Bio Factsheet

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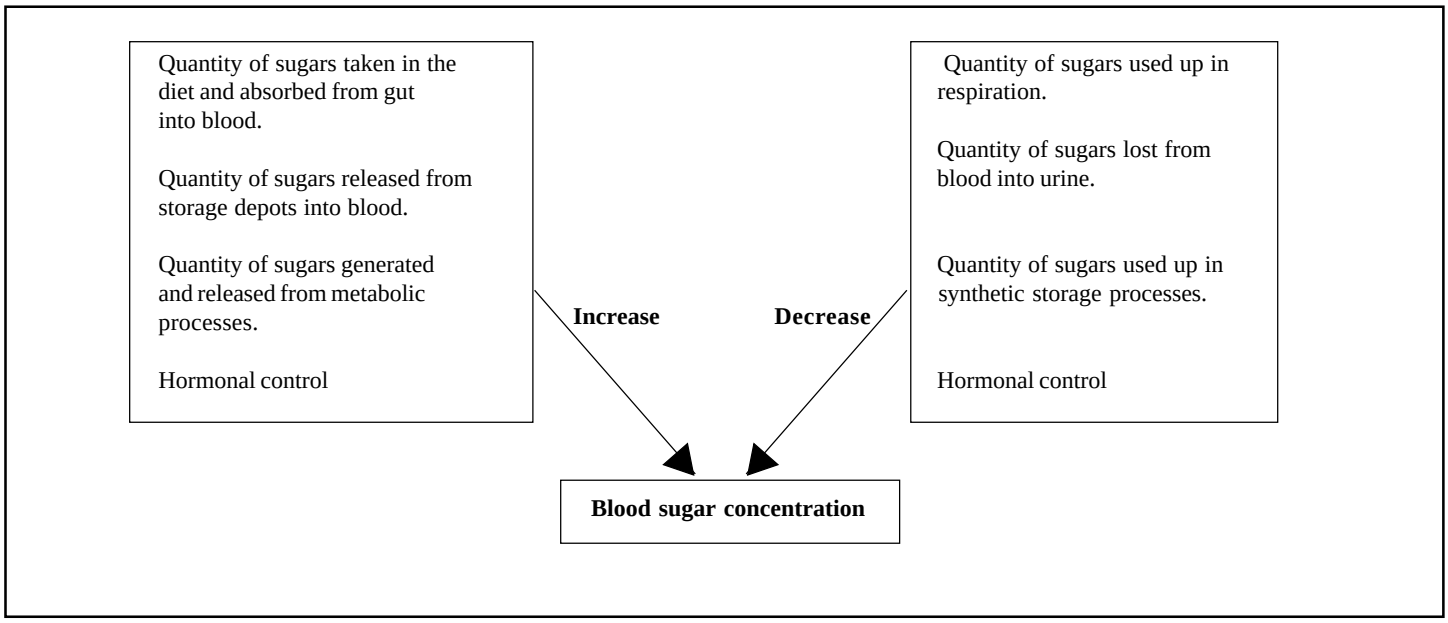
Blood Sugar and its Control

The main sugar carried in blood is glucose but many other sugars, for example, fructose, galactose, lactose, ribose, arabinose and xylose may be present in small quantities.

Fig. 1. Factors affecting the concentration of sugars in the blood.



- Glucose is the main sugar used as respiratory substrate in the body and its concentration in the blood is carefully controlled. This is so that the respiring cells and tissues receive a regulated quantity of glucose and this, in turn, regulates the rate of respiration.
- Concentrations of other sugars which occur in blood are not controlled. These sugars are used by the body as required and surplus in the blood is lost via the urine.

***Remember** – glucose is not normally present in urine (with a few exceptions, for example, during pregnancy). Other sugars may be present normally in urine. This is why a glucose specific test should be used to test urine when assessing sugar diabetes rather than a general reducing sugar test. Remember that a major symptom of sugar diabetes is the presence of **glucose** in the urine.*

- The normal concentration of glucose in the blood is 3.3 – 5.9 millimoles dm^{-3} which is known as the **fasting level**. This is measured after about 10 hours of fasting and represents the quantity of glucose being transported to the cells and tissues to maintain the rate of respiration.
- After a meal which contains carbohydrates, the blood glucose concentration may normally rise to 8.0 mmoles dm^{-3} as the blood carries glucose absorbed from the gut to the storage depots.
- Between 0.5 and 1.5 millimoles dm^{-3} of other sugars may normally be present in blood.

