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1998 clinical practice guidelines for the management of diabetes in Canada

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Abstract

Objective: To revise and expand the 1992 edition of the clinical practice guidelines for the management of diabetes in Canada incorporating recent advances in diagnosis and outpatient management of diabetes mellitus and to identify and assess the evidence supporting these recommendations.

Options: All aspects of ambulatory diabetes care, including organization, responsibilities, classification, diagnosis, management of metabolic disorders, and methods for screening, prevention and treatment of complications in all forms of diabetes were reviewed, revised as required and expressed as a set of recommendations.

Outcomes: Reclassification of types of diabetes based on pathogenesis; increased sensitivity of diagnostic criteria; recommendations for screening for diabetes; improved delivery of care; recommendations for tighter metabolic control; and optimal methods for screening, prevention and treatment of complications of diabetes.

Evidence: All recommendations were developed using a justifiable and reproducible process involving an explicit method for the citation and evaluation of the supporting evidence.

Values: All recommendations were reviewed by an expert committee that included people with diabetes, family physicians, dietitians, nurses, diabetologists, as well as other subspecialists and methodologists from across Canada.

Benefits, harm and costs: More aggressive screening strategies and more sensitive testing and diagnostic procedures will allow earlier detection and management of diabetes. Cost-effectiveness analyses suggest that this will lead to savings in health care costs relating to diabetes care by reducing the incidence of complications of diabetes. Similarly, tighter metabolic control in most people with diabetes, through intensive diabetes management, seeks to reduce the incidence of complications and, hence, their associated social and economic burdens.

Recommendations: This document contains numerous detailed recommendations pertaining to all aspects of ambulatory diabetes care, ranging from service delivery to prevention and treatment of diabetes-related complications. The terms "insulin-dependent diabetes mellitus" and "non-insulin-dependent diabetes mellitus" should be replaced by the terms "type 1" and "type 2" diabetes. Testing for diabetes using fasting plasma glucose (FPG) level should be performed every 3 years in those over 45 years of age. More frequent or earlier testing should be considered for people with additional specific risk factors for diabetes. The FPG level at which diabetes is diagnosed should be reduced from 7.8 to 7.0 mmol/L to improve the sensitivity of the main diagnostic criterion and reduce the number of missed diagnoses. Depending on the type of diabetes and the therapy required to achieve euglycemia, people with diabetes should generally strive for close metabolic control to achieve optimal glucose levels. This entails receiving appropriate diabetes education through a diabetes health care team, diligent self-monitoring of blood glucose, attention to lifestyle and adjustments in diet and physical activity, and the appropriate and stepwise use of oral agents and insulin therapies needed to maintain glycemic control. Also highlighted is the need for appropriate surveillance programs for complications and management options.

Validation: All recommendations were graded according to the strength of the evidence and consensus of all relevant stakeholders. Collateral efforts of the American Diabetes Association and the World Health Organization and the input of international experts were also considered throughout the revision process.

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These guidelines have been peer reviewed.

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Diabetes is a common chronic disease. It also meets all 3 criteria for a public health disorder: “a high disease burden, changing burden suggesting preventability, and fear that things are unknown and out of control.”¹⁻³

Currently, the diagnosis of diabetes has been made in approximately 5% of Canadians or 1.5 million people.¹ This number is expected to reach 2.2 million by the year 2000 and 3 million by 2010.² Moreover, because United States statistics demonstrate that for every person with known diabetes there is someone with undiagnosed diabetes, these numbers most likely underestimate the prevalence of the disease. Assuming that the same situation is true in Canada, up to 10% of Canadian adults may currently have diabetes.

Diabetes is a serious health problem. It is a major cause of coronary artery disease (CAD), which is the leading cause of death in Canada. It is also a leading cause of new cases of blindness and kidney disease in adults. The disease often disables people in their middle years and, as a group, people with diabetes die younger than those not affected by it.⁴

Diabetes is costly both to the affected person and to society. In general, people with diabetes have poorer health and spend more on managing their health than people without diabetes. Although the actual cost of diabetes in Canada remains unknown, data from the United States suggest that diabetes and its management consume approximately 1 in 7 health care dollars.^{5,6} These high costs, in addition to economic analyses showing that early interventions are cost-effective, emphasize the importance of the appropriate management of diabetes to society as a whole.^{7,8}

In 1992, the Canadian Diabetes Advisory Board produced the first Canadian clinical practice guidelines⁹ to address the educational needs of primary care physicians and other members of diabetes health care teams involved in the management of people with diabetes. New developments since then led the Clinical and Scientific Section of the Canadian Diabetes Association (CDA) to develop revised guidelines to provide ongoing support and guidance to health care professionals.

These guidelines are presented here as recommendations, graded according to the level of supporting evidence and accompanied by a brief explanation or description of their context. To be concise and to increase the utility of these guidelines for clinicians, only summaries

of the recommendations are presented. More detailed discussion will appear in a subsequent series of articles. Although these guidelines are not meant to be a textbook on diabetes care, they address key issues or areas of controversy related to outpatient diabetes care.

Methods

After consultation with the Canadian Diabetes Advisory Board, the CDA's Clinical and Scientific Section, undertook the task of revising and updating the “Clinical practice guidelines for treatment of diabetes mellitus” with the intention of ensuring that the recommendations are evidence-based whenever possible. A Steering Committee was assembled and identified 4 broad areas of ambulatory diabetes care: organization of diabetes care; definition, classification, diagnosis and screening; management; and complications. It then recruited an Expert Committee made up of 37 key stakeholders that included people with diabetes, family physicians, dietitians and nurse educators, diabetologists and other subspecialists, and methodologists from across Canada. These people evaluated the literature and developed recommendations for each of the 4 broad areas.

The principles used for developing these guidelines, assigning levels of evidence to the relevant citations and making and grading recommendations were drawn from the guidelines literature¹⁰⁻¹⁴ and summarized in a series of documents for the Expert Committee. The system chosen for grading the recommendations is similar to that used to grade recommendations on hypertension and thrombosis^{10,11} and differed from that used to grade recommendations related to the periodic health examination.¹⁵

Key citations identified within each broad area were assigned a level of evidence based on the problem addressed and the design of the study (Table 1). Recommendations were developed and graded on the basis of these citations as well as the consensus opinion of the relevant subcommittee and the full Expert Committee (Table 2). Some recommendations were assigned a lower grade than supported by the evidence when the consensus opinion of the Expert Committee was that there was a need for further supportive evidence; recommendations were assigned a grade of “D” when they were based on the strong consensus opinion of the Expert Committee in the absence of clear supporting evidence or when evidence was weak. Before a final grade was assigned, all key citations and recommendations

Table 1: Criteria for assigning levels of evidence to the published studies

Level	Criteria
Studies of diagnosis	
1	i. Independent interpretation of test results ii. Independent interpretation of the diagnostic standard iii. Selection of people suspected (but not known) to have the disorder iv. Reproducible description of the test and diagnostic standard v. At least 50 people with and 50 people without the disorder
2	Meets 4 of the level 1 criteria
3	Meets 3 of the level 1 criteria
4	Meets 1 or 2 of the level 1 criteria
Studies of treatment and prevention	
1+	Systematic overview or meta-analysis of randomized controlled trials
1	1 randomized controlled trial with adequate power
2+	Systematic overview or meta-analysis of level 2 randomized controlled trials
2	Randomized controlled trial that does not meet level 1 criteria
3	Nonrandomized clinical trial or cohort study
4	Before–after study, cohort study with noncontemporaneous controls, case–control study
5	Case series without controls
6	Case report or case series of <10 patients
Studies of prognosis	
1	i. Inception cohort of patients with the condition of interest but free of the outcome of interest ii. Reproducible inclusion and exclusion criteria iii. Follow-up of at least 80% of subjects iv. Statistical adjustment for confounders v. Reproducible description of the outcome measures
2	Meets criterion i and 3 of the 4 other level 1 criteria
3	Meets criterion i and 2 of the 4 other level 1 criteria
4	Meets criterion i and 1 of the 4 other level 1 criteria

Table 2: Grades of recommendations for clinical practice guidelines

Grade	Criteria
A	Need supportive level 1 or 1+ evidence plus consensus*
B	Need supportive level 2 or 2+ evidence plus consensus*
C	Need supportive level 3 evidence plus consensus
D	Any lower level of evidence supported by consensus

*An appropriate level of evidence was necessary but not sufficient to assign a grade to a recommendation; consensus was required in addition.

were reviewed by 3 methodologists, who were not directly involved in the initial assessment of evidence and the grading of the recommendations. Where appropriate, the assigned level of evidence and grade of recommendation were modified on the basis of their assessment.

Submissions were reviewed by the Steering Committee as they were being developed. In June 1997, a meeting of the full Expert Committee completed a working draft that was then circulated nationally and internationally for input from stakeholders and from experts in diabetes and related fields. This input was synthesized into a set of draft recommendations that were presented in a public forum at the 1997 CDA Professional Conference; input from this public forum was subsequently incorporated into this document.

Detailed discussions regarding the development and justification of each set of recommendations will be found in specific technical documents (in preparation). A summary of these discussions and recommendations is contained here.

Organization of diabetes care

Diabetes is a complex chronic disorder with major short- and long-term health implications. Diabetes care hinges on the daily commitment of the person with diabetes to self-management, balancing appropriate lifestyle choices and pharmacologic therapy.^{16,17} To learn and use the varied, complex skills required to achieve this balance, people with diabetes need the support of an interdisciplinary team of health and other professionals who are expert in total care for diabetes. The diabetes health care (DHC) team provides this support.^{18–20}

Central to the DHC team is the person with diabetes and his or her family. Also at the core are the primary care physician (who may be a diabetes specialist), the diabetes medical specialist/endocrinologist/internist and diabetes educators (nurses and dietitians). If required, other professional and lay caregivers may be included in an expanded DHC team. These may be medical specialists (ophthalmologists, cardiologists, neurologists, nephrologists and obstetricians), other health professionals (other nurses and dietitians, social workers, psychologists and other mental health workers, pharmacists, chiropractors, podiatrists and optometrists), community and public health agencies and other health organizations.²¹

The central recommendation for diabetes care is that it be organized around the DHC team, which is interdisciplinary and provides comprehensive, shared care. The model of shared care that entails ongoing communication among, and participation of, all members of the DHC team increases the commitment and participation of the person

with diabetes.²²⁻²⁴ Care is most effective when delivered in a structured manner²⁵⁻³⁰ and when it includes ongoing education and comprehensive care as essential components.^{18,31}

One of the key properties of the DHC team is flexibility in its organization, which will allow for identification of members of the core and expanded team according to the characteristics of the community in question. Thus, the DHC team can be structured to meet the demands of urban, rural and even remote settings.^{24,26} Indeed, models of regional DHC teams exist in a number of Canadian provinces, including Manitoba, Nova Scotia and northern Ontario. Incumbent on any DHC team is the need to maintain current standards of diabetes care.

