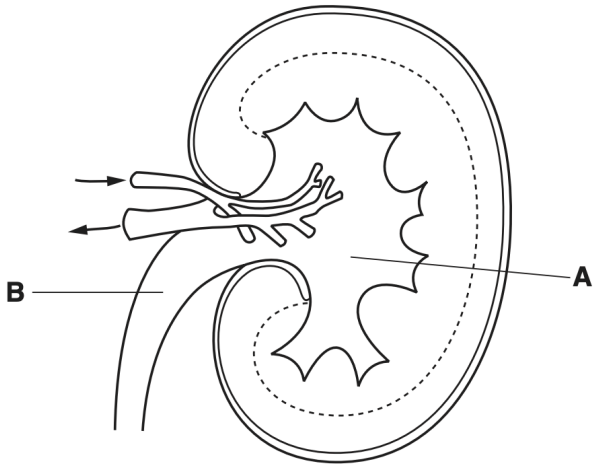


diagram of a section through a kidney:



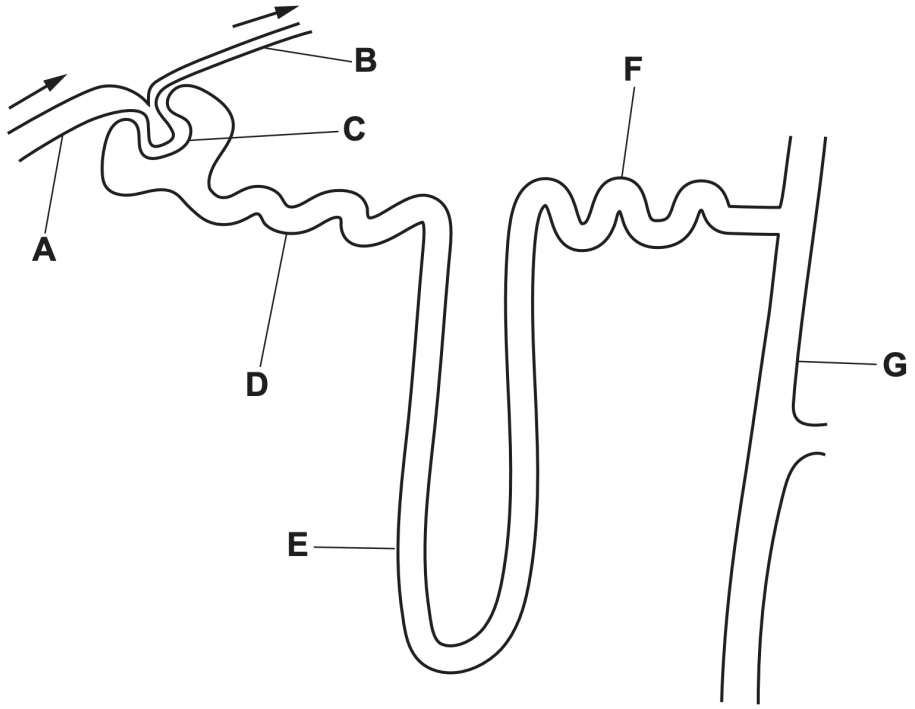
A	Pelvis
B	Ureter

State in which part of kidney blood urea concentration is low.

- Renal vein

Structure of a Nephron

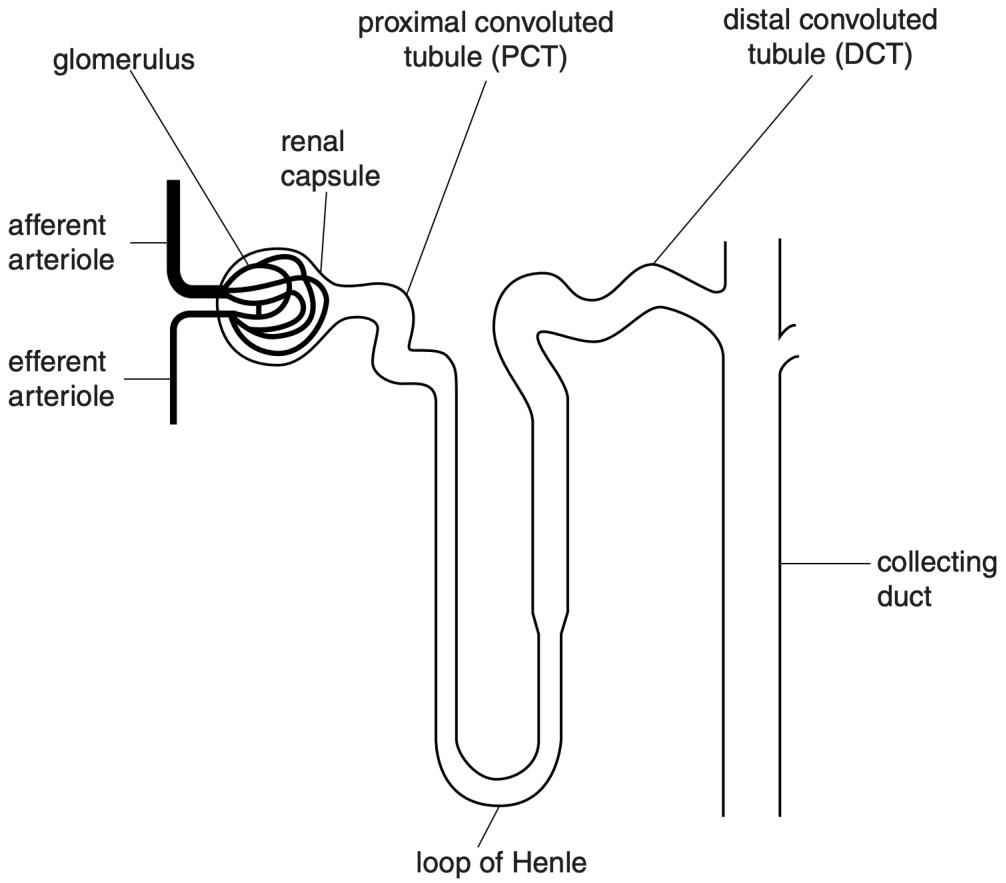
Structure of human nephron + associated blood vessels:



A	Afferent arteriole
B	Efferent arteriole
C	Bowman's capsule
D	Proximal convoluted tubule
E	Loop of Henle
F	Distal convoluted tubule
G	Collecting duct