Absorption of sugars from the gut to the blood

The principal sources of carbohydrates in the diet are:

- polysaccharides starch and glycogen → (digested) → glucose molecules
- disaccharide sucrose (cane sugar, found in most fruits) → (digested) → glucose and fructose molecules
- disaccharide lactose (milk sugar) → (digested) → glucose and galactose molecules

Rhubarb, cherries and grapes contain fairly high levels of arabinose and xylose.

All sugars must be in their monosaccharide form (glucose, fructose, galactose) for absorption. Disaccharides and polysaccharides cannot be absorbed.

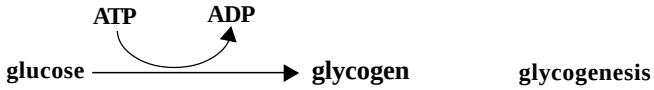
Most sugar absorption from digestive tract to blood occurs across the villi of the small intestine.

- Glucose and galactose are absorbed in combination with sodium ions. Both sodium ions and glucose (and/or galactose) molecules must bind to the outside of the appropriate membrane channel before it will open to allow the entry of sodium ions and glucose into the epithelial cells of the villi.
- Fructose is transported into the villi epithelial cells by facilitated diffusion.
- Once the monosaccharides have been transported into the villi epithelial cells they are moved by facilitated diffusion to the blood capillaries in the villi and transported to the liver in the hepatic portal vein.

Assimilation (fate) of absorbed sugars
The absorbed sugars are either absorbed into the hepatic cells of the liver, for storage as glycogen, or into other body cells and muscle fibres where they are used as respiratory substrate. Striated muscle fibres also store some glucose as glycogen.

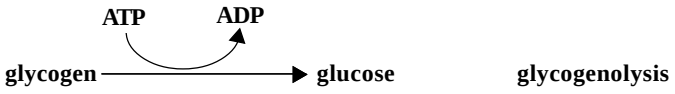
Once in cells, fructose and galactose are isomerised into glucose and metabolised as glucose.

If glucose is not needed immediately for respiration, it is combined with other glucose molecules to form the long-chained polymer glycogen. This process is called **glycogenesis** (making glycogen). It occurs mainly when glucose is being absorbed after a meal.



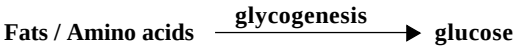
The body can store about 500g of glycogen of which about 20% is stored in the liver and 80% is stored in striated (skeletal) muscle fibres.

When the body requires energy, the glycogen stored in the liver is converted to glucose and released into the blood to be carried to the respiring cells for use. The process of converting glycogen to glucose is called **glycogenolysis** (splitting of glycogen). It usually occurs between meals.



Fat and protein molecules can also be converted in the liver to glucose. The process by which glucose is formed from non-carbohydrate sources is called **gluconeogenesis**. The process happens mainly when the liver supply of glycogen is low and the person has also not eaten recently.

Note that fatty acids break down to acetyl-coenzyme-A and ketone bodies. These ketone bodies will be referred to below because of their importance in sugar diabetes.



Sugar loss in urine

Sugars will only be lost in the urine if their blood concentration exceeds the renal threshold.

The renal threshold of a substance is its concentration <u>in the blood</u> which must be exceeded before the substance leaks via the kidney into the urine.

> ***Exam Hint:*** *a common error made by candidates is to refer to the renal threshold as 'the concentration of the substance in the urine'. Remember – the renal threshold is a blood concentration.*

- The renal threshold of glucose is 10.0 millimoles dm^{-3}. Even after a carbohydrate-rich meal, the blood concentration of glucose should not exceed the renal threshold, thus glucose should not be present in the urine.
- The renal threshold of all other sugars is zero. This means that if any of these sugars are present in the blood they can occur in the urine. Normally fructose will be immediately isomerised to glucose in the cells and so does not have time to be lost in urine. However, if one eats large quantities of fruit, jams or honey, sugars such as fructose, arabinose and xylose may occur in the urine.

The first convoluted tubules of the nephrons have powerful active transport mechanisms for reabsorbing glucose from glomerular filtrate to blood. These can cope with reabsorbing all the glucose, unless the blood concentration of glucose exceeds 10 millimoles dm^{-3}. Above this concentration, too much glucose enters the glomerular filtrate and the glucose pumps cannot cope with it all.

