DIABETES

(4 Hours)

Diabetes mellitus, often referred to simply as diabetes (Ancient Greek “to pass through"), is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels (hyperglycemia). Blood glucose levels are controlled by a complex interaction of multiple chemicals and hormones in the body, including the hormone insulin made in the beta cells of the pancreas. Diabetes mellitus refers to the group of diseases that lead to high blood glucose levels due to defects in either insulin secretion or insulin action in the body.

Diabetes develops due to a diminished production of insulin (in type 1) or resistance to its effects (in type 2 and gestational). Both lead to hyperglycemia which largely causes the acute signs of diabetes: excessive urine production resulting in compensatory thirst and increased fluid intake, blurred vision, unexplained weight loss, lethargy, and changes in energy metabolism. All forms of diabetes have been treatable since insulin became medically available in 1921, but there is no cure. The injections by a syringe, insulin pump, or insulin pen deliver insulin, which is a basic treatment of type 1 diabetes. Type 2 is managed with a combination of dietary treatment, exercise, medications and insulin supplementation. Diabetes and its treatments can cause many complications. Acute complications (hypoglycemia, ketoacidosis, or nonketotic hyperosmolar coma) may occur if the disease is not adequately controlled. Serious long-term complications include cardiovascular disease (doubled risk), chronic renal failure, retinal damage (which can lead to blindness), nerve damage (of several kinds), and microvascular damage, which may cause dysfunction and poor wound healing. Poor healing of wounds, particularly of the feet, can lead to gangrene, and possible to amputation. Adequate treatment of diabetes, as well as increased emphasis on blood pressure control and lifestyle factors, may improve the risk profile of most of the chronic complication.

Classification

The term diabetes, without qualification, usually refers to diabetes mellitus, which is associated with excessive sweet urine (known as “glycosuria”) but there are several rare conditions also named diabetes. The most common of these is diabetes insipidus (DI) in which the urine is not is not sweet (insipidus meaning "without taste" in Latin); it can be caused by either kidney (nephrogenic DI) or pituitary gland (central DI) damage. It is a noninfectious diseases. Among the body system is a noninfectious disease. Among the body systems affected are the nerve, digestive, circulatory, endocrine and urinary systems.

The term "type 1 diabetes" has universally replaced several former terms, including childhood onset diabetes, juvenile diabetes, and insulin-dependent diabetes mellitus (IDDM). Likewise, the Term "type 2 diabetes" has replaced several former terms, including adult-onset diabetes, obesity related diabetes, and non-insulin-dependent diabetes mellitus (NIDDM). Beyond these two types, there is no agreed-upon standard nomenclature. Various sources have defined "type 3 diabetes" as, among others, gestational diabetes, insulin-resistant type 1 diabetes (or "double diabetes"), type 2 diabetes which has progressed to require injected insulin, and latent autoimmune diabetes of adults (or LADA or "type 1.5" diabetes). There is also maturity onset diabetes of the young (MODY) which is a group of several single gene (monogenic) disorders with strong family histories that present as type 2 diabetes before 30 years of age.

Type 1 Diabetes

Type 1 diabetes mellitus is an autoimmune disease and characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas leading to a deficiency of insulin. Most affected people are healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early states. Type 1 diabetes can affect children or adults but was traditionally termed “juvenile diabetes” because it represents a majority of the diabetes cases in children. The principal treatment of type 1 diabetes, even in its earliest stages, is the delivery of artificial insulin via injection combined with careful monitoring of blood glucose levels using blood testing monitors. Without insulin, diabetic ketoacidosis often develops which may result in coma or death. Treatment emphasis is now also placed on lifestyle adjustments (diet and exercise) though these cannot reverse the progress of the disease. Apart from the common subcutaneous injections, it is also possible to deliver insulin by a pump, which allows continuous infusion of insulin 24 hours a day at preset levels, and the ability to program doses (a bolus) of insulin as needed at meal times. Type 1 treatment must be continued indefinitely in essentially all cases. Treatment need not significantly impair normal activities, if sufficient patient training, awareness, appropriate care, discipline in testing and dosing of insulin is taken. However, treatment is burdensome for patients; insulin is replaced in a non-physiological manner, and this approach is, therefore, far from ideal. The average glucose level for the type 1 patient should be as close to normal (80-120 mg/dl, 4-6 mmol/l) as is safely possible. Values above 600 mg/dl (30 mmol/l) usually require medical treatment and may lead to ketoacidosis, although they are not immediately life-threatening. However, low levels of blood glucose, called hypoglycemia, may lead to seizures or episodes of unconsciousness and absolutely must be treated immediately

