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DIABETES MELLITUS AND THE BIOCHEMICAL CHANGES THAT OCCUR IN IT

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Annotation: this article provides information on diabetes mellitus and the biochemical changes that occur in it. The article is written in the case of using internet resources.

Key words: diabetes mellitus, biochemical changes, blood.

Diabetes mellitus is a condition in which the body is unable to control blood glucose levels adequately, resulting in high blood glucose levels (hyperglycaemia). Symptoms include frequent urination due to the osmotic effect of excess glucose in the urine, thirst due to loss of fluids and weight loss. Possible long-term complications of diabetes if blood glucose has been poorly controlled include cardiovascular disease (such as atherosclerosis and stroke) and damage to nerves, the kidney and eyes, which can potentially lead to blindness. Diabetes is a major health problem with an estimated 425 million people affected worldwide, and these numbers are predicted to rise. The rise in numbers is associated with an increase in obesity in the population and treating the complications is a major healthcare cost. In the U.K., some estimates predict the cost could reach 17% of the NHS budget.

Most people will be familiar with the classification of diabetes into the two main forms, Type 1 and Type 2; however, it is increasingly clear that there are in fact several different types of diabetes, some of which overlap to some extent. Recent research analysing nearly 15000 diabetics showed they could be clustered into five distinct groups based on specific biomarkers[1] of the condition, which is significant because this better classification system may lead to improved treatment strategies in the future. Type 1 diabetes is an autoimmune disease in which cells of the body's immune system cause destruction of insulin secreting β-cells in the pancreas, leading to a deficiency of insulin production. There are typically antibodies against key pancreatic proteins involved in insulin storage and secretion. It is a relatively rare form of the disease affecting 5–10% of diabetics, which is usually diagnosed in childhood and is not associated with excess body weight. Type 2 diabetes is the more common form of the disease, affecting 90–95% of diabetics, and is characterised by a loss of ability to respond to insulin (i.e. there is insulin resistance, also termed as insulin insensitivity). At diagnosis, individuals are typically over 30 years old, overweight, have high blood pressure and an unhealthy lipid profile (referred to as the metabolic syndrome). Established disease is associated with hypersecretion of insulin, but this is still inadequate to restore normal blood glucose levels, and the condition may progress towards insulin deficiency. The causes of diabetes are thought to be a combination of

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genetic and environmental factors, and it is recognised that being overweight is a strong risk factor for developing Type 2 diabetes.

In healthy individuals, blood glucose levels range between 3.5 and 5.5 mmol/l before meals. This range is maintained by the actions of hormones (primarily insulin and glucagon, but also adrenaline, cortisol and growth hormone) which control the production and uptake of glucose, levels of glycogen (the stored form of glucose), and fat and protein metabolism, as required following meals, during fasting and exercise. Both insulin and glucagon are polypeptides produced by the pancreas (β-cells – insulin; α-cells – glucagon).

Insulin is secreted in response to an increase in blood glucose levels and its overall effect is to store chemical energy by enhancing the uptake and storage of glucose, amino acids and fats; consequently reducing blood glucose levels, via actions on liver, muscle and adipose tissue (specifically adipocytes – fat cells). Glucagon, on the other hand, via a complex interplay with other hormones and the nervous system increases blood glucose by stimulating the breakdown of glycogen, fat and protein. When blood glucose is high, after a meal for example, insulin acts on the liver to decrease glucose synthesis (gluconeogenesis), increase glucose utilisation (glycolysis) and increases glycogen synthesis (glycogenesis). When the storage capacity for glycogen is reached, insulin increases synthesis of fatty acids (lipogenesis), via acetyl CoA as an intermediate, which is then exported for triglyceride synthesis in adipocytes. In muscle, insulin stimulates uptake of glucose, by recruiting the glucose uptake transporter type 4 (GLUT-4), and enhances glycogen synthesis and glycolysis. In adipose tissue, there is facilitated uptake of glucose which is metabolised to glycerol and subsequently used together with fatty acids to synthesise triglycerides. Insulin also inhibits pathways involved in lipolysis. In addition, insulin increases amino acid uptake and protein synthesis in muscle and is considered an anabolic hormone (i.e. one that builds up organs and tissues).

