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The testing of a patient's blood glucose is a common event both in hospital wards and at home. It is a relatively simple procedure using modern, portable monitors and almost every nurse will at some time have performed it. However, in order to interpret test results and understand pathologies that can affect glucose levels, such as diabetes, it is necessary to have some knowledge of the physiological mechanisms that regulate the body's blood glucose. In this article, Pat James and Roger McFadden outline the principles

KEY WORDS

**Glucose regulation
Insulin
Glucagon**

REFERENCE

Guthrie, D.W., Guthrie, R.A. (2002) *Nursing Management of Diabetes Mellitus: A Guide to the Pattern Approach*. New York, NY: Springer Publishing.

Understanding the processes behind the regulation of blood glucose

Glucose is one of the body's principal fuels. It is an energy-rich monosaccharide sugar that is broken down in our cells to produce adenosine triphosphate. ATP is a small packet of chemical energy that powers the millions of biochemical reactions that take place in the body every second.

We obtain glucose from the food that we eat, predominantly starch-rich foods such as potatoes, rice, bread, and pasta. Starch is a polysaccharide (a chain of glucose molecules) that is broken down by digestive enzymes into individual glucose molecules.

In the small intestine, glucose is absorbed into the blood and travels to the liver via the hepatic portal vein. The hepatocytes (liver cells) absorb much of the glucose and convert it into glycogen, an insoluble polymer of glucose.

This is stored in the liver and can be reconverted into glucose when blood-glucose levels fall. Other types of simple sugars in our diet such as fructose, sucrose and lactose are also fuels that contribute to the production of ATP.

All of the body's cells need to make energy and most can use other fuels such as lipids. However, neurons (nerve cells) rely almost exclusively on glucose for their energy. This is why the maintenance of blood-glucose levels is essential for the proper functioning of the nervous system.

If glucose levels fall to too low a concentration (hypoglycaemia) or rise too high (hyperglycaemia) then this situation can lead to the neurological processes in the brain being compromised.

At some time, most of us will have experienced the effects of low blood glucose, a feeling of being light-headed, weak and shaky, together with an inability to concentrate properly.

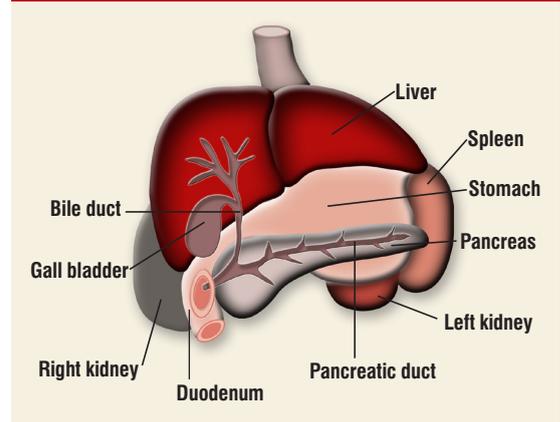
Chronic hyperglycaemia, which is a common feature of diabetes mellitus, also causes neurological problems and is a contributory factor to both atherosclerosis and renal failure.

Glucose regulation Blood-glucose levels fluctuate as a person's intake of food varies over a 24-hour period. After meals, the body is said to be in an absorptive state as it absorbs nutrients from the gut. Blood-glucose levels rise although this is buffered by glucose storage in the liver.

When digestion is complete and the absorption of nutrients decreases, the body is in a post-absorptive state and, as the body's cells use glucose to make energy, blood-glucose levels fall.

Despite these fluctuations, the body needs to maintain

FIG 1. THE POSITION OF THE PANCREAS RELATIVE TO ADJACENT ORGANS



blood-glucose levels within certain limits and the homeostatic mechanisms discussed below maintain glucose levels within these limits.

What are typical blood-glucose levels? During the absorptive state, glucose levels can vary with the type and quantity of food eaten. Therefore post-absorptive, fasting-state glucose levels are more reliable and are generally used by health care professionals when testing blood glucose (for example, imagine the test results just after an over-generous helping of sticky toffee pudding).

Typical fasting levels of blood glucose lie between 3.3 and 6.1mmol/L (Guthrie and Guthrie, 2002). Results outside this range could indicate a dysfunction in glucose regulation such as that which occurs in patients with diabetes mellitus.

The role of the pancreas The pancreas, a large gland that nestles under the stomach, plays an important part in glucose regulation and is unusual in having both an exocrine and endocrine function.