via emergency high-glucose gel placed in the patient's mouth, intravenous administration of dextrose, or an injection of glucagon. Long periods between meals should be avoided.

Type 2 Diabetes

Type 2 Diabetes Mellitus is characterized differently and is due to insulin resistance or reduced insulin sensitivity, combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin almost certainly involves the insulin receptor in cell membranes. Diabetes mellitus, due to a known specific defect, are classified separately. Type 2 diabetes is the most common type. There are numerous theories as to the exact cause and mechanism in type 2 diabetes. Central obesity (fat concentrated around the waist in relation to abdominal organs, but not subcutaneous fat) is known to predispose individuals to insulin resistance. Abdominal fat is especially active hormonally, secreting a group of hormones called adipokines that may possibly impair glucose tolerance. Obesity is found in approximately 55% of Patients diagnosed with type 2 diabetes. Type 2 diabetes may go unnoticed for years because visible symptoms are typically mild, nonexistent or sporadic, and usually there are typically mild, nonexistent or sporadic, and usually there are no ketoacidotic episodes. However, severe long-term complications can result from unnoticed type 2 diabetes, including renal failure due to diabetic nephropathy, vascular disease (including coronary artery disease), vision damage due to diabetic retinopathy, loss of sensation or pain due to diabetic neuropathy liver damage from nonalcoholic steatohepatitis and heart failure from diabetic cardiomyopathy.

Type 2 diabetes is usually first treated by increasing physical activity, decreasing carbohydrate intake, and losing weight. These can restore insulin sensitivity even when the weight loss is modest. However, the underlying tendency to insulin resistance is not lost, and so attention to diet, exercise, and weight loss must continue. The usual next step, if necessary, is treatment with oral antidiabetic drugs. Insulin production is initially only moderately impaired in type 2 diabetes, so oral medication (often used in various combinations) can be used to improve insulin production (e.g., sulfonylureas), to regulate inappropriate release of glucose by the liver and attenuate insulin resistance to some extent (e.g., metformin), and to substantially attenuate insulin resistance (by the liver and attenuate insulin resistance to some extent, e.g., metformin), and to substantially attenuate insulin resistance (e.g., thiazolidinediones).

Gestational Diabetes

Gestational diabetes mellitus (GDM) resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2%–5% of all pregnancies and may improve or disappear after delivery. Gestational diabetes is fully treatable but requires careful medical supervision throughout the pregnancy. About 20%–50% of affected women develop type 2 diabetes later in life. Even though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother. Risks to the baby include macrosomia (high birth weight), congenital cardiac and central nervous system anomalies, and skeletal muscle malformations. Increased fetal insulin may inhibit fetal surfactant production and cause respiratory distress syndrome. Hyperbilirubinemia may result from red blood cell destruction. In severe cases, prenatal death may occur. This is particularly problematic as diabetes

raises the risk of complications during pregnancy, as well as increasing the potential that the children of diabetic mothers will also become diabetic in the future.

Other Types

Most cases of diabetes mellitus fall into the two broad etiologic categories of type 1 or type 2 diabetes. However, many types of diabetes ellitus have known specific causes, and thus, fall into separate categories as diabetes due to a specific cause.