The primary care physician has an important role as the first, and at times the principal, medical contact for the person with diabetes.^{32,33} In this capacity, primary care physicians have an obligation to incorporate and evaluate clinical practice guidelines for the care of their patients with diabetes.^{28,34}

Recommendations

1. Diabetes care should be organized around an interdisciplinary diabetes health care (DHC) team. [*Grade B, Level 2*^{4,8,19,22}]
2. As an essential member of the DHC team, the primary care physician (who may be a diabetes specialist), in consultation with the other members of the team, has the responsibility to
 - a. incorporate current clinical practice guidelines for diabetes care into daily management practices^{23,24}
 - b. coordinate and facilitate the care of the person with diabetes and use a system of timely reminders for diabetes assessment and management^{23,24,35}
 - c. assure communication among all members of the DHC team.^{23,24,35} [*Grade B, Level 2*^{24,35}]
3. Initial and ongoing education of the person with diabetes should be an integral part of diabetes management and not merely an adjunct to treatment. [*Grade B, Level 2*^{4,7,18,36}]

Rights and responsibilities

Diabetes touches all aspects of a person's life. It may affect a person's ability to function successfully in both personal and work settings.^{37,38} Improved tools and self-management systems now allow many people with diabetes to function well and to achieve near-normal glucose levels. Therefore, previous blanket discrimination — in the workplace, in motor vehicle licensing and in vocational training and counselling — should now be replaced with a case-by-case review. Education and advocacy

should focus on awareness of the rights and responsibilities of people with diabetes.³⁹ Primary care physicians and other health professionals should ensure that they are knowledgeable about provincial and national laws related to people with diabetes.⁴⁰

Recommendations

4. The health care system, governments and society as a whole should recognize the rights of people with diabetes by striving to
 - a. include them in the planning of health care delivery
 - b. provide equitable access to diabetes care and education that adheres to the Clinical Practice Guidelines for the Management of Diabetes in Canada and the Standards for Diabetes Education in Canada
 - c. eliminate diabetes as an unnecessary cause of workplace injury, illness and disability
 - d. eliminate diabetes as a source of blanket discrimination with respect to health care services, employment, insurance and other related individual rights
 - e. develop a comprehensive information system to support interdisciplinary delivery of diabetes care. [*Grade D, consensus*]
5. Further, people with diabetes should strive to
 - a. become full participants in the DHC team, participate actively in planning and take responsibility for their personal health care delivery
 - b. adhere to recommended guidelines where the public interest is at stake (e.g., motor vehicle licensing). [*Grade D, consensus*]

Definition, classification, diagnosis and screening

In 1995, an international expert committee working under the auspices of the American Diabetes Association (ADA) was established to review the National Diabetes Data Group's (NDDG's) 1979 classification and diagnostic criteria for diabetes⁴¹ (adapted by the CDA in 1982) in view of more recent reported findings. This review culminated in a new classification and set of diagnostic criteria⁴² that were adopted by the ADA and that are likely to be adopted by the World Health Organization (WHO). After reviewing the new classification and all of the relevant published reports, our Expert Committee concluded that it was also appropriate for Canada to adopt these changes.

Definition of diabetes

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin

secretion, insulin action or both. The chronic hyperglycemia of diabetes mellitus is associated with significant long-term sequelae, particularly damage, dysfunction and failure of various organs — especially the kidney, eye, nerves, heart and blood vessels.

Classification

The major changes from the earlier NDDG classification and WHO recommendations are summarized as follows (Table 3):

- The new classification proposes elimination of the terms “insulin-dependent diabetes mellitus” (IDDM) and “non-insulin-dependent diabetes mellitus” (NIDDM), but retention of “type 1” and “type 2” diabetes (using Arabic rather than Roman numerals). The IDDM–NIDDM terminology was based on treatment rather than pathogenesis and caused considerable confusion. People with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, in itself, classify the patient.
- Type 1 diabetes encompasses diabetes that is primarily a result of pancreatic beta-cell destruction and that is prone to ketoacidosis. This form includes cases due to an autoimmune process and those for which the etiology of beta-cell destruction is unknown.
- Type 2 diabetes may range from predominant insulin resistance with relative insulin deficiency to a pre-

Table 3: Etiologic classification of diabetes mellitus

Type 1 diabetes mellitus (beta-cell destruction, usually leading to absolute insulin deficiency)

- Immune mediated
- Idiopathic

Type 2 diabetes mellitus (may range from predominantly insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance)

Gestational diabetes mellitus (onset or recognition of glucose intolerance in pregnancy)

Other specific types

Genetic defects of beta-cell function

- Chromosome 12, HNF-1 (formerly MODY 3)
- Chromosome 7, glucokinase (formerly MODY 2)
- Chromosome 20, HNF-4 (formerly MODY 1)
- Mitochondrial DNA
- Others

Diseases of the endocrine pancreas

- Pancreatitis
- Trauma pancreatectomy
- Neoplasia
- Cystic fibrosis
- Hemochromatosis
- Fibrocalculous pancreatopathy
- Others

Infections

- Congenital rubella
- Cytomegalovirus
- Others

Drug or chemical induced

- Vacor
- Pentamidine
- Nicotine acid
- Glucocorticoids
- Thyroid hormones
- Diazoxide
- Beta-adrenergic agonists
- Thiazine
- Dilantin
- Alpha-interferon
- Others

Genetic defects in insulin action

- Type A insulin resistance
- Leprechaunism
- Rabson–Mendenhall syndrome
- Lipoatrophic diabetes
- Others

Endocrinopathies

- Acromegaly
- Cushing's syndrome
- Glucagonoma
- Pheochromocytoma
- Hyperthyroidism
- Somatostatinoma
- Aldosteronoma
- 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
- Klinefelter'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 youth.

Source: Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.⁴²

- dominant secretory defect with insulin resistance.
- A wide variety of relatively uncommon conditions are listed under “other specific types” (Table 3). These consist mainly of specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use.
- The classification of gestational diabetes mellitus (GDM) remains unchanged. GDM refers to glucose intolerance with onset during pregnancy.⁴³

Diagnostic criteria

Previously used diagnostic criteria (level of fasting venous plasma glucose 7.8 mmol/L) lacked sensitivity; a significant proportion of people in whom a diagnosis of diabetes would have been made based on glucose level 2 h after a 75-g glucose load never received this test and, thus the diagnosis was not made.^{42,44} The diagnostic threshold of 11.1 mmol/L used for the 2-h sample in the oral glucose tolerance test (OGTT) was based on the risk of microvascular diabetic complications developing; the arbitrarily chosen fasting plasma glucose (FPG) threshold of 7.8 mmol/L actually defined a greater degree of hyperglycemia than did the 2-h plasma glucose (2hPG) threshold of 11.1 mmol/L.⁴²

A recent re-evaluation of population studies suggests that an FPG level of 7.0 mmol/L correlates most closely with a 2hPG level of 11.1 mmol/L and best predicts the development of microvascular disease.^{42,45,46} The lowering of the FPG diagnostic level from 7.8 to 7.0 mmol/L ensures that both the FPG and 2hPG define a similar degree of hyperglycemia and risk for microvascular disease. It also permits the diagnosis of diabetes to be made on the basis of a commonly available test — the FPG.

Although below the diabetic thresholds, FPG levels between 6.1 and 7.0 mmol/L are abnormally high; people with FPG levels in this range are considered to have “impaired fasting glucose” (IFG).⁴² Although they do not have the diabetes-associated risk for microvascular disease, they and people with “impaired glucose tolerance” (IGT) have a higher risk for the development of diabetes mellitus and cardiovascular disease than the general population. Preventive strategies involving lifestyle changes and increased frequency of screening for diabetes mellitus should be a priority for these people.⁴⁴ The long-term outcome and economic ramifications of identification of these new subgroups have yet to be assessed.

Recommendations

- The specific fasting plasma glucose (FPG) level used to diagnose diabetes should be reduced from 7.8 to 7.0 mmol/L. [*Grade A, Level F*;^{45,46}]

- The term “impaired glucose tolerance” (IGT) is retained, but now depends only on measurement of plasma glucose 2 h after a 75-g glucose load (2hPG). [*Grade D, consensus*]
- The term “impaired fasting glucose” (IFG) should be established to identify another intermediate stage of abnormal glucose homeostasis. [*Grade D, consensus*]
- Both IGT and IFG indicate a need for annual testing and attention to associated risk factors and lifestyle changes. [*Grade D, consensus*]

The diagnostic criteria for diabetes and the glucose thresholds for other diagnostic categories are summarized in Tables 4 and 5. These criteria are based on venous sample methods in the laboratory. Although the frequency distributions of hemoglobin A_{1c} (HbA_{1c}) levels in some studies have characteristics similar to those obtained from FPG and 2hPG tests,^{45,46} the lack of standardization of the HbA_{1c} test precludes its use in the diagnosis of diabetes.

Table 4: Diagnosis of diabetes mellitus

A confirmatory test must be done on another day in all cases in the absence of unequivocal hyperglycemia accompanied by acute metabolic decompensation. This must be based on laboratory measurements of venous plasma glucose.

- Symptoms of diabetes plus a casual plasma glucose value 11.1 mmol/L*
- OR
- A fasting plasma glucose (FPG) 7.0 mmol/L†
- OR
- A plasma glucose value in the 2-h sample (2hPG) of the oral glucose tolerance test (OGTT) 11.1 mmol/L‡

*The classic symptoms of diabetes include fatigue, polyuria, polydipsia and unexplained weight loss. Casual is defined as any time of the day, without regard to the interval, since the last meal.
 †Fasting is defined as no caloric intake for at least 8 h.

‡For details of the test see National Diabetes Data Group article.⁴¹ Only FPG and 2hPG values are required.

Table 5: Glucose levels for diagnosis

Category	FPG; mmol/L	PG 1 h after 75-g glucose load; mmol/L	PG 2 h after 75-g glucose load; mmol/L
Impaired fasting glucose (IFG)	6.1–6.9	N/A	N/A
Impaired glucose tolerance (IGT)	<7.0	N/A	7.8–11.0
Diabetes mellitus (DM)	7.0	N/A	11.1
Gestational diabetes mellitus* (GDM)	5.3	10.6	8.9

FPG = fasting plasma glucose, PG = plasma glucose, N/A = not applicable.

*A diagnosis of gestational diabetes mellitus requires 2 abnormal values among the 3 measurements.

Screening for gestational diabetes

GDM occurs in 2% to 4% of all pregnancies, and the diagnosis of GDM has implications for both the baby and mother. The established morbidity for the baby includes macrosomia (with the risk of fetal and maternal trauma during birth) and neonatal hypoglycemia;⁴⁷ other consequences are now rare. Although the value of diagnosing and treating GDM has been questioned,^{48,49} recent cost-benefit analyses^{50,51} have demonstrated the value of treating this condition primarily due to decreased costs for care of the newborn. The value of identifying a mother who is at high risk for later diabetes remains unproven; however, the incidence of postpartum diabetes mellitus, IGT and lipid abnormalities is elevated. Recognition of those at risk would allow application of preventive strategies, such as changes in nutrition and physical activity, that might help minimize the progression to more significant disease.

Due to its high prevalence and impact and because clinical criteria cannot reliably identify those with GDM, all pregnant women should be screened for GDM unless they are in a very low-risk group. Thus, screening should be carried out for all women over 25 years of age, as well as any woman under age 25 who is obese, belongs to an ethnic group predisposed to diabetes (e.g., Aboriginal people and people of Hispanic, Asian and African descent), has a family history or previous history of diabetes or has a history of giving birth to babies with a birthweight over 4 kg.^{43,52} (Low-risk people include lean Caucasian woman under age 25 years, with no personal or family history of diabetes and no history of large babies.) The evidence regarding glucose levels for screening remains unclear;⁵² therefore, no changes were made in this area.

Recommendations

10. All pregnant women should be screened for gestational diabetes mellitus (GDM) between 24 and 28 weeks' gestation, with the exception of those in a very low-risk group. [*Grade D, consensus*]
11. The preferred screening test is measurement of plasma glucose level 1 h after a 50-g oral glucose load given at any time of day.
 - If the level at 1 h is ≥ 7.8 mmol/L, a glucose tolerance test is warranted.
 - If the level at 1 h is ≥ 10.3 mmol/L, then GDM can be diagnosed. [*Grade B, Level 2*]

Diagnosis of gestational diabetes

The worldwide diversity of criteria for the diagnosis of GDM continues to be problematic. The NDDG criteria

were based on original data (100-g, 3-h oral glucose test) that predicted long-term risk of diabetes in the mother, and these levels of hyperglycemia were then found to correlate with neonatal morbidity. WHO criteria (using a 75-g, 2-h test) aim for uniformity with the nonpregnant state, but suggest treating IGT when found in pregnancy.⁵⁴

Two studies^{55,56} involving over 4000 patients in total provide statistical normative data using a 75-g, 2-h glucose test. Given the ease of the 75-g, 2-h test in terms of less nausea, less time for the patient and cost savings, and in view of the normative data available in support of it, it should be recommended as the optimum test. The fasting level found in the 2 studies was slightly different, and that derived by Carpenter and Coustan⁵⁷ by the conversion of the original O'Sullivan and Mahan data⁵⁸ lies between these 2 values. Thus, it was felt that a fasting glucose threshold of 5.3 mmol/L, which best identifies a high risk for macrosomia,^{57,59} should be used.