There are several possible causes for glucose to appear in urine:-

- inbalance of the hormones regulating glucose metabolism – this causes diabetic conditions.
- pregnancy – the developing fetus may press on the kidneys resulting in a failure to reabsorb glucose properly (a harmless condition which disappears after birth).
- a lowered renal threshold – this happens, for example, during a common cold, or during certain harmless genetic defects.

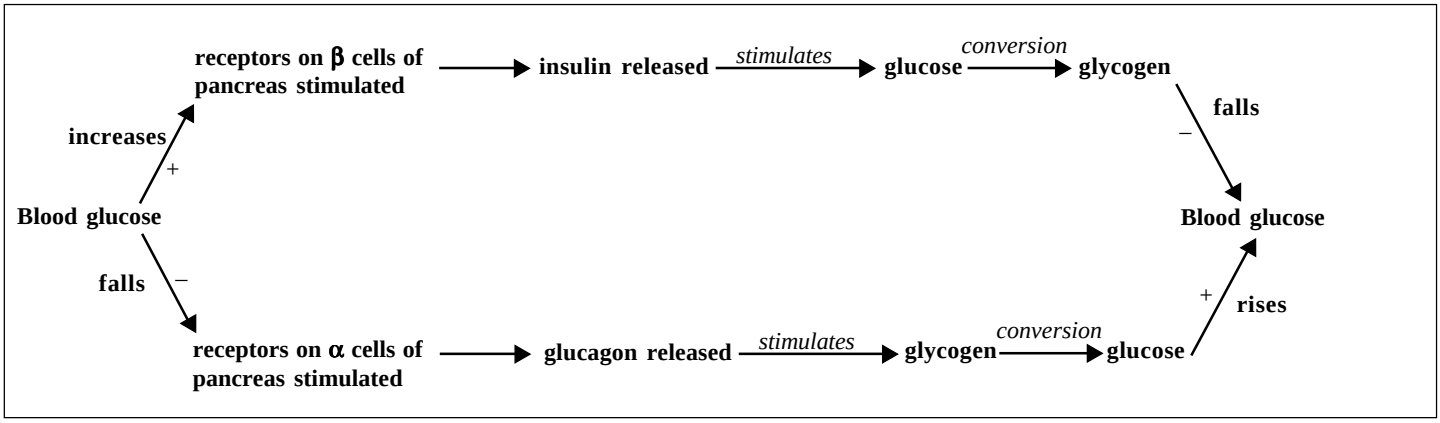
Hormonal control of blood glucose
The polypeptides insulin and glucagon are the two main hormones involved in blood glucose regulation. (Table 1).

Table 1. Hormonal control

Hormone	Secreting gland	Secreted in response to	Main effect	Modes of action
Insulin	Beta-cells of the islets of Langerhans in the pancreas	Raised blood glucose concentration	**Lowers** blood glucose concentration	• stimulates absorption of glucose from blood by muscle fibres, liver cells and adipose (fat) cells. • stimulates glycogenesis (glycogen synthesis) in liver and muscle and also stimulates oxidation/ respiration of glucose. • stimulates fat synthesis from glucose by adipose cells and protein synthesis from amino acids. • inhibits glycogen, fat and protein/ amino acid breakdown.
Glucagon	Alpha-cells of the islets of Langerhans in the pancreas	Lowered blood glucose concentration	**Raises** blood glucose concentration	• stimulates release of glucose into blood from muscle fibres, liver cells and adipose cells. • stimulates glycogenolysis causing breakdown of glycogen to glucose in liver and muscle fibres. • stimulates gluconeogenesis, forming glucose from glycerol and amino acids. • inhibits glycogenesis and fat synthesis from glucose.

Insulin and glucagon act to regulate blood glucose concentration (and thus regulate glucose and fat metabolism) by **negative feedback control**. The blood glucose receptors (sensors) which enable this control are situated on the alpha and beta cells in the islets of Langerhans (Fig 2).

Fig 2. Homeostatic control of blood glucose



Other hormones have indirect effects on the blood glucose concentration. For example:

- **Somatostatin** (growth hormone inhibiting hormone) from the delta cells of the islets of Langerhans can inhibit the secretion of insulin and glucagon.
- **Thyoxine** from the thyroid, **adrenaline** from the adrenal cortex, cortisone from the adrenal cortex and **adreno-cortico-tropic hormone (ACTH)** from the anterior pituitary, may all cause blood glucose concentration to rise.