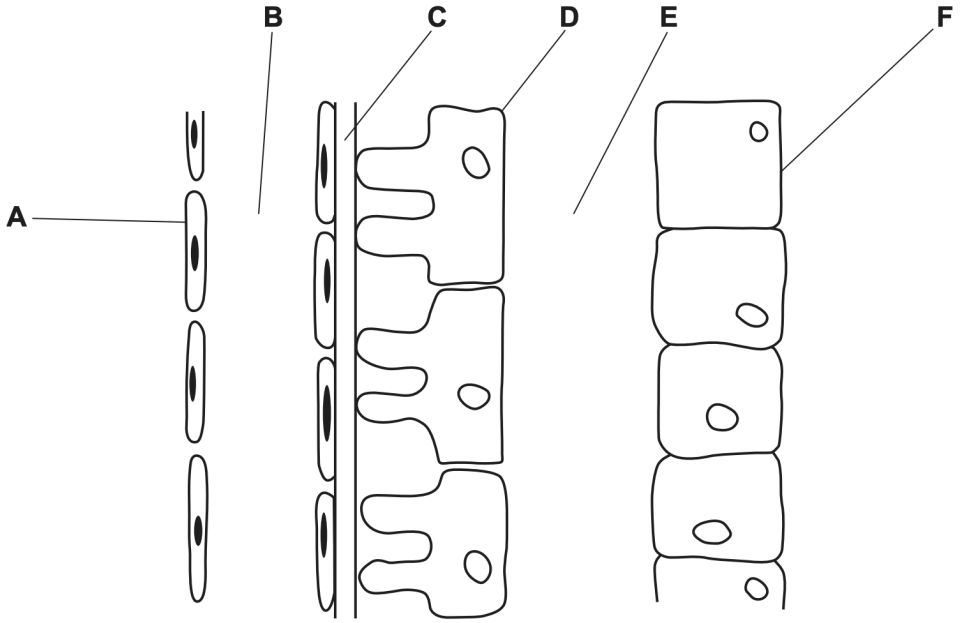
Bowman's capsule + glomerulus	cortex
Proximal convoluted tubule	cortex
Distal convoluted tubule	cortex
Loop of Henle	medulla
Collecting duct	medulla

Nephron:



Description	**Part of nephron**
Passes through the medulla	Collecting duct / Loop of Henle
Glucose is reabsorbed into the blood	Proximal convoluted tubule
ADH acts on its walls	Collecting duct / Distal convoluted tubule
Most of the water is reabsorbed into the blood	Proximal convoluted tubule
Where podocyte cells are located	Bowman's capsule

Bowman's capsule + glomerulus:



A	Capillary endothelial cell
B	Lumen of capillary
C	Basement membrane
D	Podocyte cell
E	Lumen of Bowman's capsule
F	Epithelial cell

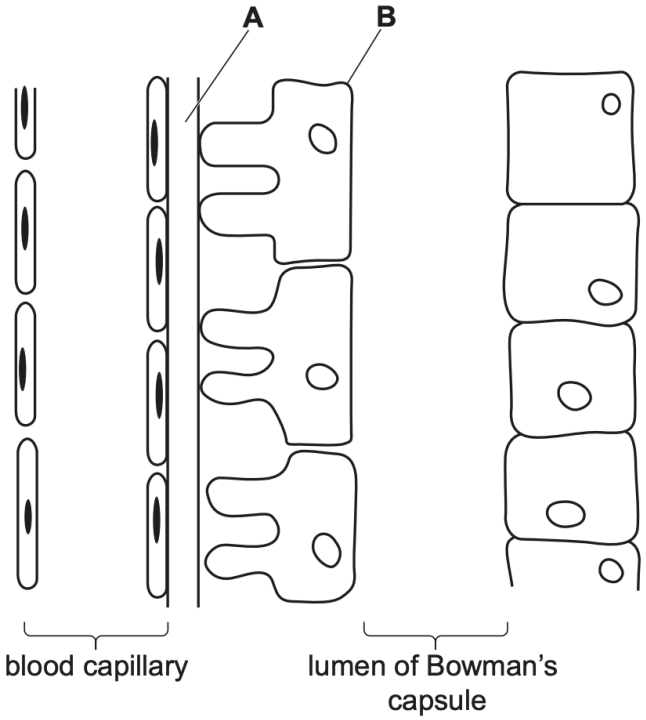
Formation of Urine in the Nephron

ULTRAFILTRATION

Describe the process of ultrafiltration in the nephron.

- Diameter of lumen of afferent arteriole is wider than efferent arteriole.
- This leads to high blood / hydrostatic pressure.
- Plasma / fluid passes through gaps / fenestrations between endothelial cells of capillaries in the glomerulus.
- Basement membrane acts as a filter / selective barrier.
- RBCs / large proteins / molecules greater than 68000 MM cannot pass through the basement membrane.
- Podocytes have gaps / slits that allow fluid / water / filtrate to pass through.
- Filtrate passes into Bowman's capsule.

Glomerulus + Bowman's capsule:



A	Basement membrane
B	Podocyte

Describe the role of basement membrane in the formation of the glomerular filtrate.

- Acts as a filter / filtration barrier.
- Only molecules less than 68 000 – 70 000 MM can pass through it: It stops RBCs / large proteins and allows urea / glucose / amino acids / ions / water.

Describe the role of podocytes in the formation of the glomerular filtrate.

- Has gaps / slits / projections / pores.
- Allows fluid / water / filtrate to pass into the lumen / Bowman's capsule.
- Contributes to the production basement membrane.

NOTE: both the endothelial cells of the glomerular capillaries and the podocytes (epithelial cells lining the inner surface of Bowman's capsule) contribute to production of basement membrane.

Explain how high blood pressure is achieved for ultrafiltration

- Afferent arteriole is wider than efferent arteriole.

Effect of afferent and efferent arteriole diameters on glomerular filtration rate (rate of flow of filtered fluid through the kidneys per unit time):

afferent arteriole lumen diameter	efferent arteriole lumen diameter	GFR
normal	normal	normal
decreased	normal	decrease ;
normal	increased	decrease ;

Explain why the lumen of the afferent blood vessel needs to be wider than the lumen of the efferent blood vessel.

- To generate a high blood pressure / hydrostatic pressure.
- To force plasma / fluid / water through the basement membrane, into the lumen of the Bowman's capsule.

Describe and explain how the structures in the Bowman's capsule and its associated blood supply are adapted to allow ultrafiltration to take place.

- Afferent arteriole is wider / has larger diameter than efferent arteriole.
- This causes high blood / hydrostatic pressure in glomerulus / capillaries.
- Pores / gaps / fenestrations in capillary endothelium.
- Basement membrane acts as a filter / filtration barrier.
- Basement membrane only allows molecules less than 68 000 – 70 000 MM to pass through it: It stops RBCs / large proteins and allows urea / glucose / amino acids / ions / water.
- Podocytes have gaps / slits that allow fluid / water / filtrate to pass through.
- Glomerulus is a network of capillaries: provides large surface area and maximises contact between the blood and filtrate.

SELECTIVE REABSORPTION

Describe and explain how all of the glucose in the glomerular filtrate is reabsorbed back into the blood as the filtrate passes through the proximal convoluted tubule.

- Na+ are actively transported / pumped out of the PCT epithelial cells into blood/ tissue fluid.
- This is done by sodium-potassium pumps in the membranes of the PCT epithelial cells.
- Na+ concentration gradient is set up: Na+ conc. decreases inside the cells.
- Thus Na+ enters the epithelial cells from filtrate.
- This occurs by facilitated diffusion.
- Na+ co-transports glucose into cells.
- This process is known as secondary / indirect active transport.

- Once inside the epithelial cells, glucose moves by facilitated diffusion out of the cells and into blood.
- This occurs through GLUT proteins in the basal membrane.