Finally, these recommendations are recognized as interim ones in the absence of clear evidence. For the next revision of the Canadian clinical practice guidelines, we hope that the criteria for the diagnosis of GDM will be based on firm outcome data.

Recommendations

12. GDM should be diagnosed by measuring FPG level and plasma glucose levels at 1 and 2 h after ingesting a 75-g glucose load. If 2 of the following 3 values are met or exceeded, a diagnosis of GDM is established. If only 1 value is met or exceeded, the diagnosis is impaired glucose tolerance of pregnancy:

Fasting	>5.3 mmol/L
1 h	>10.6 mmol/L
2 h	>8.9 mmol/L

[*Grade D, consensus*]

In view of the common use of the 100-g OGTT during pregnancy, a 100-g glucose load may be used in carrying out a diagnostic test and measuring following values as recommended by the ADA.⁶⁰

Screening for type 2 diabetes

Approximately 3% to 5% of the general adult population has unrecognized type 2 diabetes.⁶¹ Tests for hyperglycemia can identify these people, and this may result in significant benefit because many of them will have or will be at risk for preventable diabetic complications.⁶² Routine testing for type 2 diabetes is, therefore, justifiable as a routine clinical activity in some, but not all, settings.⁶³ Thus, although the relatively low prevalence of diabetes in the general population makes it unlikely that mass

screening will be cost-beneficial, testing for diabetes in people with risk factors for type 2 diabetes or with diabetes-associated conditions is likely to result in more good than harm and will lead to overall cost savings.⁸

Several widely available tests for hyperglycemia have been assessed in the context of diabetes screening. These include FPG and casual plasma glucose levels, 2hPG level during an OGTT, glycosylated hemoglobin level and glycosuria assessment.^{62,63} The FPG is the most reliable of these tests, although each has advantages and disadvantages in terms of convenience, cost, assay standardization and reliable identification of people for whom further evaluation and treatment are worthwhile. Thus, routine use of OGTTs or measurement of insulin levels to identify people at high risk for type 2 diabetes is not necessary.

Recommendations

13. Mass screening for type 2 diabetes in the general population is not recommended. [*Grade D, consensus*]
14. Testing for diabetes using a FPG test should be performed every 3 years in those over 45 years of age. [*Grade D, consensus*]
15. More frequent or earlier testing (or both) should be considered in those with additional risk factors for diabetes, i.e.,
 - a first-degree relative with diabetes
 - member of high-risk population (e.g. Aboriginal people, Hispanic, Asian and African descent)
 - obesity
 - a low level of high-density lipoprotein (HDL) cholesterol (< 0.9 mmol/L) or an elevated fasting level of triglycerides (>2.8 mmol/L). [*Grade D, consensus*]
16. Annual testing should be considered in those with one or more of the following more predictive risk factors (irrespective of the above factors), such as
 - history of IGT or IFG
 - presence of complications associated with diabetes mellitus
 - history of GDM or baby with birthweight over 4 kg
 - presence of hypertension
 - presence of coronary artery disease (CAD). [*Grade D, consensus*]

Preventing type 2 diabetes

Prospective cohort studies have identified historical, physical and biochemical variables that are associated with subsequent type 2 diabetes. These variables include older age, certain ethnic backgrounds, obesity (especially central obesity), physical inactivity, a history of GDM, overt coronary artery disease, high fasting insulin levels

and IGT.⁶⁴⁻⁶⁶ Randomized studies testing behavioural modification and sulfonylureas in the prevention of type 2 diabetes in people with IGT have followed these observations.⁶⁷⁻⁷⁰ To date, no effective treatments have been identified, with the exception of a program of diet and exercise that yielded a clinically significant absolute risk reduction (about 25%) in the rate of diabetes over 6 years in a trial conducted in Da Qing, China.⁶⁹

A large, randomized trial of behaviour modification (Diabetes Prevention Trial) being carried out by the National Institutes of Health should confirm and extend the generalizability of the Da Qing study.⁶⁹ In the meantime, in view of the promising results of that study and the accepted value of weight control, diet and exercise in reducing cardiovascular risk, these activities should be promoted. This recommendation can be made irrespective of one's risk for type 2 diabetes, including risk according to laboratory parameters. Ongoing preventive trials will also assess the efficacy and safety of other interventions including intensified lifestyle change, metformin, troglitazone and acarbose.^{65,66,71,72} However, until these trials are completed, the use of pharmacologic treatments to prevent type 2 diabetes remains experimental.

Recommendation

17. In those at increased risk, a program of weight control through diet and regular exercise is recommended and may prevent type 2 diabetes. [*Grade B, Level 1*]

Preventing type 1 diabetes

The common form of type 1 diabetes is marked by immune-mediated loss of pancreatic beta-cells. This process is incited by an interaction between genetic and environmental factors. During the asymptomatic phase, ongoing autoimmune destruction of the pancreatic beta-cells occurs. This can be identified reliably in first-degree relatives by screening for immune abnormalities, such as islet-cell antibodies, and later by metabolic abnormalities, namely reduced first-phase insulin secretion measured by an intravenous glucose tolerance test.

Two strategies to prevent the disease are, therefore, possible: altering environmental factors in people who are genetically at risk (primary prevention)⁷³ or modifying the immune process in people with subclinical beta-cell loss identified by positive screening tests (secondary prevention).^{74,75} Randomized trials of primary prevention (i.e., removal of cow's milk protein from infant feeds) and secondary prevention (i.e., nicotinamide, oral insulin and parenteral insulin) have been initiated. However, at present no preventive measures for the disease are known to be effective.

tive and safe. In the case of primary prevention, the strength of evidence for a causal link between early exposure to cow's milk protein and subsequent type 1 diabetes is not adequate to recommend that cow's milk be routinely proscribed from infant feeds (although breast feeding can be recommended given its other benefits).

Clinically important benefits of screening for prodromal type 1 diabetes are not established, and such screening carries the potential for negative psychosocial effects (specifically, informing otherwise well people that they are at increased risk for a debilitating chronic disease may do more harm than good).

Recommendation

18. Attempts to prevent type 1 diabetes — either by manipulating environmental factors or by treating people at high risk — are experimental and should be confined to formal research projects. [*Grade D, consensus*]

Management

The primary goal of therapy is to maintain the person's health in the broad sense of the word. Clearly, avoidance of acute and long-term complications is a major concern. In addition, the person's quality of life and overall sense of well-being are an integral part of management. Because virtually every aspect of daily life may be affected by management, it must always be remembered that the person with diabetes is the key member of the DHC team. For most people with diabetes, improving metabolic control will prevent the onset or delay the progression of long-term complications. Depending on the type of diabetes and the therapy required, this objective may be more or less difficult to achieve without acute adverse effects. The metabolic goals of treatment must, therefore, be tailored to the individual person and include consideration of the family and other psychosocial factors.

Examination and assessment

At the first visit of a person with newly or previously diagnosed diabetes, the primary care physician should conduct a comprehensive medical interview, focusing on the nature and extent of diabetes symptoms. A complete medical history should be obtained with special emphasis on potential risk factors for chronic disease. The information outlined in Tables 6 to 10 may have to be obtained in stages, but it is essential for comprehensive diabetes management. If diabetes has been diagnosed previously, information should be sought on a number of items, as indicated in Table 7.

A comprehensive physical examination should be per-

formed, with special attention to systems affected by diabetes. Laboratory investigations, in addition to glycated hemoglobin and plasma glucose levels (to verify the accuracy of self-monitoring and assess immediate glycemic status), should be carried out (Tables 9 and 10). This information forms the basis for a long-term care plan.

Diabetes is a chronic disease, and those with diabetes require regular medical assessment and laboratory testing to ensure optimal health. Some newly diagnosed people with diabetes may require daily visits, whereas others could require weekly or monthly visits until target goals for metabolic control are achieved. Thereafter, all people with diabetes should be followed every 2 to 4 months, although more frequent visits should be scheduled if indicated.

Targets for metabolic control

There is strong evidence that decreasing blood glucose

Table 6: History to be taken during initial visits

Symptoms	<ul style="list-style-type: none"> Onset and progression of symptoms of hyperglycemia Symptoms of acute and long-term complications of diabetes (e.g., ophthalmologic, renal, cardiovascular, neurologic, skin and foot problems)
Past history	<ul style="list-style-type: none"> Endocrine disorders Infections Cardiovascular disease Surgery (e.g., pancreatic) Obstetric (if relevant)
Family history	<ul style="list-style-type: none"> Diabetes mellitus Cardiovascular disease Dyslipidemia Hypertension, renal disease Syndrome of insulin resistance (metabolic syndrome) Infertility, hirsutism* Autoimmune diseases
Functional inquiry	<ul style="list-style-type: none"> Status of organ systems to determine other medical disorders Eating habits (e.g., food choices, meal plans, meal timing, ethnic and cultural influences) Weight history, especially recent changes Level of physical activity and limiting factors (i.e., type, duration, intensity, frequency and time of day of exercise) Risk factors for diabetes (e.g., family history, obesity, previous gestational diabetes)
Risk factors	<ul style="list-style-type: none"> Hypertension, dyslipidemia, central obesity and cigarette smoking
Social factors	<ul style="list-style-type: none"> Family dynamics, education, employment, lifestyle, coping skills
Drug history	<ul style="list-style-type: none"> Current medications, ethanol and possible drug interactions

*Hirsutism, obesity and fertility are statistically associated with increased risk for diabetes.

levels toward the normal range reduces the frequency of microvascular complications^{76,77} and that improving lipid levels reduces the frequency of CAD.⁷⁸ Nevertheless, the levels required to maximize these benefits, while keeping side effects to a minimum, remain subject to debate.

Glucose levels

The target glucose levels defined in Table 11 apply to

Table 7: Directed history for diabetes to be obtained at initial and follow-up visits

Lifestyle	<ul style="list-style-type: none"> • Details of nutrition counselling, meal plans, adherence to prescribed meal plans, ethnic and cultural influences and weight changes • Diabetes education received in the past (location and level of program), current understanding of diabetes and its management • Level of physical activity (i.e., type, duration, intensity, frequency and time of day of exercise)
Monitoring	<ul style="list-style-type: none"> • Method used and technique • Frequency, timing in relation to meals, records • Quality control of meter (correlation with laboratory)
Antihyperglycemic medications	<ul style="list-style-type: none"> • Oral agents (type, dose, compliance), any adjustment in response to monitoring • Insulin (type, source, dose, injection sites), understanding of dose adjustments in response to food, activity
Hypoglycemia	<ul style="list-style-type: none"> • Awareness, symptoms, frequency, time of occurrence, severity, precipitating causes, treatment and prevention
Social and psychological factors	<ul style="list-style-type: none"> • Support of family and friends • Economic abilities • Medical insurance • Medic alert

most adults and adolescents with diabetes mellitus. “Ideal levels” are levels within the normal range for people without diabetes. This level of glucose control may be attainable early after diabetes onset in those managed with diet therapy but rarely in those requiring pharmacologic therapy (attained in less than 5% of the intensive therapy group of the Diabetes Control and Complications Trial [DCCT]⁷⁷).

“Optimal levels” are those that approach the normal range and are associated with a low risk of developing chronic complications of diabetes. However, these levels may be impossible to attain in some people without severe side effects (e.g., hypoglycemia, decreased quality of life) and difficult to obtain in many (in the DCCT, they were attained in fewer than 50% of people in the intensive therapy group⁷⁷).

“Suboptimal glucose levels” attainable in the majority of people with diabetes (90% of subjects in the intensive therapy group in the DCCT⁷⁷), range between 7.1 and 10 mmol/L before a meal and between 11.1 and 14 mmol/L after a meal. However, most people with diabetes should strive to lower glucose levels further toward optimal levels. For certain people (e.g., those under age 5, those with hypoglycemic unawareness or those with a short life expectancy), this “suboptimal” level of glucose control may be the best that is safely attainable.

“Inadequate glucose levels” are associated with acute symptoms of hyperglycemia and a markedly increased risk of chronic complications and require reassessment and readjustment of therapy.

