



# Diabetes Mellitus:

## Epidemiology, Etiology and Pathophysiology

### A SERIES OF 3 ARTICLES ON DIABETES MELLITUS FROM PHARMERICA

The American Diabetes Association estimates that 15.7 million people in the United States (5.9% of the population) have diabetes mellitus (DM), [1] and another 5.4 million have not been diagnosed with nor are aware they have this disease. [1] DM refers to metabolic disorders characterized by glucose intolerance (hyperglycemia), which results from insufficient insulin secretion or action, or both. [2,3] The most common symptoms of hyperglycemia are polyuria, polydipsia, weight loss, polyphagia, and blurred vision. [2] DM frequently is detected only after one of its life-threatening complications develops. [1]

The long-term sequelae associated with DM are responsible for most morbidity and mortality found in people with this disease. [4] Chronic hyperglycemia and altered lipid and protein metabolism contribute to the development of microvascular and macrovascular complications involving organs such as the kidneys, eyes, nerves, heart, and blood vessels. [2,4] Loss of sight occurs in 12,000 to 24,000 people with DM annually. [1] Additionally, DM is the leading cause of end-stage renal disease. [1] An estimated 60% to 70% of people with DM have nerve damage, leading to more than 56,000 amputations each year. [1] People with DM are two to four times more likely than the general population to have heart disease or suffer a stroke. [1] DM is the seventh leading cause of death in the United States and is estimated to cost between \$92 billion and \$138 billion annually. [1]

The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus recently changed the classification scheme of DM. [2] The National Diabetes Data Group developed the previous classification scheme in 1979 based on the requirement of insulin for the treatment of DM (e.g., insulin-dependent, non-insulin-dependent), rather than on

the disease etiology. [2,5] The new classification scheme defines the illness based on disease etiology, as follows [2]:

- Type 1 DM
- Type 2 DM
- Other types
- Gestational diabetes mellitus (GDM)

The guidelines discourage the use of previously accepted terms such as insulin-dependent diabetes (IDDM), non-insulin-dependent diabetes (NIDDM), type I, and type II (to avoid use of Roman numerals). [2]

Most patients with DM have type 1 or type 2 DM. [2] Type 1 DM results from pancreatic islet beta-cell destruction (leading to an

absence of insulin secretion), usually develops in childhood, and accounts for 10% of all patients with DM. [2,3] Type 1 can be further divided into immune-mediated (previously called IDDM or juvenile-onset DM) and idiopathic. [2] Immune-mediated type 1 DM is characterized by cell-mediated, autoimmune destruction of the beta cells of the pancreas. [2] The

rate of beta-cell destruction varies and usually is faster in children and slower in adults. [2] While the etiology still is poorly understood, multiple genetic and environmental factors are thought to be involved. [2]

The incidence of immune-mediated type 1 DM in the United States peaks between ages 10 and 14. The onset of symptoms is often abrupt: thirst, excessive urination, increased appetite, and weight loss can develop in just several days. [4] Affected people usually are thin and present with signs of wasting, depending on time between onset of symptoms and start of treatment, [3,4,6] and they are prone to develop diabetic ketoacidosis, a condition that can be fatal if exogenous

insulin is not provided. [3,4,6] An initial episode of ketoacidosis sometimes is followed by a period, often termed the honeymoon period, in which patients are symptom-free and require reduced amounts of insulin. [4]

Few patients with type 1 DM are classified as idiopathic. [2] The majority with this type of DM are of African or Asian descent. [2] While idiopathic type 1 DM commonly is inherited and not immune-mediated, the etiology is unknown. [2] This type of DM is characterized by episodic ketoacidosis, and the degree of insulin required between episodes varies. [2]

The most common form of DM is type 2, previously called NIDDM or adult-onset diabetes. [2] It is most prevalent among blacks, Hispanics, Native Americans, and women. [1,4] Patients with this form of DM include those with insulin resistance and varying degrees of insulin deficiency. [2,6] They usually do not have an absolute insulin deficiency, as seen in type 1 DM. [2] Rather, patients with type 2 DM have insulin resistance and deficient insulin secretion. [2] Although type 2 exhibits a strong genetic predisposition, the specific etiologies are unknown, and the pathogenic and genetic processes are not clearly defined. [2]

Type 2 DM generally develops in adulthood, around age 40 or later. [3] Obesity is common with this form of DM. [2,6] Unlike type 1, type 2 DM usually develops gradually. [6] Patients may be asymptomatic, [2,3,6] with diagnosis sometimes occurring only after an elevated glucose level is found on routine laboratory examination. [6] Patients with type 2 DM usually do not develop ketoacidosis. [2,3,6] They do, however, have a tendency to develop hyperosmolar, nonketotic diabetic coma. [6] Approximately one half of patients who present with hyperosmolar coma were previously undiagnosed with DM. [4]

Classified as other types of DM are genetic defects of the beta-cell, genetic defects in

**DM frequently is detected only after one of its life-threatening complications develops**

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## Diabetes Epidemiology, etc. Continued

insulin action, diseases of the exocrine pancreas, endocrinopathies, drug- or chemical-induced DM, infections, uncommon forms of immune-mediated DM, and other genetic syndromes.[2] The etiology and pathogenesis of each syndrome are unique, as are their manifestations, management strategies, and treatments.[2] GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[2] GDM complicates approximately 4% of pregnancies in the United States.[2]

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