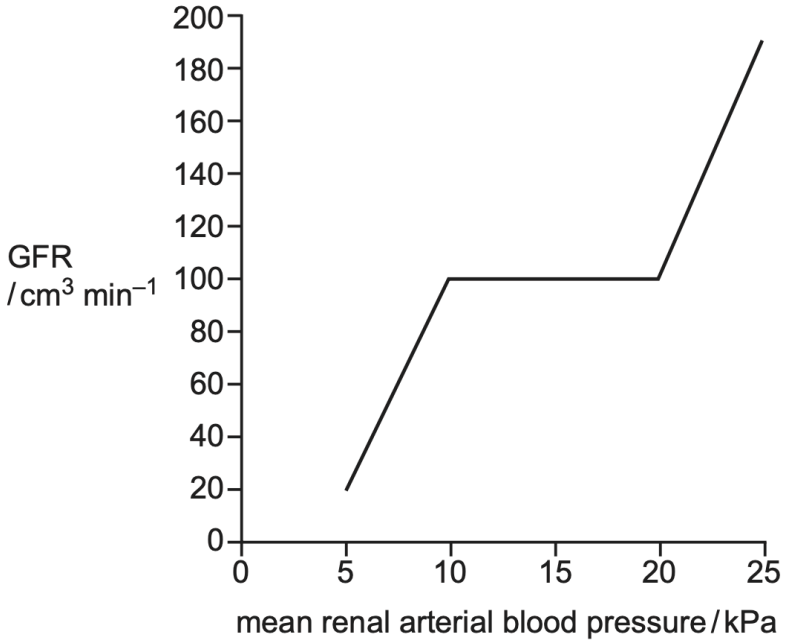
Describe and explain how the cells of the proximal convoluted tubule are adapted to carry out selective reabsorption.

- Microvilli
    - Provides large surface area for increased reabsorption.
- Many mitochondria
    - Provide ATP for sodium-potassium pumps – Sodium ions are pumped/ moved out of cell to blood / tissue fluid.
    - This is active transport and requires energy.
- Tight junctions / closely packed cells
    - Prevents leakage; fluid cannot pass between cells and substances must pass through cells.
- Many transport proteins
    - For movement of substances like glucose / amino acids / Na+: these are co-transported into the cell from filtrate / lumen.

ANALYSIS/ GRAPH QUESTIONS

<u>Question 1</u>

Glomerular filtration rate (GFR) = the rate at which blood plasma is filtered in the Bowman's capsule. *Relationship between GFR and mean renal arterial blood pressure:*



Comment on the relationship between GFR and mean renal arterial blood pressure.

- As mean arterial blood pressure increases the GFR increases, levels off and increases.

- Plateau occurs at 100 cm3 min–1 / between 10 and 20 kPa.
- Plateau is normal or healthy value.

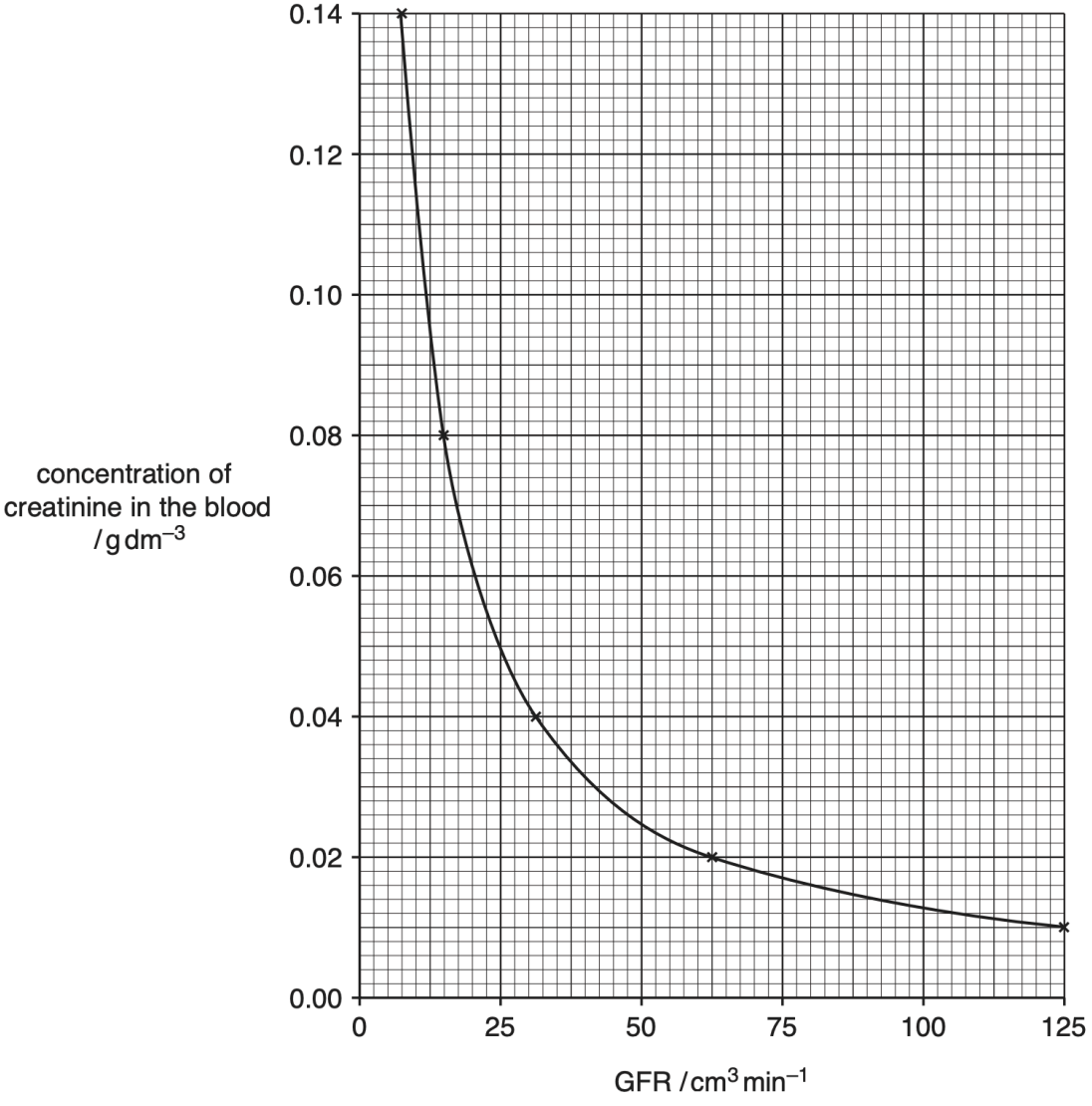
Suggest reasons why GFR of a person might decrease.

- Kidney disease / damage
- Cancer
- Dehydration
- Low blood pressure/ loss of blood

Question 2

Concentration of creatinine in the blood largely depends on the glomerular filtration rate (GFR). By measuring concentration of creatinine in the blood, the GFR can be estimated. The value of the GFR can be used to assess the efficiency of the kidneys. In humans, a normal value of the GFR is 100 cm3 min–1.

Relationship between GFR and concentration of creatinine in the blood:



Describe the relationship shown.

- Higher the creatinine concentration lower the GFR; inversely proportional.
- Exponential curve / non-linear.
- Data quote for two points + units.

Osmoregulation

Describe the roles of the hypothalamus and the posterior pituitary in osmoregulation.

- Hypothalamus detects changes in water potential of the blood.
- Osmoreceptors shrink when there is low / less water in blood.
- ADH is produced in the hypothalamus.
- Impulse / ADH is transported from hypothalamus to posterior pituitary.
- If low water potential, ADH is secreted from posterior pituitary.
- Increased number of aquaporins move to luminal membranes of collecting duct cells / distal convoluted tubule.
- Thus ADH increases permeability of collecting duct / distal convoluted tubule.
- ADH causes more water reabsorption / smaller volume of urine / more concentrated urine.