As more research is done into diabetes, many patients who were previously diagnosed as type 1 or type 2 diabetes will be reclassified as diabetes due to their known specific cause. Some cases of diabetes are caused by the body's tissue receptors not responding to insulin (even when insulin levels are normal, which is what separates it from type 2 diabetes); this form is very uncommon.

Genetic mutations (autosomal or mitochondrial) can lead to defects in beta cell function. Abnormal insulin action may also have been genetically determined in some cases. Any disease that causes extensive damage to the pancreas may lead to diabetes (for example, chronic pancreatitis and cystic fibrosis).

Diseases associated with excessive secretion of insulin antagonistic hormones can cause diabetes (which is typically resolved once the hormone excess is removed).

Signs and Symptoms

The classical triad of diabetes symptoms is polyuria (frequent urination), polydipsia (increased thirst and consequent increased fluid intake) and polyphagia (increased appetite). Symptoms may develop quite rapidly (weeks or months) in type 1 diabetes, particularly in children. However, in Type 2 diabetes, symptoms usually develop much more slowly and may be subtle or completely absent. Type 1 diabetes may also cause a rapid yet significant weight loss (despite normal or even Increased eating) and irreducible mental fatigue. All of these symptoms except weight loss can also manifest in type 2 diabetes in patients whose diabetes is poorly controlled. When the glucose concentration in the blood is raised beyond its renal threshold, reabsorption of glucose in the proximal renal tubule is incomplete, and part of the glucose remains in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume will be replaced somatically from water held in body cells and other body compartments, causing dehydration and increased thirst. Prolonged high blood glucose causes glucose absorption which leads to changes in the shape of the lenses of the eyes, resulting in vision changes; sustained sensible glucose control usually returns the lens to its original shape. Blurred vision is a common complaint leading to diabetes diagnosis; type 1 should always be suspected in cases of rapid vision change, whereas with type 2, change is generally more gradual, but should still be suspected. Patients (usually with type 1 diabetes) may also initially present with diabetic ketoacidosis (DKA), an extreme state of metabolic dysregulation characterized by the smell of acetone on the patient's breath; a rapid, deep breathing known as Kussmaul breathing; polyuria; nausea; vomiting and abdominal pain; and any of many altered states of consciousness or arousal (such as hostility and Mania or, equally, confusion and lethargy).

In severe DKA, coma may follow, progressing to death. Diabetic ketoacidosis is a medical emergency and requires immediate hospitalization.

A rarer but equally severe possibility is hyperosmolar nonketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration due to loss of body water. Often, the patient has been drinking extreme amounts of sugar-containing drinks, leading to a vicious circle in regard to the water loss. One of the significant signs of type 2 diabetes is Acanthosis Nigricans. It is a brown to black, poorly-defined, velvety hyperpigmentation of the skin. It is usually found in body folds, such as the posterior and lateral folds of the neck, the axilla, groin, umbilicus, forehead, and other areas.

The most common cause of Acanthosis nigricans is insulin resistance, which leads to increased circulating insulin levels. Insulin spillover into the skin results in its abnormal growth, and the stimulation of color-producing cells (melanocytes). It typically occurs in individuals younger than Age 40, may be genetically inherited, and is associated with obesity or endocrinopathies.

Genetics

Both type 1 and type 2 diabetes are at least partly inherited. Type 1 diabetes appears to be triggered by some (mainly viral) infections, or less commonly, by stress or environmental exposure (such as exposure to certain chemicals or drugs). There is a genetic element in individual susceptibility to some of these triggers which has been traced to particular HLA genotypes (i.e., the genetic "self" identifiers relied upon by the immune system). However, even in those who have inherited the susceptibility, type 1 diabetes mellitus seems to require an environmental trigger. There is a stronger inheritance pattern for type 2 diabetes. Those with first-degree relatives with type 2, increasing with the number of those relatives. Also, obesity (which is an independent risk factor for type 2 diabetes) is strongly inherited. Various hereditary conditions may feature diabetes, for example myotonic dystrophy and Freidreich's ataxia (an inherited disease that causes progressive damage to the nervous system resulting in symptoms ranging from gait disturbance and speech problems to heart disease). Wolfram's syndrome is an autosomal recessive neurodegenerative disorder that first becomes evident in childhood. It consists of diabetes insipidus, diabetes mellitus, optic atrophy, and deafness, hence the acronym DIDMOAD.

