CHAPTER 2
DEFINITION, CLASSIFICATION, DIAGNOSIS, SCREENING AND PREVENTION

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2.1 Definition of Diabetes Mellitus

- A metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, insulin action or both.
- Chronic hyperglycemia is associated with significant long term complications including damage, dysfunction and failure of various organs especially the kidneys, eyes and nerves and is associated with markedly increased risk of cardiovascular morbidity and mortality.

2.2 Classification

Type 1 Diabetes Mellitus - formerly "insulin dependent diabetes mellitus" **IDDM**
- Occurs as a result of beta cell destruction, usually leading to absolute insulin deficiency.
- Individuals are prone to diabetic ketoacidosis, are usually lean, and complain of weight loss, polyuria, polydipsia and fatigue at time of diagnosis.
- Tends to occur in younger people, under age 40, but can occur at any age.
- Includes cases due to an autoimmune process or other unknown etiology.

Type 2 Diabetes Mellitus - formerly "non-insulin dependent diabetes mellitus" **NIDDM**
- Occurs as a result of a range of defects from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with or without insulin resistance.
- Individuals are often obese but can be lean, may complain of symptoms of hyperglycemia but are often asymptomatic. Ketoacidosis is rare.
- Tends to occur in older people over 40 but can occur at younger ages especially in certain ethnic groups such as Native populations.

Gestational Diabetes Mellitus
- Glucose intolerance with onset during pregnancy.

Other Specific Types
- Diabetes associated with other diseases or drugs, or specific genetically defined forms.
  See Table 2.1.

TABLE 2.1 Other Specific Types

Genetic defects of beta-cell function
- Chromosome 13, IPF-1 or CPDX-1 (formerly MODY 4)
- Chromosome 12, HNF-1α (formerly MODY 3)
- Chromosome 7, glucokinase (formerly MODY 2)
- Chromosome 20, HNF-4α (formerly MODY 1)
- Mitochondrial DNA
- NeuroD1 (Chromosome 2)
- Others

Genetic defects in insulin action
- Type A insulin resistance
- Leprechaunism
- Rabson–Mendenhall syndrome
- Lipoatrophic diabetes
- Alstrom Syndrome
- Others

Diseases of the endocrine pancreas
- Pancreatitis
- Traumatic or surgical pancreatectomy
- Neoplasia
- Cystic fibrosis
- Hemochromatosis
- Fibrocalculous pancreatopathy
- Others

Endocrinopathies
- Acromegaly
- Cushing's syndrome
- Glucagonoma
- Pheochromocytoma
- Hyperthyroidism
- Somatostatinoma
- Aldosteronoma
- Others

Drug or chemical induced
- Atypical antipsychotics
- Pentamidine
- Nicotinic acid
- Glucocorticoids
- Diazoxide
- Beta-adrenergic agonists
- Thiazides
- Phenytoin
- Protease inhibitors
- Alpha-interferon
- Others

Infections
- Congenital rubella
- Cytomegalovirus
- Others

Uncommon forms of immune-mediated diabetes
- "Stiff-man" syndrome
- Anti-insulin receptor antibodies
- Others

Other genetic syndromes sometimes associated with diabetes
- Down's syndrome
- Klinfelter's syndrome
- Turner's syndrome
- Wolfram's syndrome
- Friedreich's ataxia
- Huntington's chorea
- Laurence–Biedel syndrome
- Myotonic dystrophy
- Porphyria
- Prader–Willi syndrome
- Others

DNA = deoxyribonucleic acid
HNF = hepatocyte nuclear factor
MODY = maturity onset diabetes of the young
Source: Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Reference 1.

2.3 Diagnosis of Diabetes Mellitus

- The diagnostic criteria for diabetes mellitus in non-pregnant adults and children is based on the increased risk of microvascular complications of diabetes.

- Individuals with impaired fasting glucose and impaired glucose tolerance are at increased risk of developing diabetes mellitus and are at increased risk of cardiovascular disease and should be screened annually for the development of diabetes.
- There are no diagnostic criteria at present using glycosylated hemoglobin (A1C) for the diagnosis of DM because of the lack of standardization of this test.

