# Clinical presentation and diagnosis of diabetes mellitus in adults

Author: David K McCulloch, MD
Section Editors: David M Nathan, MD, Joseph I Wolfsdorf, MB, BCh
Deputy Editor: Jean E Mulder, MD

All topics are updated as new evidence becomes available and our peer review process is complete.
**Literature review current through:** Jun 2018. | **This topic last updated:** Mar 27, 2017.

**INTRODUCTION** — The term diabetes mellitus describes several diseases of abnormal carbohydrate metabolism that are characterized by hyperglycemia. It is associated with a relative or absolute impairment in insulin secretion, along with varying degrees of peripheral resistance to the action of insulin. Every few years, the diabetes community reevaluates the current recommendations for the classification, diagnosis, and screening of diabetes, reflecting new information from research and clinical practice.

The American Diabetes Association (ADA) issued diagnostic criteria for diabetes mellitus in 1997, with follow-up in 2003 and 2010 [1-3]. The diagnosis is based on one of four abnormalities: glycated hemoglobin (A1C), fasting plasma glucose (FPG), random elevated glucose with symptoms, or abnormal oral glucose tolerance test (OGTT) (table 1). Patients with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are referred to as having increased risk for diabetes or prediabetes. (See 'Diagnostic criteria' below.)

Screening for and prevention of diabetes is reviewed elsewhere. The etiologic classification of diabetes mellitus is also discussed separately. (See "Screening for type 2 diabetes mellitus" and "Prevention of type 2 diabetes mellitus" and "Prevention of type 1 diabetes mellitus" and "Classification of diabetes mellitus and genetic diabetic syndromes".)

**CLINICAL PRESENTATION** — Type 2 diabetes is by far the most common type of diabetes in adults (>90 percent) and is characterized by hyperglycemia and variable degrees of insulin deficiency and resistance. The majority of patients are asymptomatic, and hyperglycemia is noted on routine laboratory evaluation, prompting further testing. The frequency of symptomatic diabetes has been decreasing in parallel with improved efforts to diagnose diabetes earlier through screening (see "Screening for type 2 diabetes mellitus"). Classic symptoms of hyperglycemia include polyuria, polydipsia, nocturia, blurred vision, and, infrequently, weight loss. These symptoms are often noted only in retrospect after a blood glucose value has been shown to be elevated. Polyuria occurs when the serum glucose concentration rises significantly above 180 mg/dL (10 mmol/L), exceeding the renal threshold for glucose, which leads to increased urinary glucose excretion. Glycosuria causes osmotic diuresis (ie, polyuria) and hypovolemia, which in turn can lead to polydipsia. Patients who replete their volume losses with concentrated sugar drinks, such as non-diet sodas, exacerbate their hyperglycemia and osmotic diuresis.

Rarely adults with type 2 diabetes can present with a hyperosmolar hyperglycemic state, characterized by marked hyperglycemia without ketoacidosis, severe dehydration, and obtundation. Diabetic ketoacidosis (DKA) as the presenting symptom of type 2 diabetes is also uncommon in adults but may occur under certain circumstances (usually severe infection or other illness) and in non-Caucasian ethnic groups. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis" and "Syndromes of ketosis-prone diabetes mellitus".)

Type 1 diabetes is characterized by autoimmune destruction of the pancreatic beta cells, leading to absolute insulin deficiency. Type 1 diabetes accounts for approximately 5 to 10 percent of diabetes in adults. DKA may

be the initial presentation in approximately 25 percent of adults with newly diagnosed type 1 diabetes. Compared with children, the loss of insulin secretory capacity usually is less rapid in adults with type 1 diabetes [4]. Thus, adults with type 1 diabetes typically have a longer estimated period prior to diagnosis and are likely to have a longer period with symptoms of hyperglycemia (polyuria, polydipsia, fatigue) than children [5]. In 2 to 12 percent of adults, the clinical presentation is similar to that of type 2 diabetes (not initially insulin dependent), with autoimmune mediated insulin deficiency developing later in the course of disease [4]. This is sometimes called latent autoimmune diabetes of adults (LADA). (See "Classification of diabetes mellitus and genetic diabetic syndromes", section on 'Latent autoimmune diabetes in adults (LADA)'.)

## DIAGNOSTIC CRITERIA

**Symptoms of hyperglycemia** — The diagnosis of diabetes mellitus is easily established when a patient presents with classic symptoms of hyperglycemia (thirst, polyuria, weight loss, blurry vision) and has a random blood glucose value of 200 mg/dL (11.1 mmol/L) or higher.

