Editorial

Is Diabetes Becoming the Biggest Epidemic of the Twenty-first Century?

Diabetes is a major public health problem that is approach*in*g epidemic proportions globally. Worldwide, the prevalence of chronic, noncommunicable diseases is increasing at an alarming rate. About 18 million people die every year from cardiovascular disease, for which diabetes and hypertension are major predisposing factors. Today, more than 1.7 billion adults worldwide are overweight, and 312 million of them are obese. In addition, at least 155 million children worldwide are overweight or obese. A diabetes epidemic is underway. According to an estimate of International Diabetes Federation comparative prevalence of Diabetes during 2007 is 8.0 % and likely to increase to 7.3% by 2025. Number of people with diabetes is 246 million (with 46% of all those affected in the 40-59 age group) and likely to increase to 380 m by 2025. The comparative prevalence of IGT is 7.5% in 2007 and likely to go up to 6.0 by 2025. The number of people with IGT is 308 million in 2007 and likely to be 418 m by 2025. [(1)] Almost 80% of the total adult diabetics are in developing countries. The regions with the highest rates are the Eastern Mediterranean and Middle East, where 9.2 % of the adult population is affected, and North America (8.4%). The highest numbers, however, are found in the Western Pacific, where some 67 million people have Diabetes, followed by Europe with 53 million. India leads the global top ten in terms of the highest number of people with diabetes with a current figure of 40.9 million, followed by China with 39.8 million. Behind them come USA; Russia; Germany; Japan; Pakistan; Brazil; Mexico and Egypt.

Two major concerns are that much of this increase in Diabetes will occur in developing countries and that there is a growing incidence of Type 2 Diabetes at a younger age including some obese children even before puberty. In developed countries most people with diabetes are above the age of retirement. In developing countries those most frequently affected are in the middle, productive years of their lives, aged between 35 and 64.

The risks of type 2 Diabetes mellitus in Asian countries tend to increase sharply at levels of BMI generally classified as acceptable in European and North American white people. There have been suggestions to adopt specific classifications of obesity in Asians (e.g. BMI 23 for overweight and 25 or 27 kg/m2 for obesity) and this will greatly affect the prevalence estimates of obesity worldwide currently at about 250 million people. [(2)]

Each year 7 million people develop Diabetes and the most dramatic increases in type 2 Diabetes have occurred in populations where there have been rapid and major changes in lifestyle, demonstrating the important role played by lifestyle factors and the potential for reversing the global epidemic. A person with type 2 diabetes is 2 – 4 times more likely to get cardiovascular disease, and 80% of people with Diabetes will die from it. Premature mortality caused by diabetes results in an estimated 12 to 14 years of life lost. A person with Diabetes incurs medical costs that are two to five times higher than those of a person without diabetes, and the World Health Organization estimates that up to 15% of annual health budgets are spent on diabetes-related illnesses. The annual direct healthcare costs of diabetes worldwide, for people in the 20-79 age groups, are estimated to be as much as 286 billion.

High economic and social costs of type 2 Diabetes and its ris*in*g prevalence make a compell*in*g case for its prevention. *In*tervention prior to the onset of type 2 Diabetes may be the only way of prevent*in*g the complications of Diabetes. Because of its chronic nature, the severity of its complications and the means required to control them, diabetes is a costly disease, not only for affected individuals and their families, but also for the health systems.

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and life-style choices. Type 1A DM results from autoimmune beta cell destruction, which leads to insulin deficiency. Individuals with Type 1B DM lack immunologic markers indicative of an autoimmune destructive process of the beta cells.

For low and middle-income countries, economic advancement can lead to alterations to the living environment that result in changes in diet and physical activity within a generation or two. Consequently, people can develop Diabetes despite relatively low gains in weight. In the developed world, diabetes is most common among the poorest communities. Either way, wherever poverty and lack of sanitation drive families to low cost-per-calorie foods and packaged drinks, type 2 diabetes thrives.

Progress has been achieved in identifying some genes that predispose individuals to developing type 2 Diabetes. Identification of susceptibility genes for Diabetes and its complications will enable earlier implementation of prevention measures targeted to those at highest risk. Identification of genes will also reveal new targets for drug development.

Obesity is one of the principal risk factors for type 2 diabetes. Weight gain leads to insulin resistance through several mechanisms. Clinical trials show that as little as 5% weight loss is sufficient to prevent most obese subjects with impaired glucose tolerance developing type-2 diabetes.

Diabetes is the fourth leading cause of death in most developed countries. Complications from Diabetes, such as coronary artery and peripheral vascular disease, stroke, diabetic neuropathy, amputations, renal failure and blindness are resulting in increasing disability, reduced life expectancy and enormous health costs for virtually every society. Diabetes is certain to be one of the most challenging health problems in the 21st century.