Diabetes Mellitus (DM)
Any of the following are diagnostic of DM*:

1. Symptoms of diabetes including fatigue, polyuria, polydipsia, and unexplained weight loss plus a random plasma glucose ≥ 11.1 mmol/L

   OR

2. A fasting plasma glucose (FPG) ≥ 7.0 mmol/L†

   OR

3. A plasma glucose in the 2h sample (2h PG) of the 75 gm oral glucose tolerance test (OGTT) of ≥ 11.1 mmol/L

* A confirmatory test must be done on another day in the absence of unequivocal hyperglycemia accompanied by acute metabolic decompensation.
† Fasting defined as at least 8h with no caloric intake

Impaired Fasting Glucose (IFG)
- Defined as FPG 6.1-6.9 mmol/L

Impaired Glucose Tolerance (IGT)
- FPG <7.0 and PG 2h after the 75 gm oral glucose tolerance test of 7.8-11.0 mmol/L

Gestational Diabetes
See Section 9.1.

2.4 Screening

Type 2 Diabetes
- Because diabetes may be asymptomatic until potentially preventable long term complications have occurred, screening of high risk populations is advocated. Certain genetic, environmental and biochemical variables have been identified which increase the risk developing Type 2 DM.
- **Risk Factors** include: older age, ethnicity, a family history of DM, obesity (especially abdominal obesity), a sedentary lifestyle, history of GDM or delivery of an infant weighing > 4 kg, high fasting insulin levels, impaired glucose tolerance (IGT) or impaired fasting glucose (IPG), HDL < 1.0 mmol/L or triglyceride ≥ 1.7 mmol/L, polycystic ovarian syndrome, acanthosis nigricans, schizophrenia or presence of complications associated with diabetes.

Based on Consensus, the CDA Recommends:
1. FPG on all individuals ≥ 40 years of age, every 3 years
2. More frequent and earlier testing of individuals with additional risk factors i.e.
   - a first degree relative with DM

- member of high risk population e.g. Aboriginal people, people of Hispanic, Asian and African descent
- overweight
- features of the metabolic syndrome e.g. abdominal obesity (waist circumference > 88 cm females, 102 cm males), IFG or IGT, hypertension, or elevated triglycerides ≥ 1.7 mmol/L and low HDL < 1.0 mmol/L males, < 1.3 mmol/L females)
- history of GDM or delivery of infant over 4 kg
- polycystic ovarian syndrome
- presence of coronary artery disease or other complications associated with DM

If FPG < 5.7 mmol/ L No Diabetes Mellitus Rescreen as clinically indicated.

If FPG 5.7-6.9 mmol/L in the presence of risk factors for diabetes. Consider performing 2h 75 gm OGTT in order to classify person as normal, IFG, IGT or DM.

Type 1 Diabetes
There are no currently recommended protocols for screening the general population for Type 1 DM.

2.5 Prevention

Type 2 Diabetes
- Those individuals at increased risk of developing diabetes should be encouraged to follow a program of weight control through diet and regular exercise.
- There is evidence from the Finnish Diabetes Prevention Study and the Diabetes Prevention Program (conducted in the United States) that sustained lifestyle modification involving increased physical activity, diet modification and weight loss can delay the onset of type 2 diabetes in populations at high risk of developing type 2 diabetes. In these populations with IGT, a program of 150 minutes of physical activity per week and a weight loss of 5-7% of body weight resulted in a decrease in incidence of Type 2 DM by 58%.
- There is emerging evidence that the use of pharmacologic agents such as acarbose and metformin in those with IGT may delay the onset of type 2 diabetes by 30% and 31% respectively. Consideration may be given to initiating treatment with one of these two pharmacological agents to delay the onset of diabetes in those with impaired glucose tolerance.
- However, at present there are no recommendations regarding the use of widespread screening for IGT with a 2 hr 75g OGTT.

Type 1 Diabetes
- Prevention strategies in type 1 diabetes are currently confined to research projects. The possibility of a link between early exposure to cow's milk protein and increased risk of type 1 diabetes has been raised but has not to date been proven. Trials to further study this issue are ongoing.
- There are no currently accepted prevention strategies aimed at the general population.

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