***Exam Hint**: a very common error made by candidates is to state that 'the glucose receptors are in the hypothalamus or in the pituitary gland'. This is wrong – they are in the islets of Langerhans. Another frequent error is when candidates write ' insulin changes glucose to glycogen' or 'glucagon changes glycogen to glucose'. You should write 'insulin **stimulates** the synthesis of glycogen from glucose' or 'glucagon **stimulates** the release of glucose from glycogen'.*

Diabetic conditions

Diabetes mellitus (sugar diabetes) is not a single disease but a group of diseases, all of which cause an abnormal elevation of glucose in the blood (**hyperglycaemia**) and loss of glucose in the urine as hyperglycaemia increases. Diabetic conditions are also characterised by three 'polys':-

- **polyuria** an increased volume of urine. Because the urine contains a lot of glucose it requires more water as solvent and the nephrons have difficulty reabsorbing water from the tubular fluid because of its increased osmotic pressure due to its glucose content.
- **polydipsia** which is an excessive thirst caused by the dehydrating effect of excessive urine loss.
- **polyphagia** excessive eating caused by stimulation of the hunger centre in the hypothalamus caused by falling blood glucose concentration due to its loss in the urine.

Type I diabetes (insulin-dependent or juvenile-onset diabetes) most commonly develops in people younger than age 20, but it persists throughout life. It requires daily treatment with insulin to control it. Type I diabetics appear to have certain genes which make them more susceptible to certain triggering factors, such as viral infections or Streptococcal infections. The antibodies produced against these infections, in susceptible people, probably have an autoimmune effect, so besides destroying the infecting pathogens, they rapidly cause destruction of the beta cells in the islets of Langerhans. Thus insulin secretion becomes seriously impaired or non-existent so the person quickly becomes diabetic.

The lack of insulin causes raised blood glucose concentration and loss of glucose in the urine (**glycosuria**). In themselves these symptoms are not dangerous. However, the lack of insulin accelerates fat breakdown resulting in the production of too many ketone bodies. These cause **ketosis** which increases the acidity of the blood (lowers blood pH) – this will lead to hyperglycaemic coma and death, unless controlled with insulin injections.

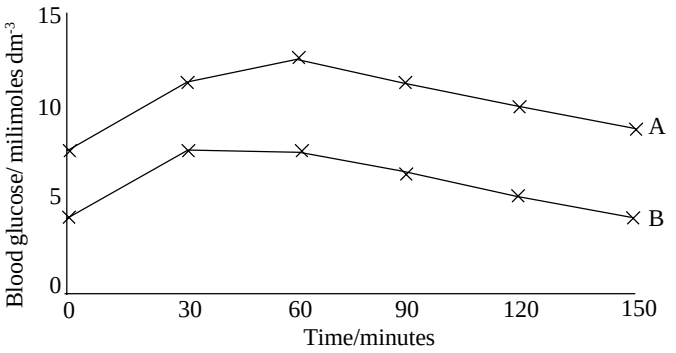
In the past, type I diabetics were treated by daily insulin injections in which the insulin had been extracted from other mammalian species, for example, sheep, goat, pig, cow insulin. Genetic engineering has enabled the mass production of human insulin (humilin) and most diabetics now use this. Attempts are being made to develop long-term cures by gene therapy, by cloning of islet cells which can then be transplanted into sufferers and by injecting sufferers with undifferentiated fetal islet cells.

Type II diabetes (non-insulin-dependent or maturity-onset diabetes) occurs commonly in people who are over 40 and overweight. It accounts for 90% of all diabetic cases. The symptoms are mild and the high blood glucose levels can usually be controlled by diet and exercise. Type II diabetics usually have a sufficient amount of insulin in their blood but for some reason it fails to act effectively. This may be due to overactivity of hormones such as thyroxine, tri-iodothyronine, cortisone, ACTH or even adrenaline. Alternatively it may be due to some molecular defect which develops on the insulin receptors or insulin mediating machinery of the cells.