Pathophysiology

Insulin production is more or less constant within the beta cells, irrespective of blood glucose levels. It is only one hormone in the body which decreases the amount of glucose in the blood while the other hormones increase it (i.e., glucagon, growth hormone [GH], and cortisol). It is stored within vacuoles pending release, via exocytose, which is primarily triggered by food, chiefly food containing absorbable glucose. The chief trigger is a rise in blood glucose levels after eating. Insulin is the principal hormone that regulates uptake of glucose from the blood into most cells (primarily muscle and fat cells, but not central nervous system cells). Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus. Most of the carbohydrates in food are converted within a few hours to the onosaccharide glucose, the principal carbohydrate found in blood and used by the body as fuel.

The most significant exceptions are fructose, most disaccharides (except sucrose and in some people, lactose), and all more complex polysaccharides, with the outstanding exception of start. Insulin and in some people, lactose, and all more complex polysaccharides, with the outstanding exception of starch. Insulin is released into the blood by beta cells found in the Islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two thirds of the body's cells to absorb glucose from the blood for use as fuel for conversion to other needed molecules, or for storage. Insulin is also the principal control signal for conversion of glucose to glycogen for internal storage in liver and muscle cells. When glucose levels fall, the results are both in the reduced release of insulin from the beta cells and in the reverse conversion of glycogen to glucose. This is mainly controlled by the hormone glucagon which acts in an opposite manner to insulin. Glucose recovered by the liver re-enters the bloodstream and muscles cells lack the necessary export mechanism. Higher insulin levels increase some anabolic ("building up") processes such as cell growth and duplication, protein synthesis, and fat storage. Insulin (or its lack thereof) is the principal signal in converting many of the bidirectional processes of metabolism from a catabolic to an anabolic direction, and vice versa. In particular, a low insulin level is the trigger for entering or leaving ketosis (the fat-burning metabolic rate). If the amount of available insulin is insufficient, if cells respond poorly to the effects of insulin (insulin insensitivity or resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by those body cells that require it nor will it be stored appropriately in the liver and muscles. The net effect is persistent high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis.

Diagnosis

The diagnosis of type 1 diabetes, and many cases of type 2, is usually prompted by recent onset symptoms of excessive urination (polyuria) and excessive thirst (polydipsia), and often accompanied by weight loss. These symptoms typically worsen over days to weeks; about a quarter of people with new type 1 diabetes have developed some degree of diabetic ketoacidosis by the time the diabetes is recognized. The diagnosis of other types of diabetes is usually made in other ways. These include ordinary health screening, detection of hyperglycemia during other medical investigations, and secondary symptoms such as vision changes or unexplainable fatigue. Diabetes is often detected when a person suffers a problem that is frequently caused by diabetes, such as a heart attack, stroke, neuropathy, poor wound healing or a foot ulcer, certain eye problems, certain fungal infections, or delivering a baby with macrosomia or hypoglycemia.

Most physicians prefer to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete. According to the current definition, two fasting glucose measurements above 126 mg/dL (7.0 mmol/l) are considered diagnostic for diabetes mellitus. Patients with fasting glucose levels from 100 to 125 mg/dL (6.1 and 7.0 mmol/l) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg, but not over 200, two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two pre-diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus as well as cardiovascular disease.