The number of deaths attributed annually to diabetes is around 3.2 million. Heart disease is taking a huge toll on people with diabetes, and most people living with diabetes do not realize it. Cardiovascular disease is responsible for between 50% and 80% of deaths in people with diabetes. Diabetic neuropathy is probably the most common complication. Diabetic retinopathy is a leading cause of blindness and visual disability. Research findings suggest that, after 15 years of diabetes, approximately 2% of people become blind, while about 10% develop severe visual handicap. Diabetes is among the leading causes of kidney failure, but its frequency varies between populations and is also related to the severity and duration of the disease. Diabetic foot disease, due to changes in blood vessels and nerves, often leads to ulceration and subsequent limb amputation. Diabetes is the most common cause of non-traumatic amputation of the lower limb.

Type 2 Diabetes generally forms part of the “metabolic syndrome”, which is characterized by insulin resistance, obesity and a range of cardiovascular risk factors. Advances in management of type 2 Diabetes include recognition of the need for early and aggressive management of insulin resistance, dyslipidaemia, hypertension and albuminuria.

Developments in diabetes care and management have evolved over the last decade and include: the introduction of recombinant human insulin; the use of second generation oral agents; home glucose monitoring and glycohemoglobin monitoring; and a better understanding of the relationship between diabetic control and complications. The effectiveness of continuous subcutaneous insulin infusion (pump therapy) has been rediscovered.

The new insulins will be important components to insulin treatment programs in the near future, improving our ability to simulate endogenous insulin action. The inhaled/oral formulations promise to provide patient acceptable systems that will translate to improved glycemic control for greater numbers of people with diabetes mellitus. Clinical trials have shown inhaled insulin to be as effective as injected regular insulin in both type 1 and type 2 Diabetes. An oral insulin spray that is absorbed rapidly through the buccal mucosa is currently in clinical trials and may also provide an alternative to injected insulin.

Many of the new insulin analogues will have a place in management of type 2 as well as type 1 Diabetes. The nuclear hormone receptor PPARγ (peroxisome proliferators-activated receptor) is involved in glucose and, to a lesser extent, lipid metabolism and is a target of the thiazolidinediones (glitizones). Drugs are currently under trial which act both on this receptor and a related receptor involved in lipid metabolism, which is targeted by the fibrates. These dual PPARγ/a agonists will probably have an important role in managing type 2 Diabetes and the metabolic syndrome within a few years.

Orlistat, a lipase inhibitor, is currently indicated for use in obesity. Clinical trials have demonstrated its usefulness as an insulin-sensitizing agent, with the added benefit of weight management.

Insulin secretagogues include the gut-derived hormones (incretins), such as glucagon-like peptide-1 (GLP1) and gastric inhibitory peptide. GLP-1 analogues and receptor agonists are currently under clinical trial and show definite promise for patients with type 2 diabetes.

The recent introduction of systems for continuous blood glucose monitoring is an exciting advance. Frequent automatic glucose readings can be obtained non-invasively through the process of reverse iontophoresis, in which a low electric current pulls glucose molecules through the skin for collection in a gel disc. A device that is worn like a wristwatch is approved for patients aged over 7 years in the United States, but its cost limits more widespread use.

Measurement of glycosylated haemoglobin (HbA1c) remains the criterion standard to judge the outcome of diabetes management. Rapid measurement with a desktop device expedites assessment and

education. With the advent of intensive therapy and its greater demands on patients and their families, counselling and education are becoming even more important in achieving compliance, particularly in adolescents

Newer insulins and automated methods of delivery via programmable pumps are markedly improving care of the child with diabetes; a fully “closed loop” system with glucose sensing in real time providing algorithmic control of insulin delivery via a pump is not a distant dream but a likely eventuality in the near future. Modulation of the autoimmune response is increasingly being investigated. Islet transplantation is in the early stages as is stem cell therapy. At present lifelong administration of exogenous insulin is the mainstay of treatment regimens for T1 Diabetes. However, innovative treatment protocols aimed at replacing beta cells via pancreatic organ transplantation or islet cell transplantation provide a hope for a disease cure. Islet cell transplantation, in which islets cells isolated from pancreas of cadavers are perfused percutanoeusly into the portal vein, has the advantage of being a minimally invasive procedure. The elusive trigger(s) for type 1 Diabetes, if and when identified, would permit prevention and a meaningful reduction in the number of new cases of this disease worldwide.

