 Diabetes Mellitus

Diabetes Mellitus

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Learning Objectives

After attending the lecture and reading these study notes, you will be able to:

- State a definition of diabetes
- Describe a classification system of diabetes
- Explain the clinical and pathogenic differences between type 1 and type 2 diabetes
- Describe the genetic inheritance of type 1 and type 2 diabetes
- List who should be screened for diabetes
- State the diagnostic criteria for diabetes
- State the diagnostic criteria and significance of prediabetes and the metabolic syndrome
- List the major goals of the management of type 1 and type 2 diabetes
- List the components of a comprehensive management plan for diabetes
- List the different ways for patient and physician to monitor the effectiveness of a management plan including self-monitoring of blood glucose and A1C testing
- Outline the principles of the nutritional management of diabetes

Extra help

Read the chapter on Diabetes in Cecil's for additional learning.

If you have any questions, don't hesitate to contact Dr. Houlden (houldenr@queensu.ca)

A Quick Overview

Diabetes is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, insulin action or both.

The chronic hyperglycemia of diabetes is associated with significant long-term sequelae including:

Microvascular complications
- retinopathy, nephropathy, neuropathy

and

Macrovascular complications
- coronary heart disease, cerebrovascular disease, peripheral vascular disease
Treatment is diet, exercise, and drugs that reduce glucose levels, including insulin and non-insulin antihyperglycemic drugs.

The prognosis varies with degree of glucose control.

**Classification of Diabetes**

There are 2 main categories of diabetes mellitus - type 1 and type 2, which can be distinguished by a combination of features.

### General Characteristics of Types 1 and 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>Most commonly under 30 yr</td>
<td>Most commonly older than 30 yr</td>
</tr>
<tr>
<td>Associated obesity</td>
<td>No</td>
<td>Very common</td>
</tr>
<tr>
<td>Propensity to ketoacidosis requiring insulin treatment for control</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Plasma levels of endogenous insulin</td>
<td>Extremely low to undetectable</td>
<td>Variable; may be low, normal, or elevated depending on degree of insulin resistance and insulin secretory defect</td>
</tr>
<tr>
<td>Twin concordance</td>
<td>≤ 50%</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Associated with specific HLA-D antigens</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Islet cell antibodies at diagnosis</td>
<td>Yes, Insulitis, selective loss of most β cells</td>
<td>No, Smaller, normal-appearing islets; amyloid (amylin) deposition common</td>
</tr>
<tr>
<td>Islet pathology</td>
<td>Yes, Prone to develop diabetic complications (retinopathy, nephropathy, neuropathy, atherosclerotic cardiovascular disease)</td>
<td>Yes, Prone to develop diabetic complications (retinopathy, nephropathy, neuropathy, atherosclerotic cardiovascular disease)</td>
</tr>
<tr>
<td>Hyperglycemia responds to non-insulin antihyperglycemic drugs</td>
<td>No</td>
<td>Yes, initially in many patients</td>
</tr>
</tbody>
</table>

### Prediabetes

Prediabetes is an intermediate, transitional state between normal glucose metabolism and diabetes.

It is a significant risk factor for diabetes and may be present for many years before the onset of diabetes.
It is associated with an increased risk of cardiovascular disease, but the microvascular complications of diabetes generally do not develop.

Prediabetes can be diagnosed with either

- a fasting plasma glucose or
- an A1c test or
- a 75 gram oral glucose tolerance test in which the patient drinks 75 g of glucose and plasma glucose levels are drawn before and 2 hours later.

Lifestyle interventions (weight loss and physical activity) can prevent progression from prediabetes to diabetes.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Prediabetes Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose</td>
<td>6.1 to 6.9</td>
<td>Impaired fasting glucose</td>
</tr>
<tr>
<td>2 hour plasma glucose in a 75 gram OGTT</td>
<td>7.8 to 11.0</td>
<td>Impaired glucose tolerance</td>
</tr>
<tr>
<td>A1c</td>
<td>6.0 to 6.4</td>
<td>Prediabetes</td>
</tr>
</tbody>
</table>

**The Metabolic Syndrome**

Dysglycemia and type 2 diabetes are often manifestations of a much broader underlying disorder called the Metabolic syndrome.

The Metabolic Syndrome is highly prevalent in the North American population and becomes more common with increasing age. It affects 30% of population at age 50 and 40% at age 60.