With reference to the maintenance of the water potential of the blood, explain what is meant by negative feedback.

- Osmoreceptors are located in the hypothalamus.
- They detect decrease in water potential.
- This stimulates the release of ADH into blood
- by posterior pituitary gland.
- Increased number of aquaporins move to luminal membranes of collecting duct cells / distal convoluted tubule.
- Thus more water is reabsorbed.
- Water potential returns to set point.

Changes in the internal environment of a mammal that leads to the release of ADH:

- Decrease in water potential of the blood
- Lower blood volume
- Increase in ion / salt concentration of the blood

NOTE:

- Hypothalamus produces ADH.
- Posterior pituitary gland secretes ADH into the blood.

State what happens to the water potential and volume of the urine if cells in the distal convoluted tubule have more aquaporins in their cell surface membranes.

- Water potential decreases.
- Volume decreases.

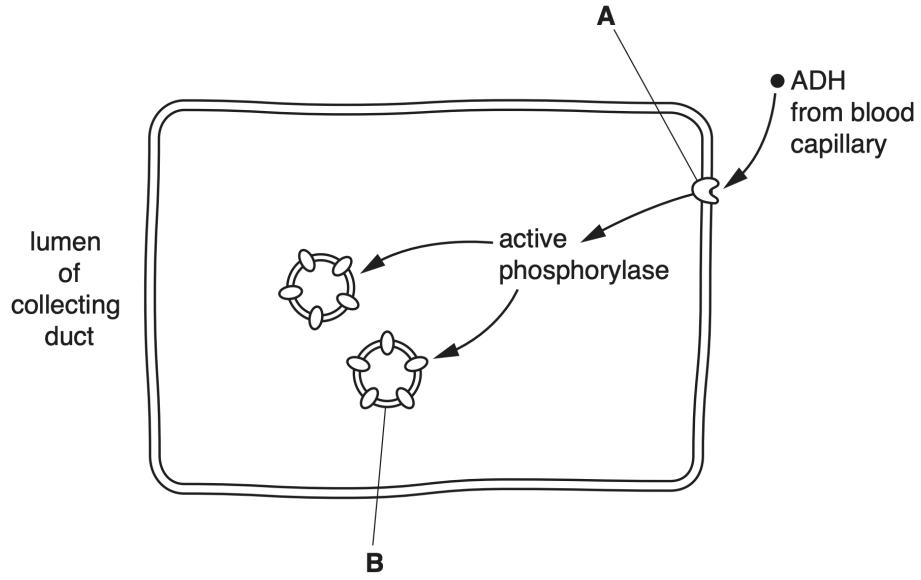
Describe the response of vesicles to stimulation by phosphorylase enzyme and describe the consequences of this response.

- Vesicles move towards / fuses with the cell surface membrane.
- Aquaporins are added to the cell surface membrane.
- Cell surface membrane becomes more permeable to water.
- Water moves from the lumen of collecting duct/ filtrate into cell/ blood/ tissue fluid.
- by osmosis / down water potential gradient.
- Water potential of blood rises / returns to set point.
- Less water is lost in urine from the body; lower volume, more concentrated urine.

Predict the effect of an increase in blood volume on ADH secretion and state one consequence for kidney function of this change in ADH secretion.

- Increase in blood volume causes decrease in ADH secretion.
- Consequence:
    - reduce water reabsorption in the collecting duct.
    - increased volume and more dilute urine formed.

A cell of one of the collecting ducts of the kidney:



Membrane protein A	Receptor protein
Cell structure B	Vesicle

ANALYSIS/ GRAPH QUESTIONS

Question 1

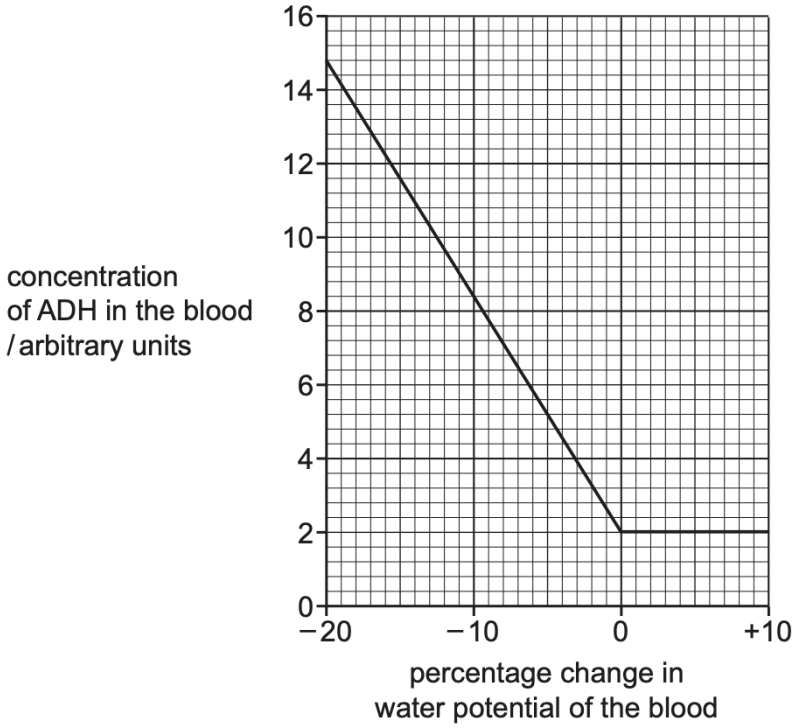
Cold diuresis = condition where people urinate more frequently in a cold environment. In a cold environment, homeostatic mechanisms keep heat loss to a minimum. Blood is diverted away from the skin so that more blood circulates around the main body organs, including the kidney.

Suggest and explain why cold diuresis occurs.

- Blood pressure increases in kidney.
- So more ultrafiltration occurs/ rate of ultrafiltration increases.
- This results in increased glomerular filtrate volume = increased urine volume.
- Exposure to cold causes concentration of ADH in blood to decrease.
- Lower levels of ADH decrease permeability of collecting ducts to water, so less reabsorption of water occurs in collecting duct = increased urine volume.
- Sweating stops in cold environments, so less water is lost through the skin and more is lost in urine.

Question 2

Concentrations of ADH in the blood at different percentage changes in water potential of the blood:



Describe the trend shown.

- As water potential of blood increases concentration of ADH in the blood decreases.
- 2 ADH figures related to 2 % change in water potential figures.
- Between 0% and +10% change in water potential, ADH concentration does not change / is constant / stays the same / plateaus.

Suggest one effect on the circulatory system of a low concentration of ADH in the blood.

- blood volume / pressure decreases

Question 3

Relative medullary thickness (RMT) indicates the proportion of a kidney that is composed of medullary tissue.

$$\text{RMT} = \frac{\text{thickness of medulla}}{\text{kidney size}} \times 10$$

Relationship between the RMT and the concentration of urine produced by four mammals from different habitats:

mammal	habitat	RMT	urine concentration / arbitrary units
beaver	rivers and lakes	1.4	0.90
warthog	savannah	2.8	2.35
human	variable	3.2	2.50
kangaroo rat	desert	8.6	10.50

Describe the relationship between the RMT and the concentration of urine produced and explain the differences between the data for the beaver and the kangaroo rat.

