

BOX 27-1

EFFECTS OF INSULIN ON METABOLISM

Carbohydrate Metabolism

- Insulin increases glucose transport into the liver, skeletal muscle, adipose tissue, the heart, and some smooth muscle organs, such as the uterus; it must be present for muscle and fat tissues to use glucose for energy.
- Insulin regulates glucose metabolism to produce energy for cellular functions. If excess glucose is present after this need is met, it is converted to glycogen and stored for future energy needs or converted to fat and stored. The excess glucose transported to liver cells is converted to fat only after glycogen stores are saturated. When insulin is absent or blood glucose levels are low, these stored forms of glucose can be reconverted. The liver is especially important in restoring blood sugar levels by breaking down glycogen or by forming new glucose.

Fat Metabolism

- Insulin promotes transport of glucose into fat cells, where it is broken down. One of the breakdown products is alpha-glycerophosphate, which combines with fatty acids to form triglycerides. This is the mechanism by which insulin promotes fat storage.

- When insulin is lacking, fat is released into the bloodstream as free fatty acids. Blood concentrations of triglycerides, cholesterol, and phospholipids are also increased. The high blood lipid concentration probably accounts for the atherosclerosis that tends to develop early and progress more rapidly in people with diabetes mellitus. Also, when more fatty acids are released than the body can use as fuel, some fatty acids are converted into ketones. Excessive amounts of ketones produce acidosis and coma.

Protein Metabolism

- Insulin increases the total amount of body protein by increasing transport of amino acids into cells and synthesis of protein within the cells. The basic mechanism of these effects is unknown.
- Insulin potentiates the effects of growth hormone.
- Lack of insulin causes protein breakdown into amino acids, which are released into the bloodstream and transported to the liver for energy or gluconeogenesis. The lost proteins are not replaced by synthesis of new proteins and protein wasting causes abnormal functioning of many body organs, severe weakness, and weight loss.

secretion involves coordination of various nutrients, hormones, the autonomic nervous system, and other factors.

Glucose is the major stimulus of insulin secretion; others include amino acids, fatty acids, ketone bodies, and stimulation of beta₂-adrenergic receptors or vagal nerves. Oral glucose is more effective than intravenous glucose because glucose or food in the digestive tract induces the release of gastrointestinal (GI) hormones (eg, gastrin, secretin, cholecystokinin, gastric inhibitory peptide) and stimulates vagal activity. Other hormones that raise blood glucose levels and stimulate insulin secretion include cortisol, glucagon, growth hormone, epinephrine, estrogen, and progesterone. Excessive, prolonged endogenous secretion or administration of pharmacologic preparations of these hormones can exhaust the ability of pancreatic beta cells to produce insulin and thereby cause or aggravate diabetes mellitus.

Factors that inhibit insulin secretion include stimulation of pancreatic alpha₂-adrenergic receptors and stress conditions such as hypoxia, hypothermia, surgery, or severe burns.

DIABETES MELLITUS

Diabetes mellitus is a chronic systemic disease characterized by metabolic and vascular abnormalities. Metabolic problems occur early in the disease process and are related to changes in the metabolism of carbohydrate, fat, and protein. A major clinical manifestation of disordered metabolism is hyperglycemia.

Vascular problems include atherosclerosis throughout the body and changes in small blood vessels, which especially affect the retina and kidney. Clinical manifestations of vascular disorders may include hypertension, myocardial infarction, stroke, retinopathy, blindness, nephropathy, and peripheral vascular disease.

Classifications

The two major classifications are type 1 and type 2. Although both are characterized by hyperglycemia, they differ in onset, course, pathology, and treatment. Other types of diabetes may be induced by disease processes, certain drugs, and pregnancy.

Type 1

Type 1 diabetes, a common chronic disorder of childhood, results from an autoimmune disorder that destroys pancreatic beta cells. Symptoms usually develop when 10% to 20% of functioning beta cells remain, but may occur at any time if acute illness or stress increases the body's demand for insulin beyond the capacity of the remaining beta cells to secrete insulin. Eventually, all the beta cells are destroyed and no insulin is produced.

Type 1 may occur at any age but usually starts between 4 and 20 years. The peak incidence for girls is 10 to 12 years, for boys, 12 to 14 years. Type 1 usually has a sudden onset; produces severe symptoms; is difficult to control; produces a high incidence of complications, such as diabetic ketoacidosis (DKA) and renal failure; and requires administration of exogenous insulin. About 10% of people with diabetes have type 1.

Type 2

Type 2 is characterized by hyperglycemia and insulin resistance. The hyperglycemia results from increased production of glucose by the liver and decreased uptake of glucose in liver, muscle and fat cells. Insulin resistance means that higher-than-usual concentrations of insulin are required. Thus, insulin is