As an exocrine gland it produces several digestive enzymes that are secreted into the duodenum via the pancreatic duct. Over 90 per cent of the pancreas is devoted to its exocrine, digestive function. The position of the pancreas relative to adjacent organs is shown in Fig 1.

As an endocrine gland, the pancreas secretes a variety of hormones that are concerned with the regulation of blood glucose, including insulin, glucagon, and somatostatin.

These hormones are produced by groups of cells that under the microscope appear as small clusters, or islands. They were discovered by the German anatomist

WEBSITES

Sanger Institute – Insulin Signal Transduction Resource Site: www.sanger.ac.uk/PostGenomics/signaltransduction/insulin
The Internet Pathology Laboratory for Medical Education: <http://medstat.med.utah.edu/WebPath/webpath.html>
UK Government National Statistics: www.statistics.gov.uk/StatBase

TABLE 1. SUMMARY OF THE ACTION OF PRINCIPAL HORMONES THAT ARE INVOLVED IN THE REGULATION OF BLOOD GLUCOSE IN THE BODY

HORMONE	SITE OF PRODUCTION	SUMMARY OF ACTION
Insulin	Pancreatic islets (beta cells)	Stimulates cells to take up glucose from the blood and so lowers blood glucose
Glucagon	Pancreatic islets (alpha cells)	Stimulates hepatocytes to release glucose into the blood and so raises blood glucose
Somatostatin	Pancreatic islets (delta cells)	Reduces gut motility and further absorption of nutrients
Adrenaline (epinephrine)	Adrenal medulla	Mobilises glycogen and suppresses the

Paul Langerhans, hence they are called Islets of Langerhans, or simply pancreatic islets. A typical islet is shown in Fig 2.

Response to an increase in blood glucose

In the absorptive state, an increase in blood glucose is detected by the beta cells of the pancreatic islets, causing them to increase the release of insulin into the blood. Insulin stimulates cells, especially adipose and muscle cells, to take up glucose from the blood.

Insulin and the transport of glucose into cells To enter cells, glucose requires trans-membrane transporters and there is a family of these called GLUT (GLUcose Transporter). The most numerous is GLUT4, which is found on muscle and fat cells.

When insulin binds to insulin receptors on the cell membrane, cells are stimulated to increase the number of glucose transporters. The more transporters are produced, the more glucose is transported into cells – with a corresponding drop in blood glucose.

The precise mechanism whereby insulin binds to receptors causing translocation is still to be determined (Sanger Institute, see ‘websites’).

Not all tissues require insulin to take up glucose, for example brain and liver cells use GLUT transporters that are not dependent on insulin.

Further effects of insulin The hormone also has other effects on the body’s cells, all of which contribute to an increase in glucose usage and storage – and therefore a reduction in blood glucose. These include:

- The promotion of glycolysis, a process that breaks down glucose for cellular energy;
- The promotion of glycogenesis, a process that converts glucose into glycogen for storage;
- The inhibition of lipolysis, a process that breaks down

lipids to release energy.

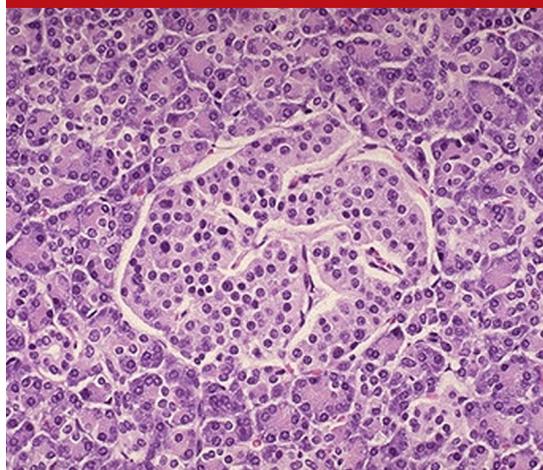
These effects of insulin actively shift the metabolism away from fat and towards glucose. In other words, insulin drives the body to utilise carbohydrates as a source of energy and to spare its fat reserves.

Response to a decrease in blood glucose

Several hours after eating a meal, when the body is in the post-absorptive state, insulin levels fall along with blood glucose and this results in the hormone glucagon being released by the alpha cells of the pancreas.

The role of glucagon Glucagon has the opposite effect to insulin in that it increases blood-glucose levels and promotes processes that spare glucose utilisation.