Lipid levels

The relation between lipid levels and CAD is discussed in the complications section. Target lipid levels for the prevention of CAD in people with diabetes are similar to those for people without diabetes. Table 12 shows

Table 8: Initial and follow-up physical examination

General	Height, weight, waist circumference (central obesity), BMI,* blood pressure (lying and standing), pulse
Head and neck	Eyes (pupillary reactions, extraocular movements, lens opacities and fundi), oral cavity (hygiene and caries), thyroid assessment
Chest	Routine
Cardiovascular system	Signs of congestive heart failure, pulses, bruits
Abdomen	Organomegaly
Genitourinary system	Rule out fungal infections
Musculoskeletal system	Foot inspections, signs of limited joint mobility and arthropathy of the hands, colour and temperature
Central nervous system	Routine evaluation for dysesthesias, change in proprioception, vibration, light touch (monofilament) and reflexes. Evaluation for autonomic neuropathy, if appropriate
Skin	Inspection for cutaneous infections, problems with injection sites and signs of dyslipidemias

*BMI = body mass index (body weight in kg divided by height in m²).

these targets and also acknowledges the fact that diabetes itself is a potent risk factor for CAD in both men and women after age 30. Thus, a 35-year-old man with diabetes already has 2 key risk factors and an associated 10-year risk of CAD of 10% to 20%.⁷⁹

Monitoring blood glucose control

The ability of people with diabetes to monitor daily changes in blood glucose has markedly improved the ability to control glucose levels. It permits recognition of low levels of blood sugars before major problems occur^{80,81} and allows people to assess the effects of diet, exercise and changes in treatment regimens. The person with diabetes, in consultation with health professionals, should decide on the frequency of blood glucose measurements, taking into account the benefits of monitoring and the cost and pain associated with the procedure.⁸² Many people treated through diet or with oral agents benefit from the assessment of fasting and postmeal testing. People with type 1

diabetes often use premeal and bedtime tests, as well as intermittent postmeal testing to adjust their insulin doses.

Optimal use of blood glucose self-monitoring requires a periodic (at least annually) verification of accuracy. The level measured in capillary blood using a meter should differ by less than 15% from a simultaneous laboratory measurement of a fasting venous blood sample.⁸³ Testing for glycosylated hemoglobin should be performed periodically to assess overall glucose control, as it reflects glucose control over the preceding 2 to 4 months. If discordance in the assessment of the glucose control is apparent between self-monitoring of blood glucose at home and the HbA_{1c} measurement, despite verified accuracy of the meter, the use of memory-equipped meters should be considered. Supplemental checking of urine for ketones and more frequent monitoring of glucose level may be required in certain situations, such as during pregnancy and in people with type 1 diabetes during intercurrent illness or when the blood glucose level is consistently over 15 mmol/L.⁸²

Recommendations

19. Glycosylated hemoglobin should be measured every 3 to 4 months in all patients taking insulin and at least every 6 months in people on nutrition therapy or oral hypoglycemic agents. [*Grade D, consensus*]
20. Self-monitoring of blood glucose level is an *essential* component of the therapeutic plan of
 - all people with type 1 diabetes [*Grade B, Level 2*]
 - all pregnant women with pre-existing diabetes or GDM [*Grade B, Level 1*]
 - all insulin-treated people with type 2 diabetes. [*Grade D, consensus*]
21. Self-monitoring of blood glucose level is an *integral* component of the therapeutic plan for the majority of people with type 2 diabetes treated with oral hypoglycemic agents. It may be useful for people with type

Table 9: Management plan to be discussed during initial visits

Nutritional and physical activity counselling	<ul style="list-style-type: none"> • Dietitian visits • Goals for lifestyle change
Monitoring	<ul style="list-style-type: none"> • Frequency of testing • Meter knowledge and laboratory correlation
Medication counselling (oral agents and/or insulin)	<ul style="list-style-type: none"> • Method of administration • Dosage adjustments
Diabetes knowledge	<ul style="list-style-type: none"> • Knowledge of value of glucose control • Hypoglycemia (prevention, recognition and treatment) • Determination of individual target goals • Appreciation of lifestyle considerations • Recognition of further educational or motivational needs

Table 10: Clinical aspects to be determined during follow-up visits

Routine clinical care	<ul style="list-style-type: none"> • Routine visit at 2–4 mo with directed history for diabetes (Table 7) • Blood pressure, foot examination at each visit • Evaluation of progress toward reduction of risks of long-term complications • Adjustment of treatment plans
Glycemic control	<ul style="list-style-type: none"> • Glycosylated hemoglobin every 2–4 mo • Laboratory–meter glucose correlation at least annually • FPG level (preferred for correlation), as needed
Complication and risk evaluation	<ul style="list-style-type: none"> • Fasting lipid profile including total, HDL, calculated LDL cholesterol and TG levels annually • Dipstick urinalysis to screen for gross proteinuria: <ul style="list-style-type: none"> —if negative, microalbuminuria screening with a random daytime urinary albumin: creatinine ratio yearly in type 2 and yearly after 5 yr of postpubertal type 1 diabetes —if positive, a 24-h urine test for endogenous creatinine clearance rate and microalbuminuria every 6–12 mo • Resting or exercise ECG if appropriate (age >35 yr)

ECG = electrocardiogram, FPG = fasting plasma glucose, HDL = high-density lipoproteins, LDL = low-density lipoproteins, TG = triglyceride.

2 diabetes controlled by diet therapy alone. [Grade D, consensus]

22. To ensure optimal self-monitoring of blood glucose level, the person with diabetes must be educated on the use of the glucose meter [Grade A, Level F], interpretation of the results and (where possible) how to modify treatment according to blood glucose levels. [Grade D, Level 5]

Metabolic therapy for type 1 and type 2 diabetes

In people with type 1 diabetes, glucose control will depend on coordination of insulin doses, food intake and physical activity. In those with type 2 diabetes, deterioration of control over the disease over time is common and is associated with progressive deterioration of beta-cell function that occurs independently of the initial therapeutic approach chosen.^{88,89} Therefore, it can be expected that therapy for people with diabetes will have to be progressively augmented over time. *If the individually determined target levels for people with type 2 diabetes have not been attained within 2 to 4 months, the next level of therapy should be introduced, as indicated in the stepwise approach outlined in Figure 1.*

Nutritional approaches

Nutrition is often said to be the cornerstone of diabetes care, but it is a controversial and complex topic. The following is not intended to be a complete discussion of the many issues involved, but merely to highlight some of the general principles and recommendations of the CDA. A detailed review of the nutritional management of diabetes is being prepared by CDA's National Nutrition Committee.

Everyone with diabetes should receive individual advice on nutrition and, whenever and wherever possible, they should be referred to registered dietitians who will assess their current intake and individual nutritional needs. In nutrition counselling, a number of factors must be considered to empower people with diabetes to achieve treatment goals. These factors are type of diabetes, lifestyle, socioeconomic issues, presence of obesity, progression of beta-cell dysfunction, type of treatment, personal preferences and the nature of any complications.

The dietitian, in cooperation with the DHC team, will provide education and development of skills to promote healthy eating habits, as well as continuing support as necessary through follow-up appointments. Nutrition

Table 11: Levels of glucose control for adults and adolescents with diabetes mellitus

	Level			
	Ideal (normal nondiabetic)	Optimal* (target goal)	Suboptimal† (action may be required)	Inadequate‡ (action required)
Glycated Hb (% of upper limit) e.g., HbA _{1c} assay	100 (0.04–0.06)	115 (< 0.07)	116–140 (0.07–0.084)	>140 (> 0.084)
Fasting or premeal glucose level (mmol/L)	3.8–6.1	4–7	7.1–10	>10
Glucose level 1–2 h after meal (mmol/L)	4.4–7	5.0–11	11.1–14	>14

Hb = hemoglobin.

*These levels are likely related to minimal long-term complications but may be impossible to achieve in most patients with type 1 diabetes with current therapies.

†Attainable in the majority of people with diabetes but may not be adequate to prevent complications.

‡These levels are related to a markedly increased risk of long-term complications, requiring a reassessment and readjustment of therapy (see specific recommendations).

Table 12: Evaluation of plasma lipid levels in people with diabetes

Risk factors*	10-yr risk; %	Target lipid level†		
		LDL cholesterol; mmol/L	Total:HDL cholesterol ratio	TG; mmol/L
Diabetes and either CAD or 3 or more other risk factors	>40	<2.5	<4	<2.0
Diabetes and 2 other risk factors	20–40	<3.5	<5	<2.0
Diabetes and 1 other risk factor	10–20	<4.0	<6	<2.0
Diabetes and no other risk factor	0–10	<5	<7	<3.0

CAD = coronary artery disease, HDL = high-density lipoprotein, LDL = low-density lipoprotein, TG = triglycerides.

*Major risk factors: family history of premature CAD, smoking, hypertension, low HDL (< 0.9 mmol/L) and age over 30 yr in both men and women

†All 3 target values must be achieved.

Source: Adapted from the 1998 Canadian guidelines by the Working Group on Hypercholesterolemia and Other Dyslipidemias,⁷⁹ by including the presence of diabetes as a risk factor.

counselling should be an ongoing process, with a stepwise increase in the complexity of the information given to the patient. Other members of the DHC team should

discuss and reinforce dietary strategies with the person with diabetes.

In type 2 diabetes, nutritional approaches are oriented

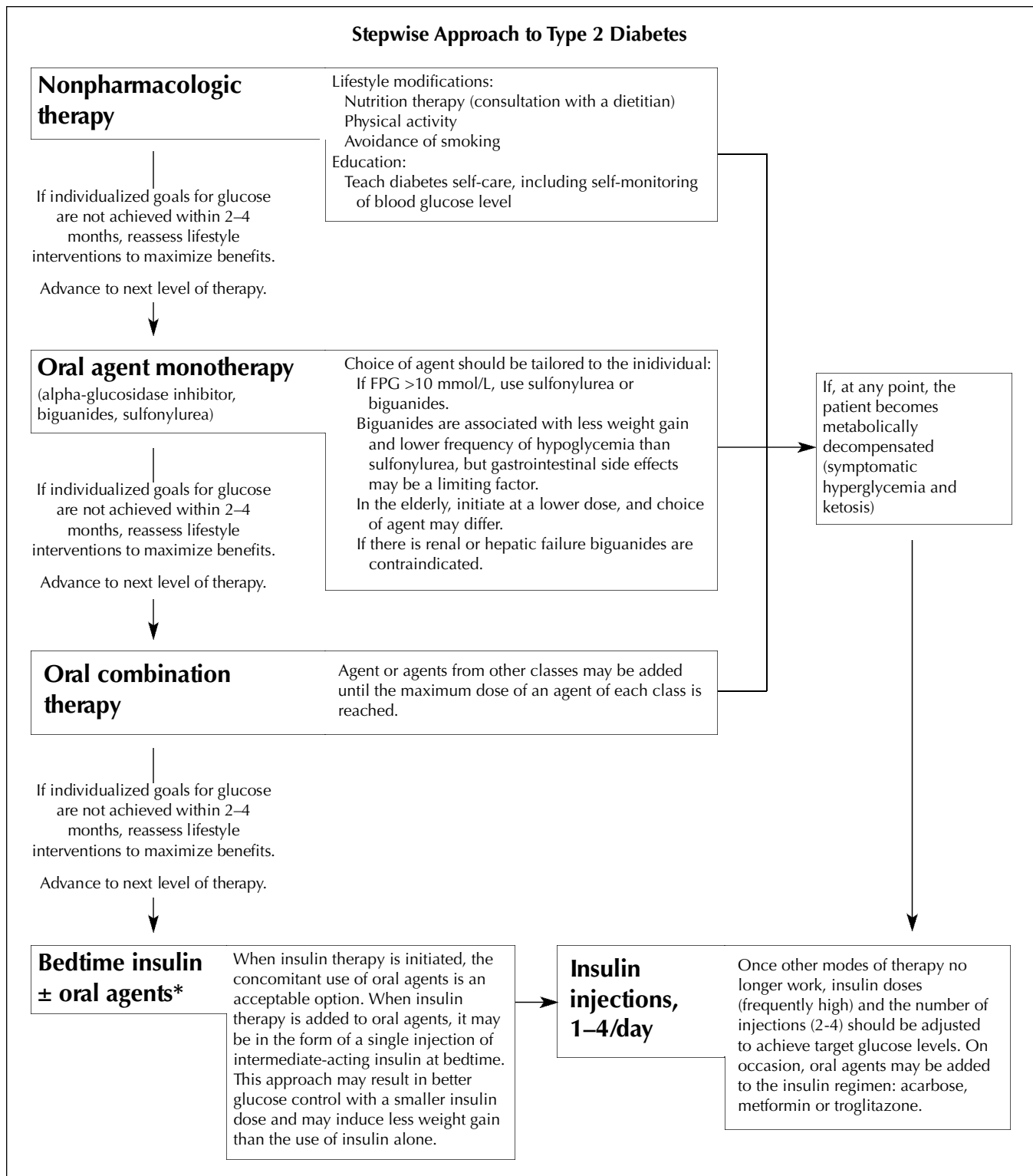


Fig. 1: A stepwise approach to type 2 diabetes. *As of September 1998, troglitazone was not yet marketed in Canada.

toward improving glucose and lipid levels through diet modification and weight loss when appropriate.⁹⁰ If weight reduction is needed, it should be attempted gradually (0.25 to 1.0 kg/wk). In type 1 diabetes, the major efforts are directed toward coordination of food intake (particularly carbohydrates) and insulin dosages to improve glycemic control.