**Asymptomatic** — The diagnosis of diabetes in an asymptomatic individual can be established with any of the following criteria (table 1):

- Fasting plasma glucose (FPG) values ≥126 mg/dL (7.0 mmol/L)
- Two-hour plasma glucose values of ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT)
- A1C values ≥6.5 percent (48 mmol/mol)

In the absence of unequivocal symptomatic hyperglycemia, the diagnosis of diabetes must be confirmed on a subsequent day by repeat measurement, repeating the same test for confirmation. However, if two different tests (eg, FPG and A1C) are available and are concordant for the diagnosis of diabetes, additional testing is not needed. If two different tests are discordant, the test that is diagnostic of diabetes should be repeated to confirm the diagnosis [6].

The importance of confirming the diagnosis by repeat measurement on a subsequent day, especially when the diagnosis is based upon plasma glucose measurements, is illustrated by a report from the National Health and Nutrition Examination Survey (NHANES) III Second Examination [7]. The prevalence of diabetes based upon either FPG or two-hour, post-OGTT plasma glucose concentration significantly decreased when the diagnosis was contingent upon having two abnormal measurements rather than a single abnormal measurement.

If measurement of A1C test is either unavailable or uninterpretable (for example, owing to rapid red cell turnover in a patient with anemia), the previous diagnostic methods and criteria, using glucose testing (FPG, two-hour OGTT), should be used. The A1C assay and potential sources of error are reviewed separately. (See "Estimation of blood glucose control in diabetes mellitus", section on 'Glycated hemoglobin'.)

The diagnostic criteria have been developed based upon the observed association between glucose levels and the risk for developing retinopathy. FPG values ≥126 mg/dL (7.0 mmol/L); two-hour, post-OGTT values of ≥200 mg/dL (11.1 mmol/L); and A1C values ≥6.5 percent (48 mmol/mol) are associated with an increased prevalence of retinopathy [3]. Not surprisingly, since the different measures of glycemia (FPG, two-hour plasma glucose, and A1C) represent different physiologic phenomena, each of the measures will identify different proportions of the population with diabetes. For example, the shift from using the FPG to using A1C to diagnose diabetes may decrease the proportion of patients identified as having diabetes [6,8-10]. As an example, in a study of 6890 adults without a history of diabetes participating in the NHANES (1999 to 2006), the prevalence of diabetes using A1C versus FPG criteria was 2.3 versus 3.6 percent, respectively [8]. Overall, the A1C and FPG criteria resulted in the same classification for 98 percent of the population studied. Similarly, the OGTT identifies different groups than an FPG level.

**WHO criteria** — The 2006 World Health Organization (WHO) criteria define diabetes as an FPG ≥126 mg/dL (7.0 mmol/L) or a two-hour, post-OGTT value ≥200 mg/dL (11.1 mmol/L). In 2011, the WHO concluded that an A1C value of ≥6.5 percent (48 mmol/mol) can be used as a diagnostic test for diabetes [11]. A value of <6.5 percent does not exclude diabetes diagnosed using plasma glucose levels.

Impaired glucose tolerance (IGT) is defined as a FPG <126 (7.0 mmol/L), and a two-hour, post-OGTT glucose ≥140 mg/dL (7.8 mmol/L) but <200 mg/dL (11.05 mmol/L) [12]. Impaired fasting glucose (IFG) is defined as a FPG of 110 to 125 mg/dL (6.1 to 6.9 mmol/L).

**ADA criteria** — In 2003, the American Diabetes Association (ADA) recommended the use of FPG levels (no caloric intake for at least eight hours) or 75 g OGTT for diagnosing diabetes [2]. In 2009, an International Expert Committee recommended using an A1C value of ≥6.5 percent (≥48 mmol/mol) to diagnose diabetes [13], and the ADA, EASD (European Association for the Study of Diabetes), and WHO affirmed the decision (table 1) [3,11]. (See 'Glycated hemoglobin for diagnosis' below.)

The following definitions are from ADA reports (table 1 and table 2) [2,3,6,14,15]:

- Normal – FPG <100 mg/dL (5.6 mmol/L). Two-hour glucose during OGTT <140 mg/dL (7.8 mmol/L).
- Categories of increased risk for diabetes:
  - IFG – FPG between 100 and 125 mg/dL (5.6 to 6.9 mmol/L).
  - IGT – Two-hour plasma glucose value during a 75 g OGTT between 140 and 199 mg/dL (7.8 to 11.0 mmol/L).
  - A1C – Persons with 5.7 to 6.4 percent (39 to 46 mmol/mol), (6.0 to 6.4 percent [42 to 46 mmol/mol] in the International Expert Committee report [13]) are at highest risk, although there is a continuum of increasing risk across the entire spectrum of A1C levels less than 6.5 percent (48 mmol/mol).
- Diabetes mellitus – FPG at or above 126 mg/dL (7.0 mmol/L), A1C ≥6.5 percent (48 mmol/mol), a two-hour value in an OGTT at or above 200 mg/dL (11.1 mmol/L), or a random (or "casual") plasma glucose concentration ≥200 mg/dL (11.1 mmol/L) in the presence of symptoms (table 1).