While not used for diagnosis, an elevated level of glucose irreversibly bound to hemoglobin A (termed glycosylated hemoglobin HbA1c) of 6.0% is considered abnormal by most labs. HbA1c is primarily used as a treatment tracking test reflecting average blood glucose levels over the preceding 90 days (approximately) which is the average lifetime of red blood cells which contain hemoglobin in most patients. However, some physicians may order this test at the time of diagnosis to track changes over time. The current recommended goal for HbA1c in patients with diabetes is <7.0%, which is considered good glycemic control, although some guidelines are stricter (<6.5%).

People with diabetes, who have HbA1c levels within this range, have a significantly lower incidence of complications from diabetes, including retinopathy and diabetic nephropathy.

Screening

Diabetes screening is recommended for many people at various stages of life, and for those with any of several risk factors. The screening test varies according to circumstances and local policy, and may be a random blood glucose test, a fasting blood glucose test, a blood glucose test two hours after 75g of glucose, or an even more formal glucose tolerance test. Many healthcare providers recommend universal screening for adults at age 40 or 50, and often periodically thereafter. Earlier screening is typically recommended for those with risk factors such as obesity, family history of diabetes, high-risk ethnicity (Hispanic, Native American, Afro-Caribbean, and Pacific Islander).

Many medical conditions are associated with diabetes and warrant screening. A partial list includes high blood pressure, elevated cholesterol levels, coronary artery disease, past gestational diabetes, polycystic ovary syndrome, chronic pancreatitis, fatty liver, hemochromatosis, cystic fibrosis, several mitochondrial neuropathies, myopathia and myotonic dystrophy, Friedreich's ataxia, some of the inherited forms of neonatal hyperinsulinism. The risk of diabetes is higher with chronic use of several medications, including high-dose glucocorticoids, some chemotherapy agents (especially L-asparaginase), as well as some of the antipsychotics and mood stabilizers (especially phenothiazines and some atypical antipsychotics). People with a confirmed diagnosis of diabetes are tested routinely for complications. This includes yearly urine testing for microalbuminuria and examination of the retina of the eye for retinopathy.

Prevention

Type 1 diabetes risk is known to depend upon a genetic predisposition, an unknown environmental trigger (suspected to be an infection), and an uncontrolled autoimmune response that attacks the insulin producing beta cells. Some research has suggested that children's breastfeeding decreased the risk in later life and also is associated with the prevention of type 2 of the disease in mothers. Giving children 2000 IU of Vitamin D during their first year of life is associated with reduced risk of type 1 diabetes. Children with antibodies to beta cell proteins (i.e., at early stages of an immune reaction to them) but no overt diabetes, and treated with vitamin B33 (niacin), had less than half the diabetes onset incidence in a 7-year time span as did the general population, and an even lower incidence relative to those with antibodies as above, but who received no vitamin B3.

Type 2 diabetes risks can be reduced in many cases by making changes in diet and increasing physical activity. The American Diabetes Association (ADA) recommends maintaining a healthy weight, getting at least 2 hours of exercise per week (several brisk sustained walks appear sufficient), having a modest fat intake, and eating sufficient fiber (e.g., from whole grains). The ADA does not recommend alcohol consumption as a preventive, but it is interesting to note that moderate alcohol intake may reduce the risk (though heavy consumption absolutely and clearly increases damage to bodily systems significantly), a similarly confused connection between low dose alcohol consumption and heart disease is termed the French Paradox. There are numerous studies which suggest connections between some aspects of Type II diabetes with ingestion of certain foods or with some drugs. Some studies have shown delayed progression to diabetes in predisposed patients through prophylactic use of metformin, rosiglitazone or valsartan. In patients on hydroxychloroquine for rheumatoid arthritis, incidence of diabetes was reduced by 77% though causal mechanisms are unclear.