Recommendations

23. All people with diabetes should receive individual advice on nutrition from a registered dietitian. [*Grade D, consensus*]
24. In obese people with type 2 diabetes, diet therapy as well as lifestyle changes incorporating increased physical activity should be the initial therapy, as this can result in improved metabolic control and weight loss. [*Grade B, Level 1*]
25. Nutritional recommendations for people with diabetes are the same as those of Health and Welfare Canada for the general population. This includes choosing a variety of foods from the 4 food groups (grain products, vegetables and fruits, milk products and meat and alternatives), attaining a healthy body weight, decreasing saturated fat intake to less than 10% of calories and having an adequate intake of carbohydrate, protein, vitamins and minerals. The distribution of nutrients may be tailored to the individual patient depending on needs and personal preferences. Meal-planning, using approximately 55% carbohydrate and 30% fat content often serves as a starting point in the development of specific recommendations. [*Grade D, consensus*]
26. Sucrose and sucrose-containing foods can be substituted for other carbohydrates as part of mixed meals, up to a maximum of 10% of calories, provided adequate control of blood glucose and lipids is maintained.⁹² [*Grade B, Level 2*]

Physical activity and exercise

An active lifestyle promotes cardiovascular fitness and well-being,⁹⁴ increased insulin sensitivity, lower blood pressure and a healthy lipoprotein profile in all people with diabetes. A consistent, stepwise increase in physical activity may also improve glycemic control and reduce the need for medications in people with type 2 diabetes.⁹⁵

Knowledge of the acute effects of exercise is mandatory for any person treated with insulin. Unless considerable hyperglycemia (i.e., >15 mmol/L) is present, low to moderate intensity exercise lowers glucose levels both during and after the activity, increasing the risk of a hypoglycemic episode. Conversely, intense exercise systematically raises glucose levels, both during the activity and for variable dura-

tions afterward, and can lead to progressive hyperglycemia (and even ketosis in people with type 1 diabetes), particularly in those who are hyperglycemic before exercising.

These effects on glucose levels can be moderated by altering diet, insulin and the type and timing of exercise. Systematic self-monitoring of glucose level before, during and *especially* for many hours after exercise is, therefore, important for establishing the patient's response to exercise and guiding the appropriate management of exercise. In patients with type 1 diabetes, the use of intensive diabetes management regimens with either multiple daily injections or continuous subcutaneous insulin infusion (CSII) provides additional flexibility in appropriately modifying the insulin dose for exercise.^{96,97}

Finally, the advantages of increased activity levels must be balanced against the risks.⁹⁸ For example, patients with macroangiopathy are susceptible to cardiac or other ischemic events and to cardiac arrhythmias; patients with proliferative retinopathy are at risk for vitreous hemorrhage; and patients with neuropathy are susceptible to lower extremity (particularly foot) injuries.

Recommendations

27. A stepwise increase in physical activity that is integrated into the person's lifestyle should be part of the therapeutic plan for everyone with type 2 diabetes who is able to increase activity. It should be prescribed with specific modifications for people with known occlusive vascular disease (or at high risk of subclinical disease), significant sensory polyneuropathy or advanced microvascular complications. [*Grade D, consensus*]
28. In anyone treated with insulin, recommendations regarding alterations of diet, insulin regimen, injection sites and self-monitoring should be appropriate for the general level of physical activity or specific types of exercise undertaken. Oral agent doses may need to be decreased. [*Grade D, consensus*]
29. The initiation of a vigorous exercise program requires an appropriate, detailed history and physical examination and specific laboratory investigations (e.g., exercise-stress cardiography in those over 35 years of age). [*Grade D, consensus*]
30. General advice regarding physical activity for everyone with diabetes includes:
 - use proper footwear, inspect both feet daily and after each exercise session, if indicated, and use adequate protective devices
 - avoid exercising during any period of poor metabolic control
 - ingest rapidly absorbed carbohydrate if pre-exercise glucose level is under 5 mmol/L

- avoid exercise in extreme hot or cold conditions.
- administer insulin into a site away from the most actively exercising extremities. [*Grade D, consensus*]

Oral antihyperglycemic agents

Current approved categories of oral agents include sulfonylureas, biguanides, alpha-glucosidase inhibitors and thiazolidinediones. (As of September 1998, thiazolidinediones had been approved but not yet marketed in Canada.) Sulfonylureas (acetohexamide, chlorpropamide, glyburide, gliclazide, tolbutamide, tolazamide) stimulate pancreatic insulin release. Biguanides (metformin) primarily decrease hepatic glucose production and may also delay glucose absorption and enhance insulin-mediated glucose uptake. Alpha-glucosidase inhibitors (acarbose) slow absorption of starch and sucrose in the gut. Thiazolidinediones (troglitazone) potentiate insulin action, although the full range of mechanisms is not fully understood. Sulfonylureas may increase the risk of hypoglycemia; this effect is not seen with metformin, acarbose or troglitazone unless they are combined with insulin or a sulfonylurea. Specific details regarding the actions, metabolism and side effects of these drugs can be found in a number of review articles.⁹⁹⁻¹⁰⁹

All people with type 1 diabetes require insulin therapy to prevent hyperglycemia and life-threatening ketoacidosis. Although type 1 diabetes is usually acute, some adults with newly developed type 1 diabetes may present with a slowly progressive disease that could be misdiagnosed as type 2 diabetes; indeed it may even respond initially to oral agents. However, if these patients are started on oral agents instead of insulin, they will be at risk of decompensating relatively rapidly and developing ketoacidosis as their pancreas stops producing insulin. Therefore, the possibility that an adult with new-onset diabetes has type 1 diabetes (particularly if that person is not obese) and, thus, requires insulin must be carefully considered.

Recommendations

31. When changes in lifestyle fail to result in achievement of target glucose levels in 2 to 4 months or if symptoms or severe hyperglycemia persist, oral hypoglycemic agents should be initiated. If lifestyle changes and oral agents are unsuccessful or in the presence of signs of deterioration with significant symptoms of hyperglycemia, the person must begin insulin therapy directly. [*Grade A, Level 1^o*]
32. The initial oral agent used can be (in alphabetical order) an alpha-glucosidase inhibitor, a biguanide or a sulfonylurea; the choice depends on the individual, taking into consideration the following points.
 - For those with a high degree of hyperglycemia (FPG >10 mmol/L), metformin or a sulfonylurea may be chosen as a first agent. [*Grade A, Level 1^o*]
 - Metformin is associated with less weight gain and less hypoglycemia than sulfonylureas [*Grade B, Level 1^{o,111}*], but gastrointestinal side effects may be a limiting factor.
 - Metformin is contraindicated in the presence of significant renal or hepatic insufficiency, as it may cause lactic acidosis. [*Grade D, consensus*]
 - Acarbose may be added to diet, metformin or sulfonylurea therapy to improve glucose control [*Grade A, Level 1²*], but gastrointestinal side effects may be a limiting factor.
33. If target glucose levels are not attainable with a single agent, an agent or agents from other classes may be added, until the maximum dose of an agent of each class is reached. [*Grade A, Level 1²* for the addition of acarbose to other oral agents; Grade A, Level 1¹¹¹ for the addition of metformin to sulfonylurea; Grade D, Level 4^{88,105} for the addition of sulfonylurea to other agents]

Insulin therapy

Insulin is available in human, analogue and animal formulations. Human insulin is associated with less anti-insulin antibody formation than animal insulin¹¹³ and should be used for people initiating insulin therapy. Insulin regimens should be adapted to an individual's treatment goals, lifestyle, diet, age, general health, motivation, capacity for hypoglycemia awareness and self-management, and social and financial circumstances. Anyone beginning insulin therapy must receive initial and ongoing education that includes comprehensive information on its care and use, recognition and treatment of hypoglycemia, management of sick days, and adjustments for food intake and physical activity. If the person with diabetes is not already self-monitoring blood glucose, he or she should learn or review the procedures.

Insulin preparations can be classified according to their time of onset and duration; in ascending order these include lispro, regular, NPH, lente and ultralente insulin. A variety of protocols using combinations of these insulins can successfully control glucose levels. The most frequently used protocols include

- multiple daily injections (basal-bolus protocol: regular or lispro insulin before each meal, NPH or ultralente as the basal type)
- 2 injections per day (split-mixed protocol: mixture of regular and NPH administered before breakfast and dinner)
- a single injection of NPH insulin at bedtime with

oral agents during the day (for patients with type 2 diabetes only)

Premixed insulin preparations (mixtures of regular and NPH insulins in various proportions) are available and may facilitate the use of the split-mixed protocol, particularly in the elderly. Insulin pen devices are gaining in popularity because of their greater ease of use. Intensive insulin therapy using a subcutaneous pump (CSII) is an alternative to multiple daily injections, primarily in patients with type 1 diabetes.¹¹⁴

Insulin use in type 1 diabetes

Insulin is essential for life in people with type 1 diabetes. The associated significant beta-cell destruction occurs very quickly in the young and more slowly when the disease presents later in life.

As already noted, insulin is available in a number of formulations defined by their absorption rate, peak activity and duration of action. Long-acting (ultralente) and intermediate-acting (NPH and lente) insulins are best used as a background (basal) insulin, but may be used at mealtime. Short-acting insulins (regular and lispro) are rapidly absorbed and best used as mealtime (bolus) insulins. Combinations of these insulins and adjustment of the time of their administration are required for optimal blood glucose control.

Lispro is a new insulin analogue that is absorbed more rapidly than regular insulin after subcutaneous injection. It results in lower postprandial glucose levels, fewer nocturnal hypoglycemic events and improved quality of life in some people.^{115,116} There is no strong evidence that it can result in lower HbA_{1c} compared with regular insulin, except in those using pump therapy.¹¹⁷ It should be used with caution in the presence of gastroparesis and should not be combined with acarbose. At present, lispro insulin is not recommended during pregnancy, as there are insufficient data to support its safety.^{115,116}

Recommendations

34. Most people with type 1 diabetes should aim for optimal glucose levels to prevent or delay microvascular complications of diabetes. [*Grade A, Level T*]
35. To achieve target glucose levels, multiple daily injections (3 or 4 per day) or the use of continuous subcutaneous insulin infusion (CSII) as part of an intensified diabetes management regimen are usually required. [*Grade A, Level T*]
36. Regular or lispro insulin, or both, can be used before meals in intensified therapy (multiple daily injections and CSII). Lispro has been associated with lower post-

prandial glucose levels and lower rates of hypoglycemia than regular insulin. [*Grade A, Level T^{115,116}*] Lispro is the preferred insulin for use in CSII. [*Grade B, Level 2⁷*]

Insulin use in type 2 diabetes

Most people with type 2 diabetes will initially attain acceptable glucose control through diet and use of oral agents. Insulin therapy may be required temporarily during periods of illness or stress. Many others will become refractory to diet and oral agents and will require insulin for metabolic control. In these people, insulin doses (frequently high) and the number of injections (1–4) should be adjusted to achieve target glucose levels.⁸⁸ A combination of insulin and oral agents may effectively control glucose levels.