- As RMT increases concentration of urine increases; positive correlation.
- 2 pairs of comparative figures.
- For kangaroo rat, little water is available.
- For kangaroo rat, loop of Henle / collecting duct is longer.
- So more reabsorption of water occurs.
- So urine of kangaroo rat is more concentrated / small volume of urine.

Warthogs (lives in dry areas) and humans have similar values of RMT and concentration of urine. Suggest how a warthog is able to survive several months without drinking water (while humans can only survive few days).

- Makes use of metabolic water / water from respiration.
- It obtains water through the food it eats.
- Behavioural responses: no or less sweating.

Question 4

One risk associated with a blood transfusion is a condition known as transfusion-associated circulatory overload (TACO). TACO is caused by a large

increase in blood volume over a short period of time. This increase in blood volume can be harmful.

(c) People with kidney disease may be at a higher risk of TACO following a blood transfusion.

A study carried out in 2019 investigated whether there is a link between kidney disease and TACO. This study included data from:

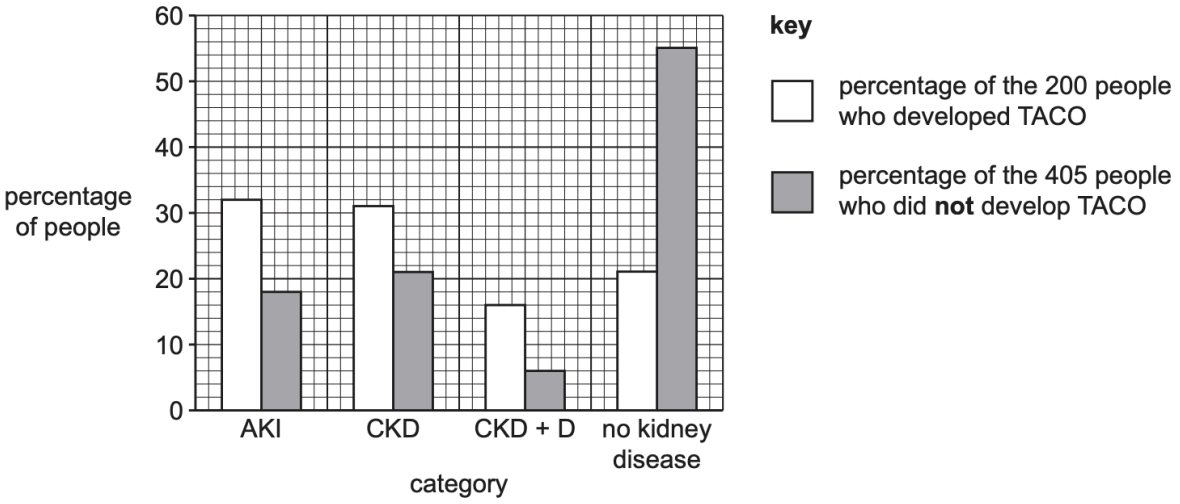
- 200 people who developed TACO after a blood transfusion
- 405 people who did **not** develop TACO after a blood transfusion.

The people in the study were put into one of four categories:

- people with acute (short-term) kidney injury (AKI)
- people with chronic (long-term) kidney disease (CKD) who do **not** require dialysis
- people with severe chronic kidney disease who do require dialysis (CKD + D)
- people who do **not** have kidney disease.

In dialysis, a machine is used to carry out the function of the kidneys.

The results of this study are shown in Fig. 3.1.



Describe the effect of having kidney disease on the risk of developing TACO.
Suggest reasons for this effect.

<u>Describe</u>

- Having kidney disease increases the risk of TACO.
- AKI has highest risk of TACO.
- Data quote comparison.

<u>Reasons</u>

- Kidney disease reduces ability to remove excess water.
- More water retained increases blood volume.
- CKD + D less risk as dialysis helps to restore water volume.

Patients who are at high risk of developing TACO following a blood transfusion can be given a type of drug called a loop diuretic. In normal urine production, 99% of sodium ions in the glomerular filtrate are reabsorbed and 1% are excreted. In urine production of people who take loop diuretics, 80% of sodium ions in the glomerular filtrate are reabsorbed and 20% are excreted.

Explain how loop diuretics affect water reabsorption in the kidneys and suggest why this reduces the risk of developing TACO following a blood transfusion.

- Fewer sodium ions reabsorbed / more sodium ions in filtrate
- This decreases water potential of filtrate / increases water potential of medulla
- Thus less water is reabsorbed by osmosis / down water potential gradient.
- This increases volume of urine.
- So blood volume from transfusion is reduced.

Control of Blood Glucose

Sequence of events that occur when the blood glucose concentration decreases below the set point:

- Decrease in blood glucose conc. is detected by α cells.
- Glucagon is secreted by α cells in the pancreas.
- Glucagon binds to receptors in the cell surface membranes of liver cells.
- Conformational change occurs to glucagon receptor, which activates G-protein.
- Activated G-protein activates adenylyl cyclase enzyme.
- Active adenylyl cyclase acts on ATP to produce second messenger – cyclic AMP (cAMP)
- Cyclic AMP binds to protein kinase and activates it.
- This activates an enzyme cascade.
- Enzyme cascade amplifies glucagon signal.
- Glycogenolysis: glycogen stored in liver cells is broken down to glucose.
- Glucose diffuses out of liver cells through GLUT transporter proteins and is released into blood so blood glucose concentration increases.

State how glucagon reaches liver cells.

- Bloodstream / circulation.

State the role of the enzyme cascade.

- Amplifies signal / expands message.

State the function of the final enzyme in the pathway, glycogen phosphorylase.

- Glycogenolysis: breaks down glycogen to glucose.

Name the location of the receptors in a non-diabetic person that detect a change in blood glucose concentration.

- β cells / pancreas / islets of Langerhans / hypothalamus

State the precise cellular location of insulin receptors.

- cell surface membrane / plasma membrane

State the type of biological molecule that forms an insulin receptor.

- glycoprotein / protein / polypeptide

Name the homeostatic mechanism by which blood glucose concentration is maintained.

- Negative feedback

Suggest the role of glycogen synthetase in the regulation of blood glucose concentration.

- catalyses glycogen production OR decreases blood glucose concentration

Describe two processes in the liver that are stimulated by glucagon.

- Glycogenolysis: Breakdown of glycogen to glucose.
- Gluconeogenesis: Production of glucose from non-carbohydrate sources like amino acids & fatty acids.

Name the type of membrane component that forms a receptor in the cell surface membrane.

- Glycoprotein / lipoprotein

Describe the role played by insulin in the control of blood glucose concentration.

- Insulin binds to receptors on liver / muscle / adipose tissue cells.
- In muscle & adipose tissue cells, insulin stimulates GLUT proteins to be added to the membranes, which increases permeability of these cells to glucose so more glucose enters by facilitated diffusion.
- In liver cells, Insulin causes activation of glucokinase which phosphorylates glucose, causing increased rate of diffusion of glucose into liver cells.
- More / faster respiration of glucose occurs.
- Insulin activates glycogen synthase enzyme, which causes glycogenesis (glycogen synthesis).
- Insulin causes lipid / triglyceride / fatty acid synthesis OR decreases glycogenolysis (glycogen breakdown) / lipolysis (lipid breakdown).
- As a result, blood glucose concentration decreases back to normal.

Name the process by which insulin is secreted from β cells.