Recombinant DNA technology has led to the development of new insulin analogs that provide more physiologic insulin delivery. Inhaled and oral insulin formulations may replace multiple injections in future insulin therapy regimens. Several laboratories are working intensively to develop noninvasive glucose monitoring using novel technologies such as infrared radiation spectroscopy. Numerous companies are developing systems to extract interstitial fluid glucose through minimally invasive methods such as transdermal patches similar to the Glucowatch and microneedles. The interstitial fluid extraction devices are being applied in clinical testing, whereas most noninvasive infrared technology requires further refinement. The implantable glucose sensor with long-term stability is still in its infancy but is a necessary component to the future artificial pancreas.

There is an urgent need for strategies to curb the ris*in*g prevalence of this disease, and prevention appears a logical approach. Lifestyle modifications with weight loss and moderate exercise can reduce the *in*cidence of *diabetes* by >50% *in* patients with impaired glucose tolerance (IGT). The use of metform*in*, acarbose and other agents have been shown *in* randomized prospective trials to prevent type 2 *diabetes in* high-risk subjects with IGT. *In*tervention prior to the onset of type 2 Diabetes may be the only way of prevent*in*g the complications of Diabetes.

Clinical trials have clearly demonstrated that lowering of blood pressure and LDL cholesterol can prevent heart disease and stroke in people with diabetes. D*iabetes prevention is proven, possible, and powerful.* Studies show that people at high risk for type 2 Diabetes can prevent or delay the onset of the disease by losing 5 to 7 percent of their body weight.

Widespread use of the FPG9 as a screening test for type 2 DM1 is recommended because. The American Diabetes Association (ADA) recommends screening all individuals >45 years every 3 years and screening individuals with additional risk factors at an earlier age. The morbidity and mortality of DM1-related complications can be greatly reduced by timely and consistent surveillance procedures. These screening procedures are indicated for all individuals with DM. Screening for dyslipidemia and hypertension should be performed annually. In addition to routine health maintenance, individuals with diabetes should also receive the pneumococcal and tetanus vaccines (at recommended intervals) and the influenza vaccine (annually). Aspirin therapy should be considered in many patients with diabetes.

Type 2 Diabetes can be prevented, but it will take enormous political will on the part of governments to make this a reality. They can achieve this by creating the environment that allows individuals to make lifestyle changes. History will record December 20th 2006 as the turning point in the fight against diabetes. On this day the United Nations General Assembly passed landmark Resolution recognizing diabetes as a chronic, debilitating and costly disease associated with major complications that pose severe risks for families, countries and the entire world. The real beneficiaries of the Resolution will be people living with diabetes, their families and many more at risk.

There is a need for all countries to endorse the UN Resolution and to target entire populations through the development and implementation of National Diabetes Prevention Plans. All individuals at high risk of developing type 2 Diabetes should be identified through opportunistic screening by doctors, nurses, pharmacists and through self-screening. There is overwhelming evidence from studies in the USA, Finland, China, India and Japan that lifestyle changes (achieving a healthy body weight and moderate physical activity) can help prevent the development of type 2 Diabetes in those at high risk. [3-6]

Learning how to eat right is an important part of controlling diabetes. Physical activity is a key factor in leading a healthy lifestyle and reducing chronic illnesses. Urgent action is needed to plan for the demands that patients with diabetes will place on healthcare systems and the global economy. The intricacies of healthcare delivery require an individualized program for each patient, addressing issues such as weight management, smoking cessation, and psychological concerns, while considering the patient's culture, age, and ability for self-care. Concerted effort is needed to plan for the demands that patients with diabetes will place on healthcare systems and the global economy. Resources will be needed to manage the projected global explosion in the prevalence of diabetes (particularly in developing countries), the increase in early onset insulin dependent diabetes mellitus, and the improved treatment for preventing late complications of diabetes.

Some pharmacological *in*terventions are currently be*in*g exam*in*ed *in* large prospective studies. It is likely that one or a comb*in*ation of these approaches could make *diabetes* prevention a reality *in* the near future. New understanding of the molecular links between obesity and insulin resistance will inform the development of new therapeutic targets for preventing and treating type 2 Diabetes. By finding all the genes and environmental factors (e.g., viruses, toxins, dietary factors) that contribute to type 1 Diabetes, researchers will develop ways to safely prevent or reverse the autoimmune destruction of insulin-producing cells. Methods for safely imaging the insulin-producing beta cells will help scientists better understand the disease process and assess the benefits of treatments and preventions that are under study. New technologies, such as a closed loop system that automatically senses blood glucose and adjusts insulin dosage precisely, will become available.

With this knowledge, personalized treatments could then be developed to preempt complications. Life means responsibility, a journey wherein change is constant and difficulties are relentless in their onslaught. The small steps one can take to delay or prevent the disease and live a long, healthy life will bring great rewards.

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