Recommendations

37. Intensive insulin therapy may prevent microvascular complications in people with type 2 diabetes. [*Grade B, Level F⁶*]
38. If individual treatment goals have not been reached on a regimen that includes appropriate use of diet, exercise and oral agents, then insulin therapy should be initiated to improve glycemic control. [*Grade A, Level F¹⁸*]
39. When insulin therapy is initiated, the concomitant use of oral agents is an acceptable option. When insulin therapy is added to oral agents, a single injection of intermediate-acting insulin may be added at bedtime. [*Grade B, Level F⁹*] This approach may result in better glucose control with a smaller insulin dose [*Grade A, Level 1⁴⁰*] and may induce less weight gain than with the use of insulin alone.
40. Poor glucose control despite insulin therapy can be improved by the addition of one of the following oral agents:
 - acarbose [*Grade A, Level F¹*]
 - metformin [*Grade B, Level F²*]
 - troglitazone [*Grade A, Level F³*]

On initiating troglitazone therapy, liver enzymes should be evaluated due to potential, severe hepatic dysfunction; evaluation should occur before therapy, monthly for the first 8 months, bimonthly for the next 4 months and periodically thereafter. [*Grade D, Level F⁴*]

Diabetes in children and adolescents

Specific recommendations have been developed for children and adolescents because of considerations that are relevant for this age group.

Type 1 diabetes

The insulin regimen and distribution of carbohydrates in the meal plan must be flexible in children and adolescents to allow for normal growth and development while balancing the need for reasonable glycemic control. Ongoing education of the child or adolescent is essential, to achieve age-appropriate knowledge and skills and eventual self-sufficiency. Intensive education, with ongoing reinforcement regarding sick-day management and prevention of diabetic ketoacidosis, must be provided for all families.^{125,126} All parents must be taught the use of glucagon for severe hypoglycemia.¹²⁷ Adolescents must receive ongoing counselling regarding disordered eating patterns,¹²⁸ smoking, contraception, alcohol and drug abuse, and driving, as these activities relate to diabetes care.

All children should be screened for associated autoimmune diseases, such as hypothyroidism, by determining thyroid-stimulating hormone (TSH) level. Selected children with poor growth, poor glycemic control or unpredictable, frequent hypoglycemia should be tested for celiac disease using antigliadin antibodies¹²⁹ and for Addison's disease by determining adrenocorticotropic hormone (ACTH) level.

Planning the transition from pediatric to adult diabetes care must be undertaken with sensitivity to the needs of the adolescent and recognition of the factors that predict noncompliance with medical follow-up.^{130,131}

Recommendations

41. The metabolic goals and therapeutic strategies for adolescents over 12 years of age are the same as those for adults. [Grade A, Level T^{1,32}] The target HbA_{1c} for prepubertal children is 120% to 140% of the upper limit of normal with targets for glucose and HbA_{1c} graduated according to the child's age. [Grade D, consensus] Extreme caution is required to avoid hypoglycemia in children under 5 years of age, because of the permanent cognitive deficit that may occur in this age group. [Grade D, Level 4^{133,134}]
42. All children with diabetes should have access to an experienced DHC team. The complex physical, developmental and emotional needs of children and their families require specialized care to ensure the best long-term outcome. [Grade D, Level 4¹³⁵]
43. In children and adolescents with new-onset diabetes, initial outpatient education and management should be considered if appropriate personnel and a 24-h telephone consultation service are available in the community. [Grade C, Level 3¹³⁶]

Type 2 diabetes

Type 2 diabetes (as distinct from genetic maturity-onset diabetes of the young or MODY forms), occurs in special groups of children. Currently, it occurs in 1% to 2% of children of Aboriginal, Hispanic or black origin and up to 4% of adolescent girls. In Canada, type 2 diabetes has been reported in Aboriginal children aged 7 and older. Most children are not symptomatic and are currently identified by screening programs in high-risk populations.

Due to the relatively low frequency and short history of this problem, which was recognized only in the 1980s, the most appropriate screening guidelines have not been developed. However, owing to the devastating consequences of early-onset complications, it is prudent to consider screening in Aboriginal children. The best management strategy for this age group is unknown. Intensive programs to increase physical activity and nutritional interventions have proven beneficial in the summer camp setting and must be encouraged in the home and community. There are no controlled trials of safety or efficacy of oral agents or insulin for type 2 diabetes in this age group (see "Diabetes in Aboriginal people" for further discussion).

Diabetes in the elderly

Because the renal threshold for glucose increases with age, elderly people frequently do not have classic symptoms of hyperglycemia (polyuria, polydipsia) until blood glucose values are markedly elevated. When symptoms are present, they are generally nonspecific (fatigue, depression, failure to thrive).

A wide variety of factors affect the ability of elderly people to follow treatment regimens. Management plans must account for limited abilities, comorbidities and potentially limited lifespans.¹³⁶⁻¹³⁸ Although the interpretation of biologic status must be considered, "elderly" in the present context refers to people over 70 years of age.

Recommendations

44. The same glucose targets apply to otherwise healthy elderly as to younger people with diabetes. In people with multiple comorbidity, the goal should be to avoid symptoms of hyperglycemia and prevent hypoglycemia. [Grade D, consensus] Closer to normal glucose levels are associated with a lower risk of complications in elderly people with type 2 diabetes. [Grade A, Level T^{6,138}]
45. Elderly people with diabetes should be referred to a DHC team. Interdisciplinary interventions have been shown to improve glycemic control in the elderly. [Grade B, Level 2⁹⁻¹⁴¹]

46. In chronic care institutions, specific dietary restrictions may not be useful in improving glycemic control. [Grade D, Level 4²] The recommended distribution of nutrients is as suggested for the general aging population. [Grade D, consensus]
47. Moderate exercise is beneficial for elderly people with type 2 diabetes; however, comorbid conditions may prevent aerobic physical training [Grade D, Level 4²], and any increase in activity levels may be difficult to achieve. [Grade D, consensus]
48. In elderly people, sulfonylureas should be used with caution because the risk of hypoglycemia increases exponentially with age. [Grade D, Level 4²] In general, initial doses should be half those for younger people, and doses should be increased more slowly. [Grade D, consensus] Gliclazide may be the preferred sulfonylurea, as it is associated with a reduced frequency of hypoglycemic events compared with glyburide. [Grade A, Level 1⁵]
49. In elderly people, the use of premixed insulins as an alternative to mixing insulins may minimize dosage errors. [Grade B, Level 2⁹]

Diabetes and pregnancy

Currently, the major problems associated with excess glucose crossing the placenta in pregnancy include teratogenicity and metabolic and growth abnormalities in the fetus. Long-term metabolic sequelae for women with GDM and the offspring of women with any form of diabetes in pregnancy may also occur.^{147,148}

Pre-existing diabetes

In the absence of prepregnancy planning and careful follow-up, maternal diabetes may be associated with an increased risk of spontaneous abortion, perinatal mortality and perinatal morbidity. Congenital malformations continue to be the major cause of perinatal mortality in diabetic women and are 2 to 7 times more common than in nondiabetic women.¹⁴⁹

Both retinal and renal disease may become more severe during pregnancy. Because significant background retinopathy may lead to deterioration of vision, affected women must have their eyes carefully monitored before and during pregnancy. Similarly, women with significant proteinuria before pregnancy are at risk for hypertension during pregnancy (with or without eclampsia), as well as worsened renal function after pregnancy.

Thus, any woman planning a pregnancy should work with a specialized DHC team to assess the level of glycemic control and the status of microvascular complications,¹⁵⁰

and to plan appropriate ongoing monitoring of glucose, blood pressure and maternal and fetal status until delivery. Women taking oral hypoglycemic agents should discontinue them and initiate use of insulin before conception.

Recommendations

Before pregnancy

50. Pregnancy in women with diabetes should be carefully planned, preferably in consultation with a high-risk prepregnancy clinic. [Grade C, Level 3⁹]
51. All women with diabetes should attempt to attain "ideal" blood glucose control (see Table 11). Glycated hemoglobin (HbA_{1c}) levels greater than 140% of the upper limit of normal nonpregnant values should be avoided as they are clearly associated with increased risk of spontaneous abortion and malformations. [Grade B, Level 2¹]
52. Both diabetic nephropathy and diabetic retinopathy may progress during pregnancy and should be evaluated and followed carefully. [Grade B, Level 2^{2,153}] Women should also be assessed for CAD. [Grade D, consensus]

During pregnancy

53. All women with diabetes should aim for ideal glucose levels without significant hypoglycemia. [Grade D, Level 3⁴]
54. Any woman on diet therapy alone who does not achieve target values should be started on insulin. Use of oral agents is not recommended. [Grade D, consensus]
55. Ketosis should be avoided, especially during the third trimester. [Grade B, Level 2³] Weight gain should be monitored, normal weight gain should be the goal and weight-reducing diets should be avoided. [Grade D, consensus]
56. Retinal examination should be performed regularly, at least once in the first trimester with subsequent frequency adjusted to the severity of the retinopathy. [Grade B, Level 2³]

Gestational diabetes mellitus

Gestational diabetes is glucose intolerance of varying severity detected or first recognized during pregnancy. Its prevalence varies widely according to the population studied and criteria used for diagnosis; it often reflects the prevalence of diabetes in a given population. It is associated with an increased risk of fetal macrosomia, neonatal hypoglycemia, hyperbilirubinemia, hypocalcemia and polycythemia. Perinatal mortality is rare today in women

with diagnosed GDM. The children of mothers with GDM may have an increased risk of childhood obesity and diabetes as young adults.^{147,148,155} The recognition of GDM indicates an increased risk of future diabetes in the mother (primarily type 2). The basis for therapy is diet adjustment, monitoring of maternal and fetal well-being and glucose control. Use of insulin is appropriate if glucose control is not attained with diet alone.¹⁵⁶

Recommendations

57. Women with GDM should receive dietary counselling and carry out frequent FPG and postprandial glucose monitoring. [Grade C, Level 3] The goals associated with the best neonatal outcome are an FPG level <5.3 mmol/L [Grade C, Level 3], a 1-h postprandial glucose level <7.8 mmol/L [Grade A, Level 1st] and a 2hPG level <6.7 mmol/L. [Grade D, Level 3]
58. Dietary counselling should be provided to ensure a well-balanced diet, with a goal of achieving normal maternal glucose levels and normal weight gain in the mother and the fetus. Because of the risk of ketonemia, weight-reducing diets are not recommended. [Grade D, consensus]
59. FPG and postprandial glucose levels should be monitored. [Grade A, Level 1st] If diet therapy does not result in achievement of glucose target values, insulin therapy should be initiated. [Grade D, consensus]
60. Regular and moderate exercise, particularly of the upper body, should be encouraged. [Grade A, Level 1st]
61. Women who have had GDM should be advised to achieve a healthy body weight and exercise regularly postpartum to reduce the risk of subsequent diabetes. [Grade D, consensus]
62. Women who have had GDM are at high risk for subsequent diabetes or glucose intolerance. [Grade C, Level 3rd,161] An OGTT (75-g, 2-h) should be performed 6 weeks to 6 months postpartum to rule out the presence of glucose intolerance or diabetes. [Grade D, consensus]

Diabetes in Aboriginal people

Over the past 50 years, dramatic changes in lifestyle in Aboriginal communities across North America have had a profound impact on the social, environmental and health status of this population. Although morbidity associated with infectious diseases and starvation has decreased, chronic diseases such as obesity, diabetes and cardiovascular disease have emerged. Type 2 diabetes mellitus is now recognized as a major health problem among Aboriginal people. Indeed, recent population-

based epidemiologic surveys in Canada have revealed age-adjusted prevalence rates of 19% to 26%, which are among the highest reported rates in the world.^{162,163}

Due to the relatively recent onset of this epidemic in Aboriginal populations, complications associated with diabetes are only beginning to emerge as significant health problems. Therefore, aggressive screening for CAD, neuropathy, nephropathy and retinopathy should accompany visits to physicians by Aboriginal people according to the recommended practice guidelines.

