present but unable to work effectively (ie, inhibit hepatic production of glucose and cause glucose to move from the bloodstream into liver, muscle, and fat cells). Most insulin resistance is attributed to impaired insulin action at the cellular level, possibly related to postreceptor, intracellular mechanisms.

Type 2 may occur at any age but usually starts after 40 years. Compared with type 1, it usually has a gradual onset; produces less severe symptoms initially; is easier to control; causes less DKA and renal failure but more myocardial infarctions and strokes; and does not necessarily require exogenous insulin because endogenous insulin is still produced. About 90% of people with diabetes have type 2; 20% to 30% of them require exogenous insulin.

Type 2 is a heterogenous disease, and etiology probably involves multiple factors such as a genetic predisposition and environmental factors. Obesity is a major cause. With obesity and chronic ingestion of excess calories, along with a sedentary lifestyle, more insulin is required. The increased need leads to prolonged stimulation and eventual "fatigue" of pancreatic beta cells. As a result, the cells become less responsive to elevated blood glucose levels and less able to produce enough insulin to meet metabolic needs. Thus, insulin is secreted but is inadequate or ineffective, especially when insulin demand is increased by obesity, pregnancy, aging, or other factors.

In the United States, African Americans, Hispanics, Native Americans, and some Asian Americans and Pacific Islanders are at high risk for development of type 2 diabetes. Prevalence rates are about 9.6% in African Americans and 10.9% in Hispanic Americans, compared to 6.2% in whites. Undiagnosed diabetes is reportedly common in Mexican-Americans.

Signs and Symptoms

Most signs and symptoms stem from a lack of effective insulin and the subsequent metabolic abnormalities. Their incidence and severity depend on the amount of effective insulin and they may be precipitated by infection, rapid growth, pregnancy, or other factors that increase demand for insulin. Most early symptoms result from disordered carbohydrate metabolism, which causes excess glucose to accumulate in the blood (hyperglycemia). Hyperglycemia produces glucosuria, which, in turn, produces polydipsia, polyuria, dehydration, and polyphagia.

Glucosuria usually appears when the blood glucose level is approximately twice the normal value and the kidneys receive more glucose than can be reabsorbed. However, renal threshold varies, and the amount of glucose lost in the urine does not accurately reflect blood glucose. In children, glucose tends to appear in urine at much lower or even normal blood glucose levels. In older people, the kidneys may be less able to excrete excess glucose from the blood. As a result, blood glucose levels may be high with little or no glucose in the urine.

When large amounts of glucose are present, water is pulled into the renal tubule. This results in a greatly increased urine output (polyuria). The excessive loss of fluid in urine leads to increased thirst (polydipsia) and, if fluid intake is inadequate, to dehydration. Dehydration also occurs because high blood glucose levels increase osmotic pressure in the bloodstream, and fluid is pulled out of the cells in the body's attempt to regain homeostasis.

Polyphagia (increased appetite) occurs because the body cannot use ingested foods. People with uncontrolled diabetes lose weight because of abnormal metabolism.

Complications

Complications of diabetes mellitus are common and potentially disabling or life threatening. Diabetes is a leading cause of myocardial infarction, stroke, blindness, leg amputation, and kidney failure. These complications result from hyperglycemia and other metabolic abnormalities that accompany a lack of effective insulin. The metabolic abnormalities associated with hyperglycemia can cause early, acute complications, such as DKA or hyperosmolar hyperglycemic nonketotic coma (Box 27–2). Eventually, metabolic abnormalities lead to damage in blood vessels and other body tissues. For example, atherosclerosis develops earlier, progresses more rapidly, and becomes more severe in people with diabetes. Microvascular changes lead to nephropathy, retinopathy, and peripheral neuropathy. Other complications include musculoskeletal disorders, increased numbers and severity of infections, and complications of pregnancy.

HYPOGLYCEMIC DRUGS

Insulin

Insulin is described in this section, and individual insulins are listed in Drugs at a Glance: Insulins.

- Exogenous insulin used to replace endogenous insulin has the same effects as the pancreatic hormone.
- Insulin and its analogs (structurally similar chemicals) lower blood glucose levels by increasing glucose uptake by body cells, especially skeletal muscle and fat cells, and by decreasing glucose production in the liver.
- The main clinical indication for insulin is treatment of diabetes mellitus. Insulin is the only effective treatment for type 1 because pancreatic beta cells are unable to secrete endogenous insulin and metabolism is severely impaired. Insulin is required for clients with type 2 who cannot control their disease with diet, weight control, and oral agents. It may be needed by anyone with diabetes during times of stress, such as illness, infection, or surgery. Insulin also is used to control diabetes induced by chronic pancreatitis, surgical excision of pancreatic tissue, hormones and other drugs, and pregnancy (gestational diabetes). In nondiabetic clients, insulin is used to prevent or treat hyperglycemia induced by intravenous (IV) hyperalimentation solutions and to treat hyperkalemia. In hyperkalemia, an IV infusion of insulin and dextrose solution causes potassium to move from the blood into the cells; it does not eliminate potassium from the body.