**GLYCATED HEMOGLOBIN FOR DIAGNOSIS** — There has been longstanding interest in the use of A1C values for screening and identification of impaired glucose regulation and diabetes [16-19]. A1C values were not previously recommended to diagnose diabetes, because of variation in A1C assays. However, the National Glycohemoglobin Standardization Program (NGSP) has standardized more than 99 percent of the assays used in the United States to the Diabetes Control and Complications Trial (DCCT) standard. A strict quality control program has improved precision and accuracy of assays in the United States and many international assays. There are also several technical advantages of the A1C assay over plasma glucose testing, increased patient convenience (since there is no special preparation or timing required for the A1C test), and the correlation of A1C levels with mean glucose concentrations and diabetes complications [3,13,20,21]. (See "Estimation of blood glucose control in diabetes mellitus", section on 'Assay'.)

In a systematic review of studies assessing the accuracy of A1C in the detection of type 2 diabetes, A1C and fasting plasma glucose (FPG) were found to be similarly effective in diagnosing diabetes [19]. Using an A1C cut-off of >6.1 percent to diagnose diabetes, sensitivity ranged from 78 to 81 percent and specificity from 79 to 84 percent when compared with diabetes diagnosed with FPG.

A1C values also correlate with the prevalence of retinopathy [22,23]. As an example, in the 2005 to 2006 National Health and Nutrition Examination Survey (NHANES), 1066 individuals ≥40 years had retinal fundus photography and measurements of A1C and FPG concentration [24]. The prevalence of retinopathy increased above an A1C of 5.5 percent and a FPG of 104 mg/dL (5.8 mmol/L). A1C was more accurate than FPG in identifying cases of retinopathy.

**A1C, FPG, AND OGTT AS PREDICTORS OF DIABETES** — Although the lifetime risk of type 2 diabetes is high, our ability to predict (and subsequently prevent) type 2 diabetes in the general population is limited. Nevertheless, in some individuals with clinical risk factors for diabetes, it may be helpful to perform glycemic testing to identify those at highest risk for developing type 2 diabetes as these patients may be candidates for preventive therapy. Our approach to identifying candidates for diabetes prevention is reviewed separately. (See "Prevention of type 2 diabetes mellitus", section on 'Our approach'.)

There is currently no consensus on using one glycemic test in preference to the other to identify individuals with increased risk for diabetes. While the two-hour oral glucose tolerance test (OGTT) is a more sensitive test in most populations, glycated hemoglobin (A1C) and fasting plasma glucose (FPG) are more convenient (table 2). Although most of the high-risk groups have been defined categorically (eg, impaired fasting glucose [IFG] or impaired glucose tolerance [IGT]), the risk for developing type 2 diabetes follows a continuum across the entire spectrum of subdiabetic glycemic values. Higher fasting or two-hour OGTT plasma glucose values or higher A1C values convey higher risk than lower values. (See "Risk factors for type 2 diabetes mellitus", section on 'Abnormal glucose metabolism'.)

A1C criteria for identifying patients with impaired glucose regulation were derived using data from the National Health and Nutrition Examination Survey (NHANES), 2005 to 2006 [3]. Compared with other cut-points, an A1C cut-point of 5.7 percent (39 mmol/mol) had the best sensitivity (39 percent) and specificity (91 percent) for identifying cases of IFG (FPG ≥100 mg/dL [5.6 mmol/L]).

Although the natural history of IFG and IGT is variable, approximately 25 percent of subjects with either will progress to type 2 diabetes over three to five years [14]. Subjects with additional diabetes risk factors, including obesity and family history, are more likely to develop diabetes.