- Exocytosis

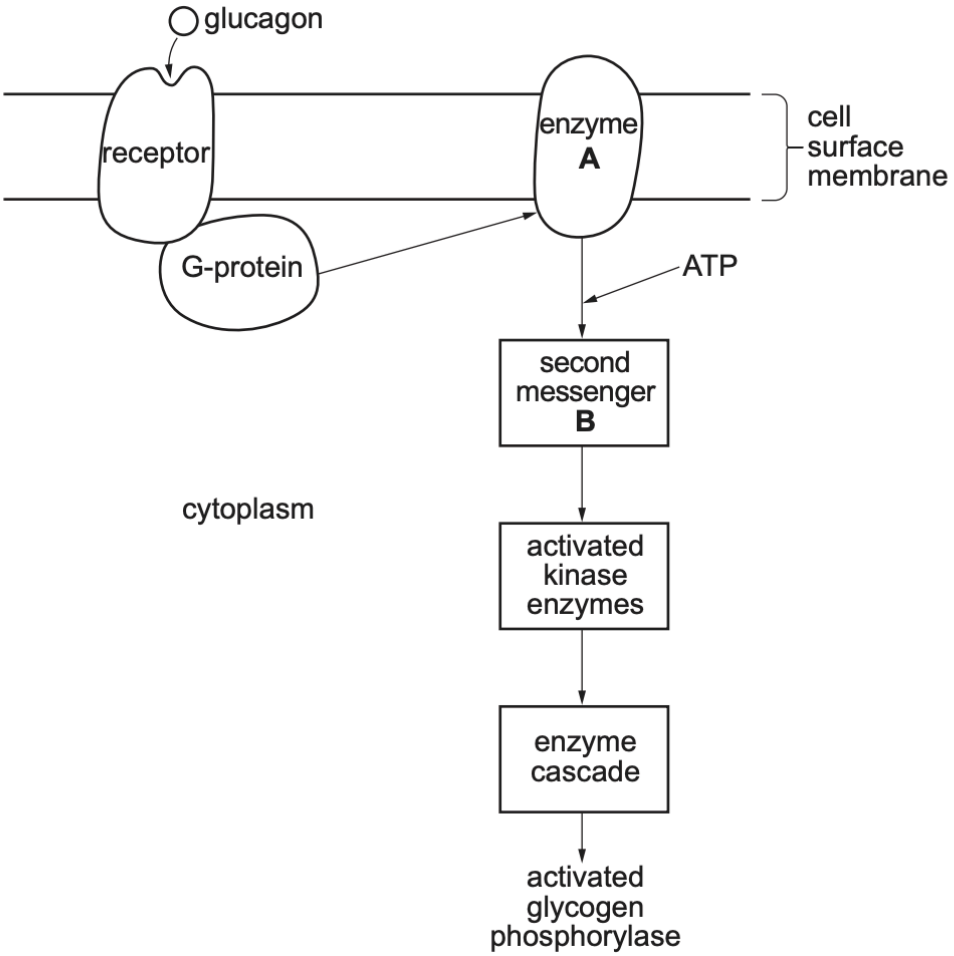
Describe the effects of insulin on muscle cells.

- Insulin causes glucose uptake / increases permeability of cells to glucose.
- Insulin adds GLUT (transport) proteins to cell surface membrane/ sarcolemma.
- This increases respiration rate/ more glucose respired.
- Causes glycogenesis: conversion of glucose to glycogen.

When pancreas cannot secrete sufficient insulin, suggest why there is a tendency to drink a lot of water and a loss of body mass.

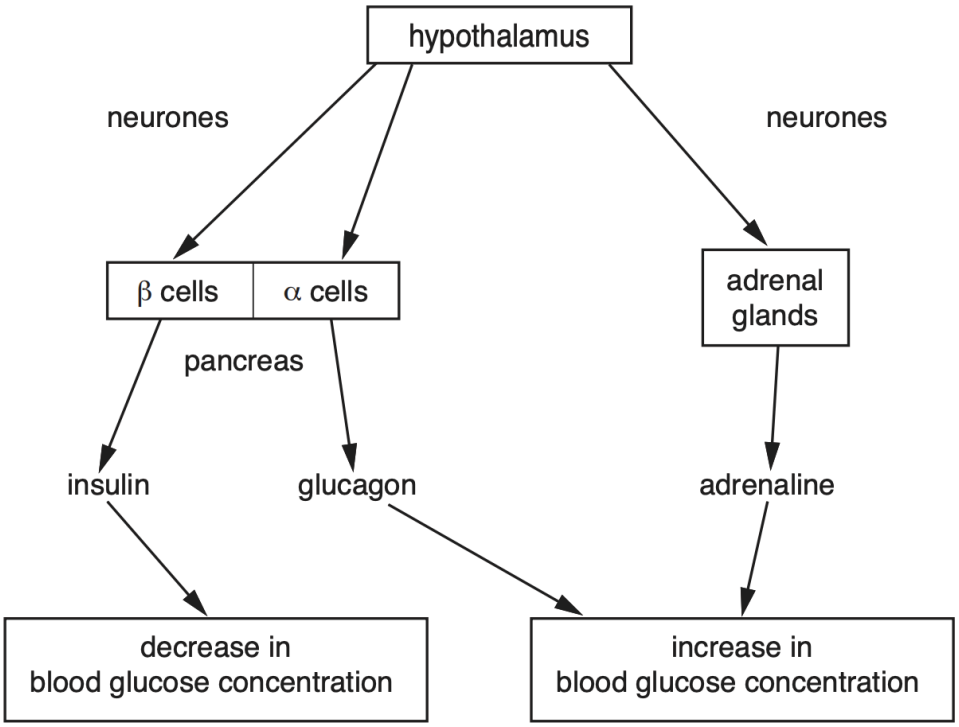
- There us high blood glucose concentration / hyperglycemia.
- This causes decrease in water potential of blood.
- This is detected by osmoreceptors in the hypothalamus.
- This causes feelings of thirst.
- Less / no glucose is converted to fat / glycogen.
- Glucose is lost in urine / not all glucose reabsorbed / blood glucose concentration is above the renal threshold.
- Glucose not taken up by cells.
- So fats / proteins are respired / metabolised, resulting in loss of body mass.

Response of liver cells to glucagon:



Enzyme A	adenylyl cyclase
Second messenger B	cyclic AMP / cAMP

role of nervous and endocrine systems in the control of blood glucose concentration:



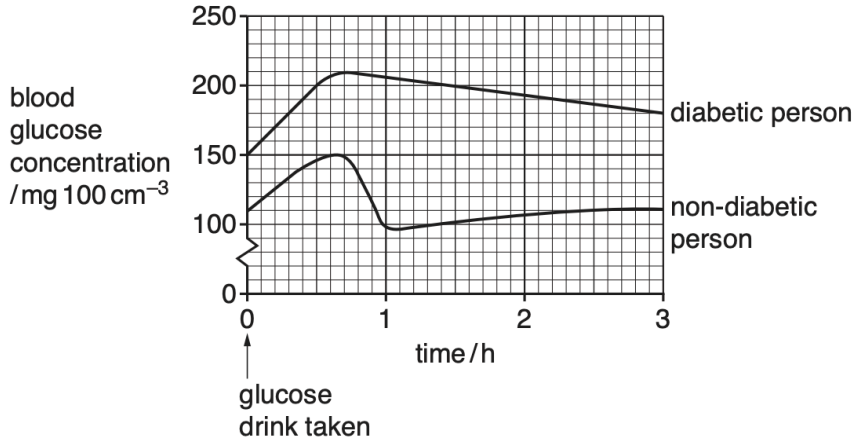
Describe the role of nervous system in the control of blood glucose concentration.