It consists of a clustering of cardiovascular disease risk factors including...
• Abdominal obesity
• Hypertension
• Dyslipidemia
• Dysglycemia

The underlying pathophysiology is related to insulin resistance.

Individuals with the Metabolic Syndrome are at risk for developing type 2 diabetes and cardiovascular disease.

**Etiology of Type 1 diabetes**

In type 1 diabetes, insulin production is absent because of **autoimmune pancreatic β-cell destruction** possibly triggered by an environmental exposure in genetically susceptible people.

The destruction progresses subclinically over months or years until β-cell mass decreases to the point that insulin concentrations are no longer adequate to control plasma glucose levels. This typically occurs when >95% of the islet cells have been destroyed.

Type 1 diabetes generally develops in childhood or adolescence and until recently was the most common form diagnosed before age 30; however, it can also develop in adults. When this occurs it is called "latent autoimmune diabetes of adulthood [LADA]."

Type 1 accounts for < 10% of all cases of diabetes.

The pathogenesis of the autoimmune β-cell destruction is incompletely understood and involves interactions between susceptibility genes, autoantigens, and environmental factors. Susceptibility genes include those within the major histocompatibility complex (MHC)—especially HLA-DR3 and HLA-DR4, which are present in > 90% of patients with type 1 diabetes—and those outside the MHC, which seem to regulate insulin production and processing and confer risk of diabetes in concert with MHC genes.

Susceptibility genes are more common among some populations than among others and explain the higher prevalence of type 1 diabetes in some ethnic groups (Scandinavians, Sardinians).

Several viruses (including coxsackievirus, rubella virus, cytomegalovirus, Epstein-Barr virus, and retroviruses) have been linked to the onset of type 1 diabetes. Viruses may directly infect and destroy β cells, or they may cause β-cell destruction indirectly by exposing autoantigens.

The risk for developing type 1 diabetes with:

- One parent affected is: father 6%; mother 2%
- Both parents affected is: 30%
Sibling affected is: 5%
Identical twin affected is: 30%

Etiology of Type 2 diabetes

Type 2 diabetes is characterized by

- Resistance to insulin action
- Defective insulin secretion
- Impaired ability of insulin to enhance glucose disposal in skeletal muscle

Insulin levels are often very high, early in the disease, but peripheral insulin resistance and increased hepatic production of glucose make insulin levels inadequate to normalize plasma glucose levels. Insulin production then falls, further exacerbating hyperglycemia.

The disease generally develops in adults and becomes more common with age. Over 90% of adults with diabetes have type 2 diabetes.

Type 2 diabetes is becoming increasingly common among children as childhood obesity has become epidemic: 40 to 50% of new-onset diabetes in children is now type 2.

There are clear genetic determinants, as evidenced by the high prevalence of the disease within ethnic groups (especially Aboriginals, African, Hispanics, and Asians) and in relatives of people with the disease. Although several genetic polymorphisms have been identified over the past several years, no single gene responsible for the most common forms of type 2 diabetes has been identified.

Obesity and weight gain are important determinants of insulin resistance in type 2 diabetes. They have some genetic determinants but also reflect diet, exercise, and lifestyle. Adipose tissue increases plasma levels of free fatty acids that may impair insulin-stimulated glucose transport and muscle glycogen synthase activity. Adipose tissue also appears to function as an endocrine organ, releasing multiple factors (adipocytokines) that favorably (adiponectin) and adversely (tumor necrosis factor-α, IL-6, leptin, resistin) influence glucose metabolism.

The risk for developing type 2 diabetes:
One parent affected: 40%
Both parents affected: 50%
Identical twin affected: 90%

Miscellaneous causes

Miscellaneous causes of diabetes that account for a small proportion of cases include:

- genetic defects affecting β-cell function, insulin action, and mitochondrial DNA (often referred to as MODY or maturity-onset diabetes of youth);
- pancreatic diseases (eg, cystic fibrosis, pancreatitis, hemochromatosis);
- endocrinopathies (eg, Cushing's syndrome, acromegaly);
- drug-induced diabetes, most notably from glucocorticoids

Pregnancy causes some insulin resistance in all women, but only a few develop "gestational diabetes" (new onset of diabetes during pregnancy).

**Symptoms and Signs**

Patients with type 1 diabetes usually present with symptoms of hyperglycemia including

- Polydipsia and polyuria secondary to an osmotic diuresis caused by glycosuria
- Polyphagia
- (known as the "3 p's").

