CHAPTER 1

INTRODUCTION TO DIABETES MELLITUS

Kirti Kaul, Joanna M. Tarr, Shamim I. Ahmad, Eva M. Kohner and Rakesh Chibber

Abstract: The chronic metabolic disorder diabetes mellitus is a fast-growing global problem with huge social, health, and economic consequences. It is estimated that in 2010 there were globally 285 million people (approximately 6.4% of the adult population) suffering from this disease. This number is estimated to increase to 430 million in the absence of better control or cure. An ageing population and obesity are two main reasons for the increase. Furthermore it has been shown that almost 50% of the putative diabetics are not diagnosed until 10 years after onset of the disease, hence the real prevalence of global diabetes must be astronomically high.

This chapter introduces the types of diabetes and diabetic complications such as impairment of immune system, periodontal disease, retinopathy, nephropathy, somatic and autonomic neuropathy, cardiovascular diseases and diabetic foot. Also included are the current management and treatments, and emerging therapies.

INTRODUCTION

Diabetes was first documented by the Egyptians and is characterised by weight loss and polyuria. However, it was the Greek physician Aetarneus who coined the term diabetes mellitus (DM). In Greek, diabetes means “to pass through” and mellitus is the Latin word for honey (referring to sweetness). Diabetes is an important cause of prolonged ill health and premature mortality, and claims more lives per year than HIV-AIDS with nearly 1 death every 10 seconds.

With the advent of industrialisation worldwide and the staggering rise in obesity, diabetes has manifested as a global epidemic. Although it is very difficult to reach an accurate measure of prevalence for two main reasons: the standard and methods of
data collection varying widely in different parts of the world; recent surveys predict an increase in the prevalence of diabetes in adults from 4% in 1995 to 6.4% by the year 2025.\(^1\) Furthermore, it is estimated to change rapidly with a 42% increase from 51 to 72 million in the developed countries and a 170% increase from the 84 to 228 million in the developing world. Worldwide the number of adults suffering from diabetes will rise from 194 million in 2003 to nearly 380 million in 2025. The countries most affected by this epidemic in the year 2025 will be India, China and the USA.\(^2\) The second and fairly alarming reason is that even today there is a large population (almost 50%) of the patients remaining undiagnosed.

The change in life expectancy and lack of improvement in healthcare are in part responsible for the astounding rise in the incidence of DM. As a result there is an upward trend of occurrence of diabetes, especially in the urban areas. Consequently, countries across the globe will face a significant increase in the burden for health care, as patients with diabetes are prone to both short-term and long-term complications and premature death.

**Pathophysiology of Diabetes**

In the human body a number of systems and pathways function in synchrony to bring about and maintain a healthy physiological state. At the core of these processes lies the ability of the organism to maintain a constant stable state or homeostasis. An aberration of the homeostasis leads to the development of an injury or a pathological state in various organs. DM reduces the ability of an individual to regulate the level of glucose in the blood stream resulting in a number of major and some minor complications.

**Regulation of Blood Glucose**

Regulation of the levels of glucose in the blood is based on a negative feedback loop and acts via the release of insulin and glucagon. When glucose levels in blood are high, the \(\beta\) cells of the islet of langerhans in the pancreas are triggered to release insulin, a 51-amino acid polypeptide that is composed of two chains (A and B) connected by disulphide bridges. Insulin is synthesised from pro-insulin by the pro-hormone convertases (PC1 and PC2), and exo-protease carboxypeptidase.\(^3\) The action of these enzymes generates insulin and C-peptide.\(^3\)

Insulin binds to the tyrosine kinase insulin receptor which is made up of two \(\alpha\) subunits (extracellular) and two \(\beta\) subunits (intramembrane) linked by disulfide bonds (Fig. 1). The binding of insulin to the \(\beta\) subunit of tyrosine kinase insulin receptor promotes autophosphorylation of the \(\beta\) subunit. Insulin signals the liver to convert the excess glucose to glycogen for storage; it also triggers other cells in the body (adipose/ skeletal muscle cells) to take up more glucose by the translocation of glucose transporter (GLUT4) to the cell surface. This helps to bring the circulating glucose concentrations to normal levels (Fig. 2). When the glucose concentration in the blood is low, the \(\alpha\) cells of the pancreas are stimulated to release glucagon. Glucagon signals the liver to convert stored glycogen into glucose which is released into the blood to achieve homeostasis.

In diabetes, there is an aberration either in the synthesis or secretion of insulin as seen in Type 1 diabetes mellitus (T1DM) and stenosis in the pancreatic duct, or the development of resistance to insulin or its subnormal production as in the case of Type 2 diabetes (T2DM) and certain secondary diabetes.