- Hypothalamus detects change in blood glucose concentration.
- Autonomic / motor / nerve impulses are sent.
- So β cells secrete insulin when blood glucose increases.
- So α cells secrete glucagon when blood glucose decreases.
- So adrenal gland secretes adrenaline either when blood glucose decreases or due to fear / shock / excitement / stress.
- Nervous control supplements endocrine control / control by pancreas.

ANALYSIS/ GRAPH QUESTIONS

Question 1

Blood glucose concentrations of a type 1 diabetic person and a non-diabetic person, at regular intervals after drinking a glucose drink:



Describe the results shown.

- Blood glucose concentration rises in both with drink.
- Diabetic always/ initially has higher blood glucose concentration.
- Diabetic has higher peak/ steeper rise in blood glucose concentration.
- Diabetic blood glucose concentration has slower fall/ does not return to normal in 3 hours/ is still high after 3 hours.
- Compare two data points with x and y figures and units.

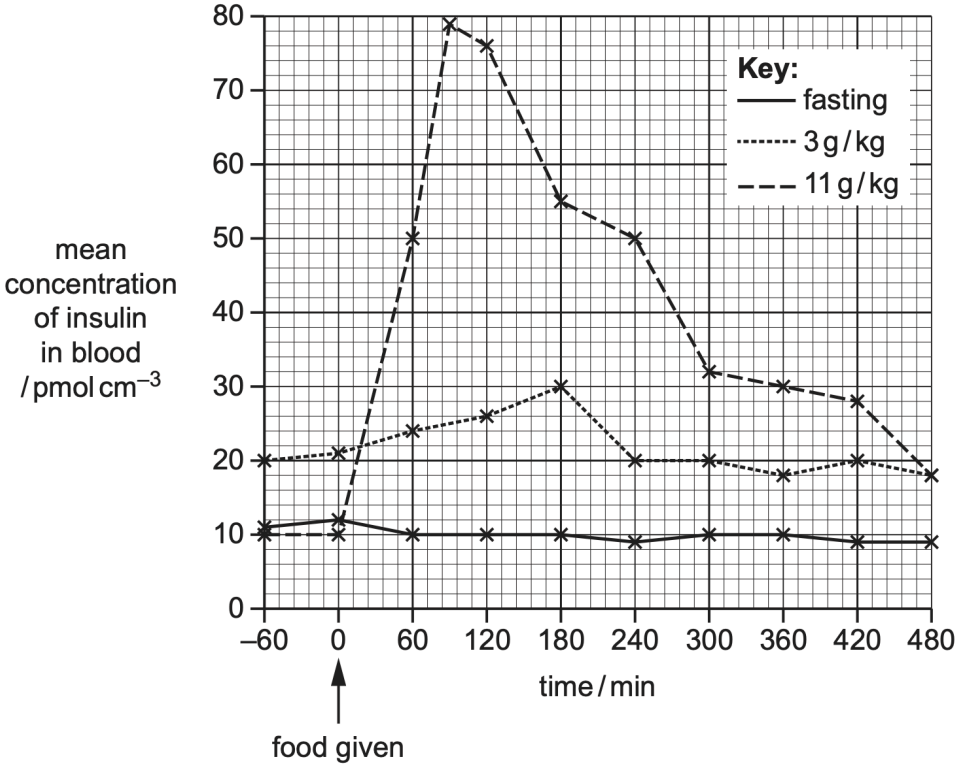
Question 2

Control of blood glucose concentration in dolphins is same as in most mammals. A study was carried out to investigate the concentration of insulin in the blood of dolphins that were provided with a diet of fish, supplemented with glucose.

- One group of dolphins ate fish with 3 g of glucose for every kg of fish.
- Another group ate fish with 11 g of glucose for every kg of fish.

The concentration of insulin in the blood was measured 60 minutes before being fed, at the time of being fed and at regular intervals afterwards. Measurements were also taken for a third group of dolphins, at the same time intervals, that were not fed any fish (fasting).

Results of the study:



Describe the trends shown.

- Concentration of insulin relatively constant for all groups before being fed.
- Fasting dolphins: very little change in insulin concentration.
- Fed dolphins: insulin concentration increases then decreases.

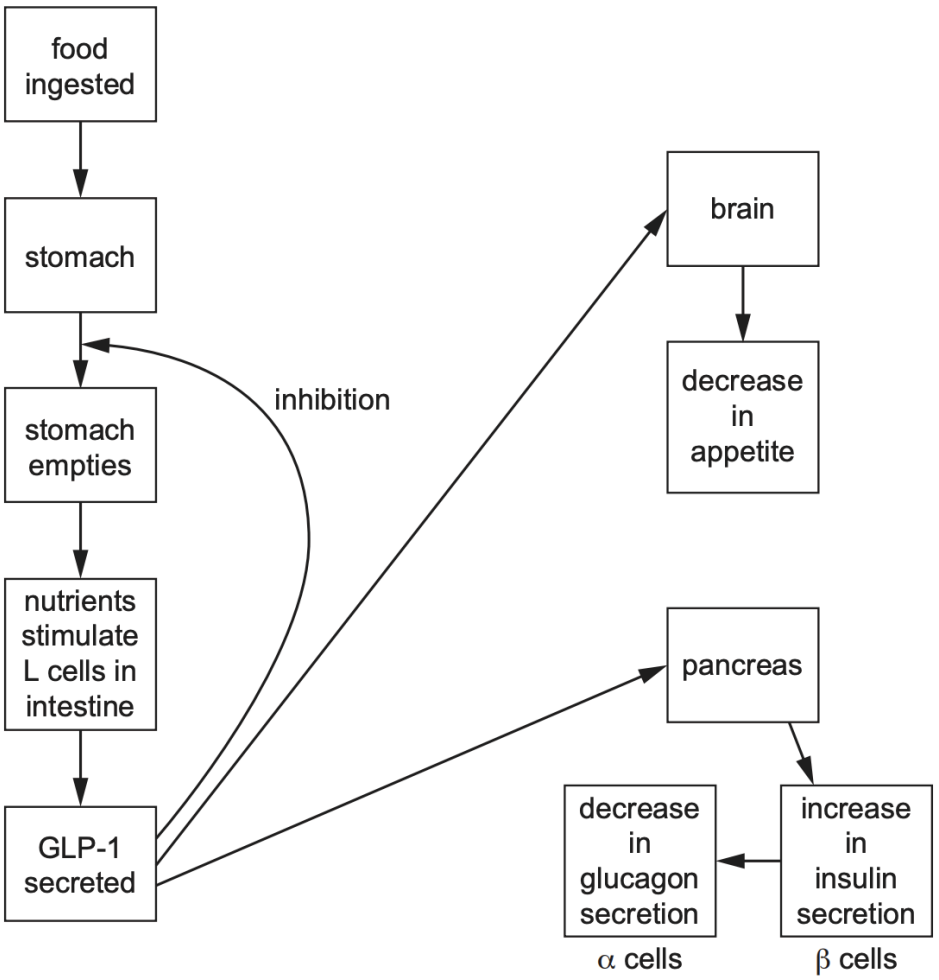
- Fed dolphins – 11 g / kg dolphins: steep increase / decrease in insulin concentration.
- Fed dolphins – 11 g / kg dolphins: highest peak in insulin concentration.
- Data quote with time in min:

3 kg	21 at 0 min	30 at 180 min	20 at 240 min
11 kg	10 at 0 min	79 at 90 min	18 at 480 min

Question 3

GLP-1 = hormone that inhibits secretion of glucagon by α cells in the pancreas.