Treatment and Management

Diabetes mellitus is currently a chronic disease, without a cure, and medical emphasis must necessarily be on managing/avoiding possible short-term as well as long-term diabetes-related problems. There is an exceptionally important role for patient education, dietetic support, sensible exercise, self-monitoring of blood glucose, with the goal of keeping both short-term blood glucose levels, and long term levels as well, within acceptable bounds. Careful control is needed to reduce the risk of long term complications. This is theoretically achievable with combinations of diet, exercise and weight loss (type 2), various oral diabetic drugs (type 2 only), and insulin use (type 1 and for type 2 not responding to oral medications, mostly those with extended duration diabetes). In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications should be undertaken to control blood pressure and cholesterol by exercising more, smoking less or ideally not at all, consuming an appropriate diet, wearing diabetic socks, wearing diabetic shoes, and if necessary, taking any of several drugs to reduce blood pressure. Many type 1 treatments include combination use of regular or NPH insulin, and/or synthetic insulin analogs (e.g., Humalog, Novolog or Apidra) in combinations such as Lantus/Levemir and Humalog, Novolog or Apidra. Another type 1 treatment option is the use of the insulin pump (e.g., from Deltec Cozmo, Animas, Medtronic Minimed, Insulet Omnipod, or ACCU-CHEK). A blood lancet is used to pierce the skin (typically of a finger), in order to draw blood to test it for sugar levels.

Peer support links people living with diabetes. Within peer support, people with a common illness share knowledge and experience that others, including many health workers, do not have. Peer support is frequent, ongoing, accessible and flexible and can take many forms—phone calls, text messaging, group meetings, home visits, and even grocery shopping. It complements and enhances other health care services by creating the emotional, social and practical assistance necessary for managing disease and staying healthy.

Cures for Type 1 Diabetes

There is no practical cure, at this time, for type 1 diabetes. The fact that type 1 diabetes is due to the failure of one of the cell types of a single organ with a relatively simple function (i.e., the

failure of the beta cells in the Islets of Langerhans) has led to the study of several possible schemes to cure this form of diabetes mostly by replacing the pancreas or just the beta cells.

Only those type 1 diabetic who has received either a pancreas or a kidney-pancreas transplant (often when they have developed diabetic kidney disease (ice, nephropathy) and become insulin independent) may now be considered "cured" from their diabetes. A simultaneous pancreas kidney transplant is a promising solution, showing similar or improved survival rates over a kidney transplant alone. Still, they generally remain on long-term immunosuppressive drugs and there is a possibility that the immune system will mount a host versus graft response against the transplanted organ.

Cures for Type 2 Diabetes

Type 2 has had no definitive cure, although recently it has been shown that a type of gastric bypass surgery can normalize blood glucose levels in 80-100% of severely obese patients with diabetes. The precise causal mechanisms are being intensively researched; its results are not simply attributable to weight loss, as the improvement in blood sugars precedes any change in body mass. This approach may become a standard treatment for some people with type 2 diabetes in the relatively near future. This surgery has the additional benefit of reducing the death rate from all causes by up to 40% in severely obese people. A small number of normal to moderately obese patients with type 2 diabetes have successfully undergone similar operations.

Prognosis

Patient education, understanding, and participation is vital since the complications of diabetes are far less common and less severe in people who have well-controlled blood sugar levels. Wider health problems accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise. According to a study, women with high blood pressure have a threefold risk of developing diabetes. Anecdotal evidence suggests that some of those with type 2 diabetes who exercise regularly, lose weight, and eat healthy diets may be able to keep some of the disease or some of the effects of the disease in 'remission.' Certainly these tips can help prevent people predisposed to type 2 diabetes and those at pre-diabetic stages from actually developing the disorder as it helps restore insulin sensitivity. However patients should talk to their doctors about this for real expectations before undertaking it (especially to avoid hypoglycemia or other complications). Few people actually seem to go into total 'remission,' but some may find they need less of their insulin medications since the body tends to have lower insulin requirements during and shortly following exercise. Regardless of whether it works that way or not for an individual, there are certainly other benefits to this healthy lifestyle for both diabetics and no diabetics.