Most Aboriginal communities are aware of diabetes and its many complications; the establishment of the National Aboriginal Diabetes Association (NADA) in 1996 reflects this. However, diabetes is often not a priority for communities in which other important political and health issues predominate. According to some, diabetes is a social disease or, more appropriately, a result of social conditions. Geographic isolation, poor eating patterns, minimal physical activity, substance abuse, psychosocial issues and even absence of basic health care in isolated communities may be significant barriers to the recognition of diabetes as a priority.

Much of the responsibility for diabetes care in communities lies with community health representatives, who are usually overburdened with other duties. In some cases, community health representatives are able to provide better care with more training, and a number of initiatives across Canada are addressing this need. Expanded community-based prevention programs are also required.

Major challenges face health care professionals and policymakers in terms of providing appropriate and practical diabetes screening and treatment programs to Aboriginal populations. Culturally appropriate community-based intervention strategies must be developed by supporting community initiatives and providing technical and financial resources. Cooperation and partnership with political leaders in grassroots organizations are essential elements in the support of innovative strategies. Local input combined with the knowledge and experience of multidisciplinary teams is required.

The major focus of this strategy should be primary prevention, and a number of such initiatives are under way¹⁶⁴ (e.g., in Kahnawake, Que., and Sandy Lake, Ont.). Programs aimed at schoolchildren and their parents are critical for the prevention of diabetes in future generations. In addition to prevention strategies, efforts to improve metabolic control and assure regular surveillance for complications, are also needed. High-risk groups such as children and women in the childbearing ages require particular attention.¹⁶⁵⁻¹⁶⁸ Despite the significant challenges that accompany the institution of such programs, the management and prevention of diabetes and associat-

ed complications in Aboriginal populations should be a high priority in health care planning and delivery.

At present there is no evidence that therapeutic strategies should differ from those used for the general population.

Recommendations

63. Community-based screening programs based on measuring blood glucose levels should be established in Aboriginal communities. Urban people of Aboriginal origin should be screened for diabetes in primary care settings. [*Grade D, consensus*]
64. Primary prevention programs initiated by Aboriginal communities should be encouraged. [*Grade D, consensus*]
65. There must be recognition of, respect for and sensitivity regarding the unique language, culture and geographic issues as they relate to diabetes care in Aboriginal communities across Canada. [*Grade D, consensus*]

Complications

Major acute complications of diabetes are hypoglycemia and hyperglycemic crises including ketoacidosis and hyperglycemic-hyperosmolar states. A person with diabetes experiencing an acute complication may be treated in an ambulatory setting or require emergency admission to a hospital ward or an intensive care unit. Once a patient has recovered from such an episode, appropriate education by the DHC team is necessary to prevent recurrences.

Long-term complications may occur in both type 1 and type 2 diabetes. These include macrovascular complications (CAD, cerebrovascular disease, and peripheral vascular disease) and microvascular complications (retinopathy, neuropathy, and foot problems).

Regular, systematic surveillance for these acute and long-term complications is an integral component of comprehensive diabetes care. An organized and coordinated approach should be implemented for follow-up visits.

Retinopathy

Diabetic retinopathy is the major cause of adult blindness in North America and likely the most feared of the long-term complications. Diabetes is the sole or contributing cause of blindness in about 86% of the eyes of people with type 1 diabetes, and in 33% of the eyes of people with type 2 diabetes.¹⁶⁹ Proliferative retinopathy occurs in 23% of patients with type 1 diabetes, 14% of people with type 2 diabetes taking insulin and 3% of peo-

ple with type 2 diabetes not taking insulin;¹⁷⁰ macular edema occurs in 11%, 15% and 4% of these groups, respectively.¹⁷¹ Patients with diabetes are also at increased risk of developing cataracts.¹⁷² Evidence for increased risk of primary open-angle glaucoma is conflicting.^{173,174}

Screening strategies for sight-threatening retinopathy (i.e., proliferative retinopathy or macular edema) must reflect differences in the incidence and prevalence of retinopathy in type 1 and type 2 diabetes.¹⁷⁵⁻¹⁷⁸ Development of diabetic retinopathy in children under 10 years of age with type 1 diabetes is rare regardless of the duration of diabetes.¹⁷⁷ The prevalence rate increases sharply after 5 years duration of diabetes in postpubertal people with type 1 diabetes.¹⁷⁷ Conversely, retinopathy may be present in 21% of people soon after clinical diagnosis of type 2 diabetes, but is vision-threatening in only about 3%.^{171,173-176} Important predictors of the progression of retinopathy are longer duration of diabetes, higher level of glycated hemoglobin, more severe retinopathy, higher blood pressure, higher lipid levels and, in type 1 diabetes, pregnancy.^{152,175-180}

The "gold standard" for assessing diabetic retinopathy is 7-standard field, stereoscopic-colour fundus photography.¹⁸¹ Seventy-nine per cent agreement in the detection of proliferative retinopathy can be achieved by fundus examination by direct ophthalmoscopy through dilated pupils carried out by highly trained personnel (regardless of professional designation).¹⁸² Examinations by inexperienced observers or examinations through undilated pupils fail to detect proliferative retinopathy in about 50% of patients and macular edema in all cases.^{183,184} Contact lens fundus biomicroscopy by retinal specialists results in 81% agreement in the detection of clinically significant macular edema.¹⁸⁵ The Early Treatment Diabetic Retinopathy Study's final scale is the best means of categorizing the severity of retinopathy and provides important prognostic information.¹⁸⁶

In type 1 diabetes, the onset of retinopathy can be delayed or its progression slowed by intensive insulin therapy, with achievement of improved control.⁷⁷ In type 2 diabetes, epidemiologic studies show that hyperglycemia is an independent risk factor for the incidence and progression of retinopathy; however, the risks and benefits of insulin therapy have not been completely established.^{4,187}

In both types of diabetes, elevated diastolic blood pressure is a risk factor for the development of macular edema,^{180,188} and elevated systolic blood pressure is a risk factor for loss of vision.¹⁸⁹ People with elevated serum cholesterol, low-density lipoprotein (LDL) cholesterol or triglyceride levels are more likely to have or develop retinal hard exudate, which can be associated with risk of loss

of vision independent of the extent of macular edema.¹⁷⁹ Retinopathy can become worse during pregnancy, independent of higher levels of glycated hemoglobin.¹⁵²

Focal/grid laser treatment for clinically significant macular edema reduces loss of vision by 50%.¹⁹⁰ Full implementation of scatter laser treatment and vitrectomy reduces legal blindness by 90% in patients with severe nonproliferative or proliferative retinopathy.¹⁹¹⁻¹⁹³ In type 1 diabetes, early vitrectomy performed for nonclearing, severe vitreous hemorrhage provides a better chance of visual recovery than if treatment is deferred. In type 2 diabetes, early vitrectomy has no such benefit and carries a 2-fold higher overall risk of serious untoward events than if deferred for 1 year.¹⁹⁴ In people with type 1 or type 2 diabetes, early vitrectomy for advanced active proliferative retinopathy unresponsive to laser treatment achieves significant recovery of visual acuity compared with conventional management.¹⁹⁵

Recommendations

66. The development and progression of retinopathy may be prevented through intensive diabetes management achieving optimal metabolic control [*Grade A Level I*^{6,77}] and treatment of elevated blood pressure or lipid levels. [*Grade D, Level F*^{9,188,189}]
67. In people with diabetes, screening for sight-threatening retinopathy should be performed by experienced professionals highly trained in direct ophthalmoscopy through dilated pupils or by retinal specialists. [*Grade A, Level I*^{182,183,185} Level 2¹⁸⁴]
68. Screening and evaluation for retinopathy should be performed annually 5 years after the onset of diabetes in postpubertal patients (age 15 years or over) with type 1 diabetes and in everyone with type 2 diabetes at the time of diagnosis. [*Grade A, Level F*] The interval for follow-up assessments should be tailored to the severity of the retinopathy. In those with type 2 diabetes who have no or minimal retinopathy, the recommended interval is 2 years and should not exceed 4 years. [*Grade A, Level F*^{6,178}]
69. Women with type 1 diabetes should have an ophthalmic assessment before conception in a planned pregnancy and in the first trimester of pregnancy and be followed up as needed during pregnancy. [*Grade A, Level I*⁵²]
70. Proliferative or severe nonproliferative retinopathy necessitates referral to an ophthalmologist or retinal specialist with access to surgical facilities. [*Grade A, Level I*⁹⁰⁻¹⁹⁵]
71. Visually disabled people should undergo low-vision evaluation and rehabilitation. [*Grade D, consensus*]

Nephropathy

Diabetic nephropathy is the number one cause of end-stage renal failure in Canada and the western world.¹⁹⁶⁻¹⁹⁸ The costs of dialysis and renal transplantation are high. In addition, people with diabetes and end-stage renal failure have high morbidity and mortality rates due to cardiovascular disease.¹⁹⁶⁻²⁰³

The focus of treatment of diabetic nephropathy is on prevention through early screening and detection. Elevated microalbuminuria is the earliest reliable and clinically detectable sign of progressive nephropathy in both type 1 and 2 diabetes.^{197,204-210} Screening for increased microalbuminuria is necessary 5 years after the onset of diabetes for people over 15 years of age with type 1 diabetes and at the time of diagnosis for everyone with type 2 diabetes to detect progressive nephropathy at the earliest stage.²¹¹⁻²¹⁵ Once nephropathy is diagnosed, intensive glucose control,^{76,77,216-224} inhibition of angiotensin-converting enzyme (ACE),²²⁵⁻²²⁹ normalization of blood pressure²³⁰⁻²⁴¹ and elimination of all cardiovascular risk factors²⁴²⁻²⁴⁴ will help prevent its progression. If overt nephropathy is evident (i.e., more than 300 mg/d of albumin in urine), all those with type 1 diabetes should receive ACE inhibitors. ACE inhibitors should also be considered for those with type 2 diabetes and overt nephropathy. Data suggest that dietary reduction of protein intake may delay progression of renal failure.²⁴⁵ Follow-up should include monitoring of serum creatinine and potassium, a 24-h creatinine clearance test and quantitation of proteinuria at least twice a year.

Recommendations

72. The best possible glucose control — if necessary intensive diabetes management — should be instituted in people with type 1 diabetes for the prevention of onset and delay in progression of early nephropathy. [*Grade A, Level F*²²⁴]
73. In people with either type 1 or type 2 diabetes, screening for microalbuminuria is recommended in those with dipstick-negative or trace proteinuria. Frequency of screening is annual for people over 15 years of age with a 5-year history of type 1 diabetes and for all people after diagnosis of type 2 diabetes. [*Grade D, consensus*] The recommended screening method is measurement of an albumin:creatinine ratio in a random, daytime urine sample. If values are greater than 2.8 for females and 2.0 for males, the test should be repeated (and confirmed in 2 out of 3 measurements over 3 months); if uncertainty about elevation still exists, it should be confirmed with a timed urine collection to measure the rate of microalbuminuria. [*Grade A, Level F*^{2,215}]

74. In type 1 diabetes, elevated microalbuminuria (30–299 mg albumin in 24 h or 20–200 µg/min) should be treated with an ACE inhibitor to decrease albuminuria, even in the absence of hypertension. [*Grade A, Level I*^{25,226,229}]
75. People with type 2 diabetes and elevated microalbuminuria (30–299 mg albumin in 24 h) may benefit from ACE inhibitor therapy to decrease albuminuria. [*Grade B, Level I*^{27,228}]
76. People with type 1 diabetes and overt nephropathy (>300 mg albumin in urine in 24 h) should be treated with an ACE inhibitor. (Blood pressure goals should be the same as for people with hypertension.) [*Grade A, Level I*³³]
77. A greater than 50% decrease in creatinine clearance rate necessitates referral to a nephrologist or internist associated with a dialysis and renal transplantation centre for adequate, well-planned long-term management. [*Grade D, consensus (best practice of the Canadian Society of Nephrology)*]

Neuropathy

Detectable neuropathy will develop within 10 years of the onset of diabetes in 40% to 50% of people with type 1 and type 2 diabetes. Although fewer than 50% of these people are symptomatic,^{77,246} neuropathic pain is frequently bothersome.^{247–249} People with type 2 diabetes may have neuropathy at the time of diagnosis, whereas it is uncommon in people with type 1 diabetes within the first 5 years after onset of diabetes. Increased risk of foot ulceration, which depends on the degree of foot insensitivity,²⁵⁰ and amputation are serious sequelae of diabetic neuropathy. Both somatic and autonomic neuropathy may occur and may require referral to a specialist experienced in managing the affected body system.