Secretion of GLP-1 hormone and its effects on the pancreas, brain and stomach:



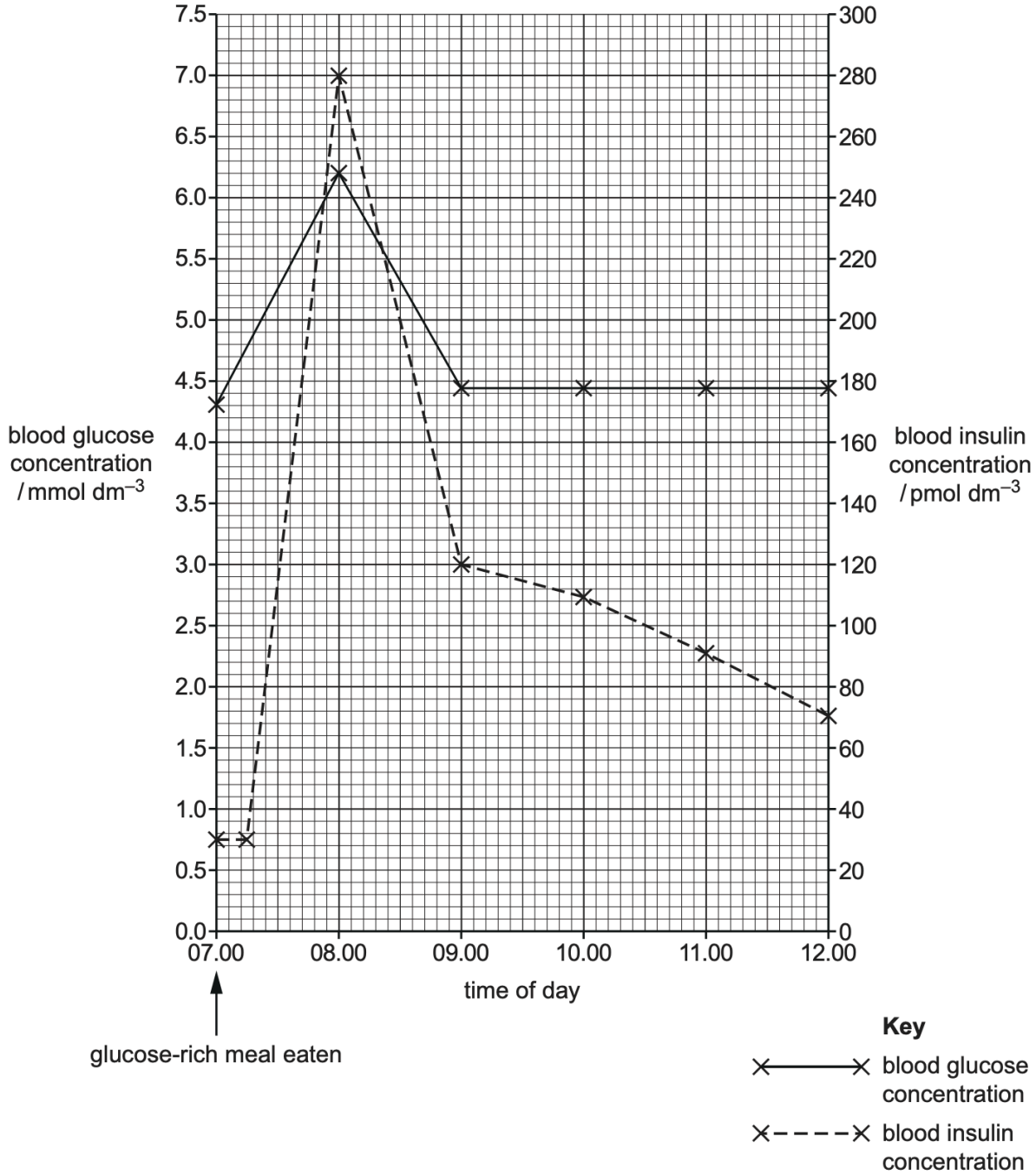
Suggest why secretion of GLP-1 causes a decrease in appetite.

- to reduce ingestion of food OR binds to receptors in brain.

Question 4

An investigation measured how blood glucose concentration and blood insulin concentration changed after a glucose-rich meal had been eaten.

Results:



Describe and explain how these results indicate a relationship between blood glucose concentration and blood insulin concentration after the consumption of a glucose-rich meal.

- As blood glucose concentration increases, blood insulin concentration increases; A positive correlation.
- Data quote + unit.
- Increase in blood glucose concentration causes release of insulin from pancreas.

- Insulin stimulates conversion of glucose to glycogen (glycogenesis) OR insulin increases permeability of liver / muscle cells to glucose.
- Insulin causes blood glucose concentration to return back to set point.
- Negative feedback mechanism.

Suggest and explain how these results would change if the meal was mostly starch rather than glucose.

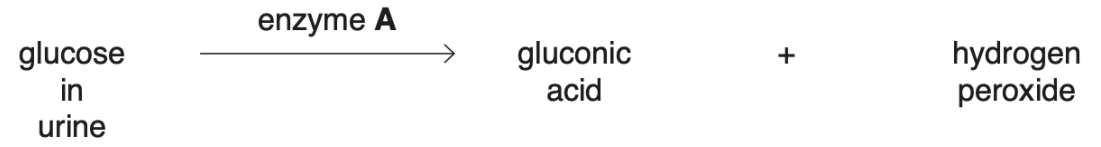
- Delay before both graphs would increase.
- Peaks for both would be lower.
- Both curves would take longer to decrease.
- Time is needed for starch to be broken down / converted to glucose.

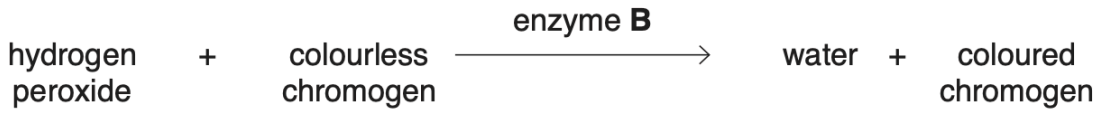
Test Strips & Biosensors

Describe how a glucose biosensor works.

- Sample of blood is placed on pad/strip and inserted into biosensor.
- Strip contains immobilised enzyme glucose oxidase which specifically reacts with glucose in the blood.
- Glucose is oxidised to produce gluconic acid and hydrogen peroxide.
- Hydrogen peroxide undergoes oxidation at the electrode, producing electric current/ flow of electrons/ voltage.
- Size of current is proportional to glucose concentration in blood.
- Electrical signal is converted to digital / numerical reading shown on screen.

How a dipstick works:





Enzyme A	glucose oxidase
Enzyme B	peroxidase

Advantages of using a biosensor to measure glucose concentration.

- rapid / immediate / 2 seconds reading
- more accurate / precise / quantitative / numerical / sensitive
- shows current blood glucose concentration
- reusable

Advantages of using a dipstick to measure glucose concentration.

- non-invasive / painless / less risk of infection
- easy to use
- cheap