At the biochemical level, insulin produces its effects by binding to the insulin receptor – a cell surface glycoprotein composed of two extracellular α subunits and two β subunits that span the membrane. The receptor has tyrosine kinase activity (i.e. enzyme activity that catalyses the transfer of a phosphate group from ATP to a tyrosine amino acid within a protein, also known as tyrosine phosphorylation). Binding of insulin to the receptor initially causes tyrosine phosphorylation of the receptor itself, and then phosphorylation of intracellular proteins termed as insulin receptor substrate (IRS)-1 and IRS-2, followed by a complex series of intracellular signalling events involving many other kinases that lead to the physiological changes in carbohydrate, fat and protein metabolism discussed above via changes in gene expression and the activity of metabolic enzymes. The effects of insulin on glucose uptake are mediated via the glucose transporter GLUT-4, which is stored in intracellular vesicles in an inactive state, and insulin stimulates the movement of these vesicles to the plasma membrane where GLUT-4 becomes inserted into the membrane forming a pore that allows glucose uptake into the cell.

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Many of the longer term complications of diabetes involve effects on both large arteries (macrovascular) and small arteries and capillaries (microvascular). High blood glucose leads to proteins and lipids becoming modified in a non-enzymatic process by exposure to sugars, forming advanced glycation end products that have been implicated in the disease process. Oxidative stress and damage to the vascular endothelium lining blood vessels is also involved. One of the diagnostic tests for diabetes involves measuring levels of glycated haemoglobin (HbA_{1c}) from red blood cells. This is a valuable test because it gives an assessment of the average plasma glucose concentration over months, because of the 120 days lifespan of a red blood cell, and it also gives an indication of how effective treatment has been.

An acute serious life-threatening condition associated with untreated Type 1 diabetes is diabetic ketoacidosis. It develops in the absence of insulin, during which there is increased glucose production by the liver but because of the absence of insulin cells in the periphery, such as muscle cells, are unable to take-up the glucose and use it. The consequent high blood glucose levels results in the kidneys filtering and removing it from the body in urine. This is associated with osmotic diuresis (loss of fluids and electrolytes) and dehydration. As an alternative energy source, triglycerides (fats) from adipose tissue are broken down to free fatty acids and taken up by the liver. Here they are converted into acetyl CoA which is the precursor for formation of ketones (acetoacetate, β-hydroxy-butyrate and acetone) within mitochondria. These are referred to as ketone bodies and released into the blood and are detectable in the breath giving a distinctive smell similar to that of acetone or pear drops. Release of ketones into the blood causes a drop in pH (acidosis) and the body tries to compensate by hyperventilating. If untreated, these events can lead to coma and death.

For treatment of Type 1 diabetes, insulin is essential. Human insulin is now produced by recombinant DNA technology, rather than via extraction from the pancreases of animals. Diet and exercise are key to treatment of Type 2 diabetes and this can be combined with drug treatment.

Atherosclerosis, also known as hardening of the arteries, is a chronic arterial disease that develops over many decades and is a major cause of deaths worldwide. A raised patch or plaque, develops in the arterial wall that is rich in fat, cholesterol and calcium, and over time this hardens and narrows the artery depriving the region supplied by the blood vessel of oxygen (ischaemia). Rupture of the plaque causes blood cell fragments called platelets to stick to the surface of the injury, leading to thrombosis (formation of a blood clot) which can result in a total blockage of the affected artery. If a coronary artery is affected, a myocardial infarction (heart attack) may result or if a cerebral artery supplying the brain is affected ischaemic stroke may result. Multiple risk factors have been identified for development of atherosclerosis. Some of these are modifiable, such as an unhealthy blood lipid profile, high blood pressure, Type 2 diabetes, smoking, obesity, stress and physical inactivity. Other factors such as age, gender, race and a family history of heart disease cannot be changed. The biochemistry of lipid metabolism and

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process of atherosclerosis are discussed below.

Literature:

1. IDF Diabetes Atlas - 8th Edition (2017) http://diabetesatlas.org/resources/2017-atlas.html
2. Diabetes UK - The Cost of Diabetes (2014) https://www.diabetes.org.uk/resources-s3/2017-11/diabetes%20uk%20cost%20of%20diabetes%20report.pdf
3. Ahlqvist E., Storm P., Karajamaki A., Martinell M., Dorkhan M., Carlsson A.. et al. (2018) Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables. *Lancet Diab. Endocrinol.* 6, 361–369 10.1016/S2213-8587(18)30051-2
4. Rich S.S. (2016) Diabetes: still a geneticist's nightmare. *Nature* 536, 37–38 10.1038/nature18906
5. Samuel V.T. and Shulman G.I. (2012) Mechanisms for insulin resistance: common threads and missing links. *Cell* 148, 852–871 10.1016/j.cell.2012.02.017