***Remember** – diabetic comas can be one of two types. In **hyperglycaemic** coma the blood glucose level is too high but the coma is caused by excessive ketone production from uncontrolled fat metabolism. It should be treated by administering insulin. In **hypoglycaemic** coma the blood glucose level is too low with the result that brain cells are starved of glucose. It can be caused by taking too large a dose of insulin. It should be treated by administering glucose and/or by injecting adrenaline. Both types of coma can cause death unless treated quickly.*

Practice Questions

1. Two people, A and B, fasted overnight and then swallowed 75g of glucose. Their blood glucose concentrations were measured every 30 minutes for 2½ hours. The results are shown in the graph below.



glucose taken at 1 minute after initial blood sample

(a) One of the graphs indicates a diabetic state. Is it A or B? Suggest three reasons to explain your answer. 4

(b) (i) Define the term 'renal threshold'. 1
(ii) Draw a line on the graph to indicate the renal threshold of glucose. 1

(c) With reference to insulin, glucagon and glucose explain the shape of curve B,
(i) from 0 minutes to 60 minutes, and 3
(ii) from 60 minutes to 150 minutes. 3

Total 12 marks

2. The following statements refer to an untreated sufferer of insulin-dependent diabetes. Explain whether each statement is true or false. An untreated sufferer of insulin-dependent diabetes has,

(a) a high concentration of ketones in the blood. 1

(b) glycosuria (glucose in the urine). 1

(c) very slow glycogen synthesis. 1

(d) a fast drop in blood glucose concentration after a meal. 1

Total 4 marks

3. (a) (i) Distinguish 'glycogenolysis' from 'gluconeogenesis'. 2
(ii) What effects do insulin and glucagon have on these processes?1

(b) What do you understand by the term 'fasting blood glucose'? 2

(c) In the early 1920s, two scientists called Banting and Best discovered insulin and managed to extract it from dogs. In one experiment they removed the pancreas from a dog and found that the dog could not control the glucose level in its blood. When they injected an extract of the dog pancreas into the dog the blood glucose level was controlled for a short time but after a few hours the dog died. Explain why the dog died. 3

(d) When experiments of this type are performed some people are likely to complain. Suggest one argument to support and one argument to ban this type of experiment. 2

Total 10 marks

Answers

1. (a) A;
initial fasting level is above the normal fasting level;
blood glucose level rises for 60 minutes whereas A only rises for minutes/ref to slow change of absorbed glucose to stored glycogen;
blood glucose level exceeds renal threshold/ref glycosuria;
final blood glucose level still above norm/insufficient glucose converted to glycogen; **max** 4

(b) (i) the concentration of a substance in the blood which must be exceeded before the substance escapes into the urine; 1
(ii) draw a horizontal line, parallel to the X-axis, from the 10 millimole dm^{-3} level on the Y-axis; 1

(c) (i) glucose is being absorbed from the digestive tract into the blood faster (over the first 30 minutes) than it is being changed to glycogen /or at the same rate (over the 30 -60 minute period);
raised blood glucose concentration is stimulating insulin release so that insulin can stimulate the change of glucose to glycogen;
glucagon release is inhibited by negative feedback; 3

(ii) most of the glucose has been absorbed from the digestive tract into the blood and the surplus blood glucose is being changed to glycogen to bring the blood glucose level back to the norm/ fasting level/respiratory level;
insulin concentration is still high but falls as blood glucose concentration becomes reduced;
eventually when the blood glucose returns to a fasting level, glucagon secretion will occur due to negative feedback stimulation; 3

2. (a) **True.** Lack of insulin results in increased fat metabolism which results in increased release of ketones from cells; 1

(b) **True.** An abnormally high blood glucose concentration exceeds the renal threshold, so glucose leaks into the urine; 1

(c) **True.** As insulin is deficient glucose will be converted to glycogen more slowly; 1

(d) **False.** Insulin stimulates the synthesis of glycogen from blood glucose, so if insulin is deficient the synthesis occurs more slowly than normal; 1

3. (a) (i) glycogenolysis is the release of glucose from glycogen;
gluconeogenesis is the synthesis of glucose from non-carbohydrate molecules such as amino acids/glycerol; 2
(ii) insulin inhibits but glucagon stimulates glycogenolysis and gluconeogenesis; 1

(b) it is the glucose level after fasting overnight/for about 10 hours; it is the amount of glucose being carried to/required by the cells to maintain respiration/metabolic rate; 2

(c) the dog became diabetic and could not produce insulin; thus fat breakdown was not inhibited and so ketone bodies were formed/ ketosis occurred; this lowered blood pH resulting in hyperglycaemic coma/death; 3

(d) **for:** it provides information to help in understanding/treating diseases common to animals and humans;
against: it is cruel/immoral to experiment on live animals; 2

Total 10 marks

Acknowledgements:
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