The way diabetes is managed changes with age. Insulin production decreases because of age-related impairment of pancreatic beta cells. Additionally, insulin resistance increases because of the loss of lean tissue and the accumulation of fat, particularly intra-abdominal fat, and the decreased tissue sensitivity to insulin. Glucose tolerance progressively declines with age, leading to a high prevalence of type 2 diabetes and post challenge hyperglycemia in the older population. Age-related glucose intolerance in humans is often accompanied by insulin resistance, but

circulating insulin levels are similar to those of younger people. Treatment goals for older patients with diabetes vary with the individual, and take into account health status, as well as life expectancy, level of dependence, and willingness to adhere to a treatment regimen.

Acute Complications Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is an acute and dangerous complication that is always a medical emergency. Low insulin levels cause the liver to turn to fat for fuel (i.e., ketosis); ketone bodies are intermediate substrates in that metabolic sequence. This is normal when periodic, but can become a serious problem if sustained. Elevated levels of ketone bodies in the blood decrease the blood's pH, leading to DKA. On presentation at hospital, the patient in DKA is typically dehydrated and breathing rapidly and deeply. Abdominal pain is common and may be severe.

The level of consciousness is typically normal until late in the process when lethargy may progress to coma. Ketoacidosis can easily become severe enough to cause hypotension, shock, and death. Urine analysis will reveal significant levels of ketone bodies (which have exceeded their renal threshold blood levels to appear in the urine, often before other overt symptoms).

Prompt, proper treatment usually results in full recovery, though death can result from inadequate or delayed treatment, or from complications (e.g., brain edema). DKA is always a medical emergency and requires medical attention. Ketoacidosis is much more common in type 1 diabetes than type 2.

Hyperglycemia Hyperosmolar State

Hyperosmolar nonketotic state (HNS) is an acute complication sharing many symptoms with DKA, but an entirely different origin and different treatment. A person with very high (usually considered to be above 300 mg/dl [16 mmol/l]) blood glucose levels, water is osmotically drawn out of cells into the blood and the kidneys eventually begin to dump glucose into the urine. This results in loss of water and an increase in blood osmolarity. If fluid is not replaced (by mouth or intravenously), the osmotic effect of high glucose levels, combined with the loss of water, will eventually lead to dehydration. The body's cells become progressively dehydrated as water is taken from them and excreted. Electrolyte imbalances are also common and are always dangerous. As with DKA, urgent medical treatment is necessary, commonly beginning with fluid volume replacement. Lethargy may ultimately progress to a coma, though this is more common in type 2 diabetes than type 1.

Hypoglycemia

Hypoglycemia, or abnormally low blood glucose, is an acute complication of several diabetes treatments. It is rare otherwise, either in diabetic or non-diabetic patients. The patient may become agitated, sweaty, and have many symptoms of sympathetic activation of the autonomic nervous system resulting in feelings akin to dread and immobilized panic. Consciousness can be altered or even lost in extreme cases, leading to coma, seizures, or even brain damage and death. In patients with diabetes, this may be caused by several factors, such as too much or incorrectly timed insulin, too much or incorrectly timed exercise (exercise decreases insulin requirements) or not enough food (specifically glucose containing carbohydrates).

In most cases, hypoglycemia is treated with sugary drinks or food. In severe cases, an injection of glucagon (a hormone with effects largely opposite to those of insulin) or an intravenous infusion of dextrose is used for treatment, but usually only if the person is unconscious. In any given incident, glucagon will only work once as it uses stored liver glycogen as a glucose source. In the absence of such stores, glucagon is largely ineffective. In hospitals, intravenous dextrose is often used.