Neuropathy is most easily detected by examining the patient for loss of ankle reflexes and perception of 128 Hz vibration in the great toe,⁷⁷ or by using a 10-g Semmes–Weinstein monofilament.²⁵¹ In people with significant symptoms of neuropathy, referral for additional neurologic evaluation and to other specialists (e.g., neurologist, podiatrist, chiropodist) may be helpful.

Intensive diabetes management is effective for the primary or secondary prevention of neuropathy in patients with type 1 diabetes.^{77,222,252} In patients with type 2 diabetes, lower glucose levels are associated with reduced frequency of neuropathy²⁴⁶ and intensified therapy may also be helpful.⁷⁶

Tricyclic antidepressants,^{247–249,253} carbamazepine,²⁵⁴ or mexiletine²⁵⁵ are often effective in controlling neuropathic pain. Adverse effects of these medications, especially mex-

iletine, must be considered before use. The effect of topical capsaicin is less certain.^{256,257} Nonaddictive analgesics may be used to alleviate pain.

Recommendations

78. Screening for peripheral neuropathy should be carried out annually to identify those at high risk of developing foot ulcers. [*Grade A, Level I*⁰]
79. Detection of peripheral neuropathy can be done through assessment for
- decrease or loss of ability to sense vibration or loss of sensitivity to a 10-g monofilament at the great toe
 - absent or decreased ankle reflexes. [*Grade D, Level 4*⁵¹]
80. People with type 1 diabetes should be treated for peripheral neuropathy with intensive management for primary prevention or secondary intervention. [*Grade A, Level I*²²²]
81. Intensified diabetes management should be considered for people with type 2 diabetes to prevent onset and progression of neuropathy. [*Grade B, Level I*]
82. Tricyclic antidepressants and carbamazepine [*Grade A, Level I*^{49,254}] should be considered for symptomatic relief of painful peripheral neuropathy. Topical capsaicin should be considered as a nonsystemic treatment for painful neuropathy. [*Grade B, Level I*⁷]
83. People with clinically significant autonomic dysfunction should be appropriately assessed and referred to a specialist experienced in managing the affected body system. Because sexual dysfunction is common, specific inquiries should be made as people may be reluctant to volunteer such information. [*Grade D, consensus*]

Foot care

Foot problems are a major cause of morbidity and mortality in people with diabetes and contribute to increased health care costs.^{258,259} The sequence of events leading to lower-extremity amputation is well known: in people with neuropathy²⁶⁰ or peripheral vascular disease (PVD),²⁶¹ minor trauma to the foot leads to skin ulceration, infection and gangrene, resulting in amputation.^{262–266} Foot complications are a major reason for admission to hospital of people with diabetes and account for approximately 20% of all admissions in the North American population.^{264,265,267,268} After amputation of one limb, the prognosis for the contralateral limb is poor.^{269,270} Of all lower-extremity amputations, 45% occur in people with diabetes; the age-adjusted rate of amputation is 11 times higher in those with diabetes than in people without diabetes.²⁷⁰ More recent data indicate that one-half to two-thirds of all lower-extremity

amputations performed in the United States are in people with diabetes, and these account for more than 50 000 amputations.^{259,266,268} In the United States, the direct costs for this common complication of diabetes, including rehabilitation, are in excess of \$500 million a year.^{267,271}

Appropriate management can prevent or heal diabetic foot ulcers, thereby greatly reducing the amputation rate.^{263,266,267,272,273} Prevention of amputations calls for the use of various measures, including regular foot examination and evaluation of amputation risk, patient education, early detection and treatment of diabetic foot ulcers and, if necessary, vascular surgery.^{267,271-274} Characteristics that have been demonstrated to confer high risk of amputation include previous ulceration, increased age, PVD, neuropathy, structural deformity, renal transplantation, poor socioeconomic status and smoking.

Recommendations

84. Foot examination in adults should be an integral component of diabetes management and decreases risk of foot ulcers and amputation. [*Grade A, Level I*^{273,274}] Foot examination should include assessment of structural abnormalities, neuropathy, vascular disease, ulcerations and evidence of infection. [*Grade D, Level 4*⁶⁶] Foot examinations should be performed at least annually in all people with diabetes who are over 15 years of age and at more frequent intervals for those at high risk. [*Grade D, consensus*]
85. Prevention of foot ulceration and amputation requires foot care education, proper footwear, avoidance of foot trauma, smoking cessation and early referral if problems occur. People at high risk of foot ulceration should receive reinforcement of foot care education. [*Grade A, Level I*^{3,274}]
86. A person with diabetes who develops a foot ulcer requires therapy by experienced health care professionals who have expertise in diabetes foot care. Any infection must be treated aggressively. [*Grade D, consensus*]

Cardiovascular disease and hypertension

Cardiovascular disease is a major cause of morbidity and mortality in both type 1 and 2 diabetes; morbidity and mortality rates are 2- to 4-fold higher than in age- and sex-matched groups in the nondiabetic population.²⁷⁵⁻²⁷⁹

The risk of CAD and stroke is increased 2-fold among men with diabetes and 3- to 4-fold among women with diabetes.²⁷⁸⁻²⁸² Silent ischemia and myocardial infarction are more common and the outcome of an infarction is worse than in nondiabetic people.²⁸³⁻²⁸⁵ In fact, after an acute myocardial infarction, men and women with dia-

betes are at greater risk for congestive heart failure, have a 4-fold greater risk of recurrent infarction, a 2-fold greater risk of arrhythmias and higher short- and long-term mortality rates than nondiabetic people.^{286,287} They also have a lower overall survival rate.²⁸⁶ In addition to the risk of CAD and stroke, diabetes is associated with increased risk of PVD, which contributes to the high rate of gangrene and lower-limb amputations.^{276,281}

The benefits of reducing CAD by modifying the major risk factors for cardiovascular disease, such as hyperlipidemia, have not been clearly assessed in people with diabetes.²⁸⁸ Nevertheless, subgroup analyses of people with diabetes who were enrolled in both primary²⁸⁹ and secondary⁷⁸ prevention trials of lipid-lowering drugs suggest that reduction of LDL cholesterol can significantly decrease morbid events.

As CAD may be asymptomatic in people with diabetes, aggressive treatment including the use of acetylsalicylic acid as a primary prevention strategy should be considered in high-risk people (over the age of 30); acetylsalicylic acid may also be effective for secondary prevention.²⁹⁰ There is no contraindication to acetylsalicylic acid therapy, even in people with severe stages of diabetic retinopathy who are at risk for (or who have) vitreous hemorrhage.^{291,292}

Hypertension complicates diabetes in all populations and is more frequent with advancing age.²⁸⁰ In type 1 diabetes, blood pressure is usually normal at presentation. Hypertension typically develops with the onset of nephropathy and is characterized by elevation of systolic and diastolic blood pressure. About half of people with type 1 diabetes with 30 or more years of diabetes have hypertension.²⁷⁹ People with type 2 diabetes are frequently hypertensive at the time of diagnosis, and the increase in blood pressure is generally correlated with obesity, decreased physical activity and older age. Isolated systolic hypertension is particularly common in type 2 diabetes.^{293,294}

Because hypertension is a major contributor to the dramatically increased morbidity and mortality of both type 1 and 2 diabetes,^{203,279} it should be recognized and treated early and aggressively. Although treatment of hypertension with any known antihypertensive agent may improve cardiovascular disease outcomes,^{241,293,294} the use of low-dose diuretics and beta-blockers may be particularly effective in the elderly.²⁹⁵ ACE inhibitors may also decrease cardiovascular events more than calcium channel antagonists in those at high risk.^{296,297} ACE inhibitors have additional advantages in the presence of diabetic renal disease. (See *Nephropathy* section.)

Recommendations

87. People with type 1 or 2 diabetes should be encouraged

- to adopt a healthy lifestyle to lower their risk of CAD: this means achieving and maintaining healthy eating habits and a desirable weight, engaging in regular physical activity and stopping smoking. [Grade D, consensus]
88. A fasting lipid profile (total cholesterol, triglycerides, HDL cholesterol and calculated LDL cholesterol) should be carried out in adults with diabetes and repeated every 1 to 3 years as clinically indicated. [Grade D, consensus]
89. Appropriate treatment of dyslipidemia to achieve target levels (as noted in Table 12) should be instituted for primary prevention of CAD [Grade D, consensus] and secondary prevention of CAD. [Grade C, Level 3]
90. Hypertension in people with diabetes (i.e., blood pressure 140/90 mmHg) should be treated to attain target blood pressure <130/85 mmHg. [Grade D, consensus]
91. First-line drug therapies for hypertension in people with diabetes and without overt nephropathy can include (in alphabetical order): ACE inhibitors, alpha-blockade agents, angiotensin II receptor antagonists and calcium channel antagonists. The choice of antihypertensive agents should be tailored to the individual and take into account the effects of these agents on cardiovascular, metabolic and renal outcomes. [Grade D, consensus]
92. Hypertension treatment goals for the elderly should be tailored to the individual. [Grade D, consensus] Low-dose diuretics and beta-blockers should be considered in the elderly to prevent cardiovascular disease. [Grade A, Level 1⁹⁵]
93. Low-dose acetylsalicylic therapy (81–325 mg/d) should be considered as primary prevention therapy in high-risk patients (over the age of 30 years) with diabetes and as a secondary prevention strategy in people with diabetes and large vessel disease. [Grade C, Level 3⁹⁰]

Summary

These are the first evidence-based clinical practice guidelines for diabetes to be published in the Americas. The method used to develop them included the review and grading of the scientific evidence for many of the recommendations, but it also revealed specific areas where evidence to support clinical practices was lacking.

Outpatient management of diabetes using a shared-care team approach is addressed in a comprehensive manner. Unsettled issues relating to such controversial areas as the treatment of GDM and the management of diabetes in Aboriginal Canadians are explicitly acknowledged and identified as targets for further investigation or strategy development.

There has been an overwhelming commitment by many key stakeholders in this process. Their desire to improve the health of Canadians with diabetes and to continue the effort begun with publication of the first guidelines in 1992⁹ was evident from the intensity of their efforts and the amount of time they committed to their tasks. They are confident that the recommendations contained in these revised clinical guidelines will lay the groundwork for significant improvement in diabetes care, and they trust that publication of these guidelines will enhance the quality of life of Canadians with diabetes. Before this can happen, the critical challenge will be to implement these guidelines in a scientific way so that the information can be used to further enhance health policies for diabetes.

This document is an executive summary of all the recommendations of the 1998 revision of the clinical practice guidelines for management of diabetes mellitus. It will be followed by in-depth assessment of each area in the form of technical review articles that will be published subsequently.

In addition to those who contributed to the development of this document, the process benefited from the valuable insights and comments of numerous national and international experts who reviewed these guidelines in detail. The members of the Clinical and Scientific Section and the Diabetes Educator Section of the Canadian Diabetes Association (CDA) and attendees at the CDA Professional Sections Conference, London, Ont., October 1997, provided valuable insight as part of the consensus process. Their contributions in enhancing the quality of this information are gratefully acknowledged. An enormous amount of work was done by the staff of the CDA; particularly important support came from Donna Lillie, director of research and professional education. The expert secretarial assistance of Shirley Grundy and Mary Richardson, the fundraising support of Nowshad Ali and the administrative details carried out by numerous other CDA staff, as well as the medical writing assistance of Arthur Tan are much appreciated. It was also of great benefit to have the funding support of our sponsors to pursue this process with the intensity required.

Note added in proof: The benefits of improved glucose and blood pressure control for the prevention of long-term complications in those with type 2 diabetes have been confirmed by recent reports of the results of the United Kingdom Prospective Diabetes Study.²⁹⁸⁻³⁰² This landmark study of over 5000 people with type 2 diabetes over 20 years confirmed the prevention of microvascular complications through improved glucose control and highlighted the major effects of blood pressure control on micro- and macrovascular complications of diabetes. After further evaluation, a position statement will be developed by the CDA on the implications of this study, which may include revision of the grading of some of the recommendations in these guidelines.

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