

## Diabetes: Advances and Controversies

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This special issue of *Clinical Chemistry* focuses on diabetes mellitus. Diabetes has been recognized for more than 3500 years, since an early description in 1552 BCE in the Ebers Papyrus. Surviving texts from the ancient Greeks, Chinese, Indians, and Persians also refer to the disease, which was subsequently named diabetes mellitus. The recent dramatic increase in the worldwide prevalence of diabetes has led to the term “diabetes epidemic.” In the US, the prevalence in the period from 1999 to 2002 was 9.3% (of which 30% was estimated to be undiagnosed) (1). More recent data from 2005 and 2006 indicate that 42 million adults in the US have diabetes (2). Of concern is that in 40% of these individuals (approximately  $16 \times 10^6$ ) the disease has not been diagnosed. Current projections are that by 2050, 33% of the US adult population will have diabetes (Fig. 1A) (3). The high prevalence and projected large increases are not confined to the US. The worldwide prevalence of diabetes among adults (20–79 years) is estimated to be currently 6.4% ( $285 \times 10^6$ ) and will increase to  $439 \times 10^6$  by 2030 (4). Between 2010 and 2030, the number of affected adults is projected to increase by 69% in developing countries and by 20% in developed countries (Fig. 1B) (4). A recent study in China demonstrated higher rates than initially projected, suggesting that these projections not only are cause for alarm but also are likely to be fulfilled in the wake of remarkable economic development and the obesity epidemic (5). These staggering numbers reveal the magnitude of the global health problem caused by diabetes.

In addition to the individual burden of diabetes, there are considerable financial costs to society. In 2007, diabetes cost the US approximately \$174 billion. In the UK, approximately 10% of National Health Service spending, equivalent to £9 billion (\$14.5 billion)

per annum (or £1 million per hour), goes for diabetes care and treatment (6). In 2007, approximately  $3.8 \times 10^6$  people worldwide are believed to have died from diabetes-related causes.

Much of the morbidity and considerable costs of diabetes are due to the complications that arise. Patients with diabetes develop numerous long-term complications, both microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (including stroke and myocardial infarction). Owing to the delay of 7 or more years between the onset of disease and diagnosis, 20%–30% of patients already have complications when first diagnosed (7).

The pathophysiology of diabetes remains incompletely understood. Type 1 diabetes, which affects 5%–10% of those with the disease, is predominantly caused by autoimmune destruction of the islet cells of the pancreas. Patients with type 2 diabetes have both insulin resistance and inadequate insulin secretion. Genetic and environmental factors are believed to contribute to the pathogenesis of the disease. Because of the lack of a unique biological marker, the diagnosis of diabetes is based exclusively on the consequences of the disrupted carbohydrate metabolism, namely hyperglycemia.

Despite the progress we have made, much work remains to be done. Areas that require attention include preventing the disease, enhancing treatment, and eliminating complications. Basic research studies are needed to enhance our comprehension of fundamental molecular mechanisms that lead to disease or protection from disease. It is important to develop sensitive and specific tests to identify individuals who are at risk for diabetes and its complications and thereby enable preventive strategies to be focused on those who would derive the most benefit. An enhanced understanding of the disease pathophysiology will permit the development of specifically targeted therapies. Finally, additional assays are required to monitor and evaluate the response to treatment and to minimize the risk of adverse effects.

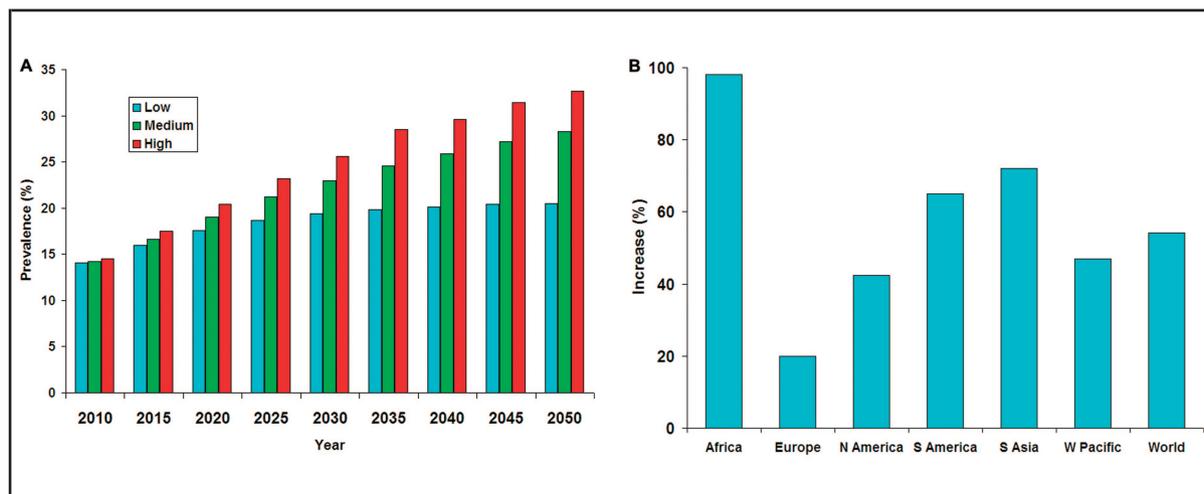
The reports selected for this issue cover a diverse array of topics and are designed to promote our knowledge of diabetes with the ultimate goal of individualizing assessments and interventional strategies. The pathophysiology and genetics of type 1 and type 2 dia-

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**Fig. 1. Projected prevalence of diabetes among adults.**

(A), Projections of diabetes prevalence as a percentage of the total US adult population. Low, medium, and high incidence projections are shown. (B), Projected increase in the number of adults with diabetes in the world by region. These figures were generated with data from Boyle et al. (3) and Shaw et al. (4), respectively.

betes are addressed. Both recently developed assays (soluble CD163 and glycated albumin) and established assays (hemoglobin A<sub>1c</sub> and LDL cholesterol) for identifying individuals at risk for the development of diabetes or its complications are described. The debate over the use of hemoglobin A<sub>1c</sub> to diagnose diabetes and the concept of the “glycation gap” are considered. The benefits of accurately identifying and treating diabetes in pregnancy are reviewed, as are the role of hypoglycemia in vascular disease and the therapeutic approaches for targeting inflammation in type 2 diabetes. Controversial areas in diabetes pathogenesis, diagnosis, treatment, and monitoring are considered. The evidence of immune system participation in the pathophysiology of type 2 diabetes and the implications for diabetes classification are presented. The clinical implications of the problems associated with intensive control of glycemia and cardiovascular mortality in patients with type 2 diabetes are also contemplated.

The objective of this special issue is to promote awareness and to enhance our comprehension of these key topics. The authors represent diverse backgrounds, ranging from basic science and statistics to the clinic and clinical chemistry. We hope that these reports will increase the interactions among these groups and stimulate advances in all these areas. Additional progress is

necessary to reduce the severe and debilitating effects of diabetes.

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