Chronic Complications - Vascular Disease

Chronic elevation of blood glucose level leads to damage of blood vessels (angiopathy). The endothelial cells lining the blood vessels take in more glucose than normal, since they don't depend on insulin. They then form more surface glycoproteins than normal, and cause the basement membrane to grow thicker and weaker. In diabetes, the resulting problems are grouped under "microvascular disease" (due to damage to small blood vessels) and "macrovascular disease" (due to damage to the arteries). The damage to small blood vessels leads to a microangiopathy, which can cause one or more of the following:

- Diabetic retinopathy, growth of friable and poor-quality, new blood vessels in the retina as well as macular edema (swelling of the macula), which can lead to severe vision loss or blindness. Retinal damage (from microangiopathy) makes it the most common cause of blindness among non-elderly adults in the US.
- Diabetic neuropathy, abnormal and decreased sensation, usually in a 'glove and stocking' distribution starting with the feet but potentially in other nerves and later, often fingers and hands. When combined with damaged blood vessels, this can lead to “diabetic foot.” Other forms of diabetic neuropathy may present as mononeuritis or autonomic neuropathy. Diabetic amyotrophy is muscle weakness due to neuropathy.
- Diabetic nephropathy, damage to the kidney which can lead to chronic renal failure, eventually requiring dialysis. Diabetes mellitus is the most common cause of adult kidney failure worldwide in the developed world.
- Diabetic cardiomyopathy, damage to the heart, leading to diastolic dysfunction and eventually heart failure.
- Macrovascular diseases leads to cardiovascular disease, to which accelerated atherosclerosis is a contributor.
- Coronary artery disease, leading to angina or myocardial infarction ("heart attack").
- Stroke (mainly the ischemic type).
- Peripheral vascular disease, which contributes to intermittent claudication as well as diabetic foot.
- Diabetic myonecrosis ('muscle wasting').

Diabetic foot, often due to a combination of sensory neuropathy (numbness or insensitivity) and vascular damage, increases rates of skin ulcers and infection and, in serious cases, necrosis and gangrene. It is why diabetics are prone to leg and foot infections and why it takes longer for them to heal from leg and foot wounds. It is the most common cause of non-traumatic adult amputation, usually of toes and or feet, in the developed world.

Carotid artery stenosis does not occur more often in diabetes, and there appears to be a lower prevalence of abdominal aortic aneurysm. However, diabetes does cause higher morbidity, mortality and operative risks with these conditions. Diabetic encephalopathy is the increased cognitive decline and risk of dementia observed in diabetes.

Epidemiology

In 2000, according to the World Health Organization, at least 171 million people worldwide suffer from diabetes, or 2.8% of the population. Its incidence is increasing rapidly, and it is estimated that by the year 2030, this number will almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence of diabetes in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. For at least 20 years, diabetes rates in North America have been increasing substantially. In 2008, there were about 24 million people with diabetes in the United States alone, and from those, 5.7 million people remain undiagnosed. The other 57 million people are estimated to have prediabetes.

The Centers for Disease Control has termed the change an epidemic. The National Diabetes Information Clearinghouse estimates that diabetes costs $132 billion in the United States alone every year. About 5%–10% of diabetes cases in North America are type 1, with the rest being type 2. The fraction of type 1 in other parts of the world differs, probably due to both differences in the rate of type 1 and differences in the rate of other types, most prominently type 2. Most of this difference is not currently understood. The American Diabetes Association cites the 2003 assessment of the National Center for Chronic Disease Prevention and Health Promotion (Centers for Disease Control and Prevention) that 1 in 3 Americans born after 2000 will develop diabetes in their lifetime. According to the American Diabetes Association, approximately 18.3% (8.6 million) of Americans age 60 and older have diabetes. Diabetes mellitus prevalence increases with age, and the number of older persons with diabetes are expected to grow as the elderly population increases in number. The National Health and Nutrition Examination Survey (NHANES III) demonstrated that, in the population over 65 years old, 18% to 20% have diabetes, with 40% having either diabetes or its precursor form of impaired glucose tolerance.