Progressive dehydration can lead to orthostatic hypotension, weakness, fatigue, and mental status changes.

Some patients experience a long but transient phase of near-normal glucose levels after acute onset of the disease (honeymoon phase) due to partial recovery of insulin secretion.

Patients with type 2 diabetes may present with symptomatic hyperglycemia but are more often asymptomatic, and their condition is detected only on routine testing.

In some patients, initial symptoms are those of diabetic complications, suggesting that the disease has been present for some time.

**Diagnosis of diabetes**

Diabetes can be diagnosed by 4 different ways:

Fasting plasma glucose ≥ 7.0 mmol/L (Fasting = no caloric intake for at least 8 hours) or

Random plasma glucose ≥ 11.1 mmol/L (random = any time of the day) or

2-hour plasma glucose in a 75-g oral glucose tolerance test ≥ 11.1 mmol/L or
A1C > 6.5%

The A1C test (also known as glycated hemoglobin or hemoglobin A1C test) involves measuring the degree of glycation of hemoglobin (sugar sticking to the amino-terminal valine of the β-subunit of hemoglobin). As RBC’s have a lifespan of 3 months, the A1C test gives a reflection of glucose control over the preceding 3 months.

Many physicians find the A1C test the easiest screening test as the patient doesn’t need to fast.

The same test should be repeated on 2 occasions to confirm the diagnosis. The only exception is for patients with symptoms of marked hyperglycemia (polyuria, polydipsia) where one random blood glucose ≥ 11.1 mmol/L is considered to be sufficient.

### Relationship between A1C and average blood glucose

<table>
<thead>
<tr>
<th>A1C</th>
<th>Average blood glucose in the last 3 months</th>
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</thead>
<tbody>
<tr>
<td>6%</td>
<td>7.0</td>
</tr>
<tr>
<td>7%</td>
<td>8.6</td>
</tr>
<tr>
<td>8%</td>
<td>10.2</td>
</tr>
<tr>
<td>9%</td>
<td>11.8</td>
</tr>
<tr>
<td>10%</td>
<td>13.4</td>
</tr>
<tr>
<td>11%</td>
<td>14.0</td>
</tr>
</tbody>
</table>

### Screening for diabetes

In 2009, the estimated prevalence of diabetes in Canada was 6.8% of the population or 2.4 million Canadians. By 2019, the number is expected to increase to 3.7 million. This will pose a major challenge for health services. Prevention efforts are urgently needed.

The prevalence of diabetes increases with age. The sharpest increase occurs after age 40 years. The highest prevalence is in the 75-79 year age group.

Factors contributing to the increasing prevalence of diabetes include
- Aging of the Canadian population
- Increased longevity of people living with diabetes.

Diabetes is also increasing worldwide and is becoming a global problem.

Given the high prevalence of diabetes in the Canadian population, screening is important.

Screening for diabetes should be performed every 3 years in individuals ≥ 40 years of age.

More frequent or earlier testing should be performed if the person has additional risk factors for diabetes.

**Risk factors for diabetes**

**Risk factors for type 2 diabetes include**

- Age ≥ 40 years
- 1st degree relative with type 2 diabetes
- Member of high risk population (Aboriginal, African, Asian, Hispanic, or South Asian descent)
- History of prediabetes (impaired glucose tolerance, impaired fasting glucose or A1C 6.0 to 6.4%)
- History of gestational diabetes or delivery of a macrosomic infant
- Presence of end organ damage associated with diabetes such as retinopathy, neuropathy, nephropathy, and coronary, cerebrovascular and peripheral vascular disease
- Presence of vascular risk factors:
  - HDL-C < 1.0 mmol/L in males, < 1.3 mmol/L in females
  - Triglycerides ≥ 1.7 mmol/L
  - Hypertension
  - Overweight or abdominal obesity
- Other disease associated with diabetes such as polycystic ovary syndrome, acanthosis nigricans, mental health disease (depression, schizophrenia), HIV infection, or obstructive sleep apnea
- Drugs associated with diabetes such as glucocorticoids, atypical antipsychotics, and highly active antiretroviral therapy

**Management of diabetes**
Diabetes care is complex, and as a result it is difficult for any single healthcare provider to provide all that is involved in diabetes care. The basic diabetes team consists of the:

- Person with diabetes + their family
- Primary care physician
- Diabetes nurse educator
- Registered dietitian
- Pharmacist
- Endocrinologist / Internist
- Ophthalmologist / Optometrist

The extended team may include a:

- Psychologist
- Social Worker
- Foot care specialist
- Nephrologist
- Neurologist
- Cardiologist
- Cardiovascular Surgeon
- Orthopedic Surgeon
- Obstetrician
- Dentist

Diabetes care should be structured and guideline driven. A number of quality improvement strategies have been shown to improve diabetes care. This can include:

- Team changes with use of multidisciplinary teams, and expansion of professional roles (e.g., nurse of pharmacist has a more active role in monitoring of the patient or adjusting drug regimens)
- Electronic patient registries,
- Patient/physician reminder systems,
• Telehealth to support diabetes self-management in underserviced communities and,
• Audit and feedback

The key components of a management plan for diabetes include:

• Nutritional therapy
• Physical activity
• Antihyperglycemic medication (insulin and non-insulin antihyperglycemic agents)
• Self-monitoring of blood glucose
• Patient education
• Early detection and treatment of complications

Nutritional Therapy

Nutritional Therapy

Adjusting diet to individual circumstances can help patients control fluctuations in their glucose level and, for patients with type 2 diabetes, lose weight.

In general, all patients with diabetes need to be educated about a diet that is low in saturated fat and cholesterol and contains moderate amounts of carbohydrate, preferably from whole grain sources with higher fiber content.

Although dietary protein and fat contribute to caloric intake (and thus, weight gain or loss), only carbohydrates have a direct effect on blood glucose levels.

Patients with type 1 diabetes should use carbohydrate counting to match insulin dose to carbohydrate intake. “Counting” the amount of carbohydrate in the meal is used to calculate the premeal insulin dose. In general, patients require 1 unit of rapid-acting insulin for each 15 g of carbohydrate in a meal.

Patients may also benefit from instruction on the glycemic index to help delineate between rapid and slowly metabolized carbohydrates.

Patients with type 2 diabetes should restrict calories, eat regularly, increase fiber intake, and limit intake of refined carbohydrates and saturated fats.

Both the patient and the person who prepares the patient’s meals should both be present during nutritional counselling.

Basic nutritional advice a physician can give while a patient with type 2 diabetes is waiting to see a dietitian:
• Have 3 meals a day
• Use 3 out of 4 key food groups per meal
• Space meals 4 to 6 hours apart
• Enjoy a variety of foods from each group
• Include high fibre foods
• Make low fat choices
• Reduce the intake of simple sugar

Here is a link to a tool to teach patients about portion sizes. https://mystarsystem.sanofi.ca/ContentDocuments/PDF/Portion%20Guide.pdf

Blood glucose monitoring

Blood glucose monitoring

Most people with diabetes monitor their blood glucose 1 to 4 times a day with a glucose meter. You will be learning how to use a glucose meter and teach a patient how to use a meter at the Diabetes Expo.

These are the recommended blood glucose targets of the Canadian Diabetes Association

<table>
<thead>
<tr>
<th>Target</th>
<th>A1C (%)</th>
<th>Fasting/Pre-Meal blood glucose (mmol/L)</th>
<th>2-hour Post-Meal blood glucose (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 and type 2 diabetes</td>
<td>7.0</td>
<td>4.0 – 7.0</td>
<td></td>
</tr>
</tbody>
</table>

5.0 – 10.0

(5.0 to 8.0 if A1C targets not being met)

Self-management education

Diabetes needs to be self-managed. Diabetes is a personal responsibility. Health professionals typically see patients with diabetes only a few minutes each year; however, 24-hour-a-day management by the patient is needed. It is crucial that all patients with diabetes receive education about

• nutritional therapy
• physical activity
• self-monitoring of blood glucose with a glucose meter
• symptoms and signs of hypoglycemia, hyperglycemia, and diabetic complications

Active, informed self-management leads to better outcomes. Diabetes education programs, conducted by diabetes nurse educators and registered dietitians are very effective in empowering patients with the skills they need. Self-management education should be culturally appropriate and may include trained lay educators.

Credits

Congratulations!

You have now completed the Diabetes Mellitus module.

Credits

• This web-based module was based on content written by Dr. Robyn Houlden for the Division of Endocrinology at Queen’s University
• The module was created using MedTech communities with support from the Queen's University School of Medicine Education Technology Unit.

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