FIG 2. ISLET OF LANGERHANS SURROUNDED BY EXOCRINE PANCREATIC TISSUE



Reproduced with permission from Professor Edward Klatt, Florida State University, US (The Internet Pathology Laboratory for Medical Education, see ‘websites’)

FURTHER READING

Guyton, A.C., Hall, J.E. (2000) *Textbook of Medical Physiology*. Philadelphia, PA: W.B. Saunders.
Sherwood, L. (1997) *Human Physiology From Cells to Systems*. Belmont, CA: West Publishing.

Glucagon works primarily on the hepatocytes in the liver to:

- Convert stored glycogen into glucose and release it into the blood;
- Promote gluconeogenesis, the manufacture of new glucose from lactic acid and other metabolites.

Glucagon binds to glucagon receptors, which are part of the G-protein-coupled receptor family. This stimulates a series of linked enzyme reactions, resulting in the activation of glycogen phosphorylase, the enzyme responsible for the mobilisation of glycogen reserves into free glucose. Glucagon release is inhibited by both insulin and somatostatin.

Homeostatic control The control of blood glucose is an excellent example of homeostatic control via negative feedback. This is where the corrective response, triggered by a deviation from normal levels, is turned off by a return to normal levels.

For example, low blood glucose results in the production of glucagon and this raises blood glucose. Consequently, as glucose levels rise, the stimulation to produce glucagon is turned off.

A summary of the contrasting actions of insulin and glucagon is shown in Fig 3.

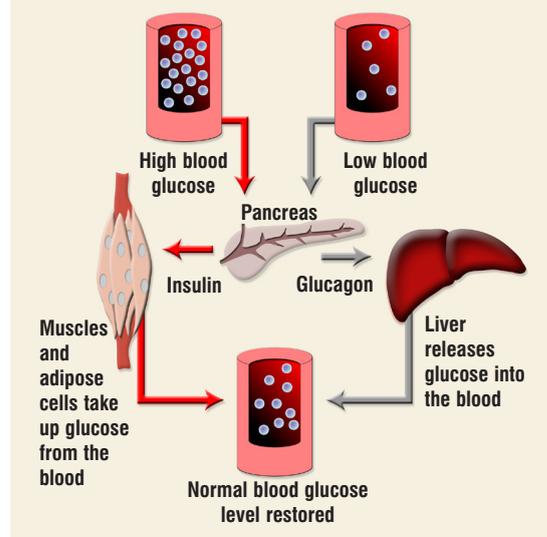
Other hormones that are involved in the regulation of blood glucose Like most of the physiological processes, the regulation of blood glucose is complex and there are many other hormones beside insulin and glucagon that play an important function, such as somatostatin.

The role of somatostatin This is released by the delta cells located in the pancreatic islets in response to a post-prandial increase in blood glucose and amino acids. It reduces gut motility and the further absorption of nutrients as well as inhibiting pancreatic exocrine secretions.

The function of gastrin and cholecystokinin The gastrointestinal tract also releases hormones such as gastrin and cholecystokinin that stimulate the pancreas to secrete insulin in anticipation of the absorption of nutrients.

The role of stress hormones When a person is experiencing stress, neuro-endocrine mechanisms cause the release of stress hormones such as adrenaline (epinephrine). These increase blood-glucose levels by mobilising glycogen and suppressing the release of insulin.

FIG 3. COMPLEMENTARY ACTION OF INSULIN AND GLUCAGON RESPONDING TO A RISE OR FALL IN BLOOD-GLUCOSE LEVELS



Other hormones such as amylin and pancreatic polypeptide (PP) are involved in glucose regulation but their roles are less well understood.

A summary of the principal hormones involved in glucose regulation is presented in Table 1.

Neuroregulation of blood glucose The autonomic division of the nervous system modulates the release of insulin and glucagon. The sympathetic stimulation that occurs with exercise stimulates glucagon production and this maintains blood-glucose levels that would otherwise fall as muscles use glucose for their energy.

During the periods when the body is at rest, parasympathetic activity stimulates digestion and also the release of insulin to deal with the expected rise in blood glucose.

Conclusion The incidence of type 1 and type 2 diabetes has been increasing annually in the UK (UK Government National Statistics, see 'websites') and researchers are working hard to determine the causes of these diseases and to develop new treatments.

Diabetes is fundamentally a dysfunction in glucose metabolism but there are many aspects of this complex issue that are yet to be resolved.

As our understanding of these processes improves, so does the possibility for advances in treatment, or even finding a cure. ■