**A1C, FPG, AND OGTT AS PREDICTORS OF CARDIOVASCULAR RISK** — Epidemiologic analyses (observational studies or secondary analyses of trials) suggest a correlation between chronic hyperglycemia and higher rates of cardiovascular disease (CVD). There is consistent evidence that the relationship between blood glucose levels and cardiovascular risk extends into the nondiabetic range [25]. In a meta-analysis of 24 prospective cohort studies with median follow-up of 9.5 years, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or increases in glycated hemoglobin (A1C) in the nondiabetic range (5.7 to 6.4 percent or 6.0 to 6.4 percent) was associated with an increased risk of coronary heart disease (CHD) compared with normoglycemia (relative risk [RR] 1.10 to 1.28) [26]. IFG or IGT (but not increases in A1C) was also associated with an increased risk of stroke (18 studies, RR 1.06 to 1.20) and overall mortality (25 studies, RR 1.13 to 1.32).

Although there is a correlation between measures of glycemia and cardiovascular risk, their addition to conventional cardiovascular risk factors is not associated with a clinically meaningful improvement in prediction of CVD risk. An analysis of individual patient data from 73 prospective studies (294,998 participants) [27] showed that the addition of A1C to prognostic models containing conventional cardiovascular risk factors (age, gender, blood pressure, total and high-density lipoprotein [HDL] cholesterol, smoking) significantly improved the models' ability to predict the development of CVD; however, the incremental improvement was small and of little clinical relevance. The improvement provided by A1C was at least equal to estimated improvements for measurement of fasting, random, or postload glucose levels. These findings suggest that in individuals without known CVD or diabetes, traditional cardiovascular risk factors are much stronger predictors of CVD than measures of glycemia. The co-incidence of and relationship between hyperglycemia and traditional risk factors makes the analysis of their individual contributions particularly challenging.

**CLASSIFICATION OF DIABETES** — Type 2 diabetes accounts for over 90 percent of cases of diabetes in the United States, Canada, and Europe; type 1 diabetes accounts for another 5 to 10 percent, with the remainder due to other causes (table 3) [6]. The etiologic classification of diabetes, including distinguishing type 2 from type 1 diabetes, and monogenic forms of diabetes (formerly referred to as maturity onset diabetes

of the young [MODY]) from type 1 and type 2 diabetes, is reviewed elsewhere. (See "Classification of diabetes mellitus and genetic diabetic syndromes".)

**DIFFERENTIAL DIAGNOSIS** — There are few causes of persistent hyperglycemia in adults other than diabetes mellitus. Transient hyperglycemia may occur during severe illness in adults without known diabetes mellitus. This is sometimes referred to as stress hyperglycemia and is a consequence of many factors, including increased serum concentrations of cortisol, catecholamines, glucagon, growth hormone, which leads to increased gluconeogenesis and glycogenolysis and insulin resistance. Uncontrolled hyperglycemia associated with critical illness has been associated with poor outcomes, potentially because such hyperglycemia is an index of the severity of the underlying illness, but possibly because of pernicious effects of hyperglycemia and hypoinsulinemia. Such patients are typically treated with insulin during hospitalization. (See "Glycemic control and intensive insulin therapy in critical illness".)

Stress hyperglycemia may simply be a marker of abnormal glucose tolerance and increased risk for developing diabetes. However, not all patients develop diabetes [28,29]. In a prospective study of 2124 patients without known diabetes admitted to a hospital with pneumonia, 1418 (67 percent) had varying degrees of stress hyperglycemia (admission plasma glucose 110 to 360 mg/dL [6.1 to 20 mmol/L]) [30]. Over five years, a greater proportion of patients with stress hyperglycemia subsequently developed diabetes (14 versus 6 percent of patients with normal glycemia). The risk of a new diagnosis of diabetes increased with increasing degrees of stress hyperglycemia: 7, 18, and 47 percent for mild (110 to 139 mg/dL [6.1 to 7.7 mmol/L]), moderate (140 to 198 mg/dL [7.8 to 11.0 mmol/L]), and severe (200 to 360 mg/dL [11.1 to 20.0 mmol/L]) hyperglycemia, respectively. In most patients with severe stress hyperglycemia, diabetes mellitus was diagnosed within one year. Thus, patients with stress hyperglycemia require follow-up testing after discharge to identify underlying diabetes.

**SOCIETY GUIDELINE LINKS** — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Diabetes mellitus in adults".)

**INFORMATION FOR PATIENTS** — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5$^{th}$ to 6$^{th}$ grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10$^{th}$ to 12$^{th}$ grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Type 1 diabetes (The Basics)" and "Patient education: Type 2 diabetes (The Basics)" and "Patient education: Hemoglobin A1C tests (The Basics)")
- Beyond the Basics topics (see "Patient education: Diabetes mellitus type 1: Overview (Beyond the Basics)" and "Patient education: Diabetes mellitus type 2: Overview (Beyond the Basics)")

**SUMMARY AND RECOMMENDATIONS**

- Type 2 diabetes is by far the most common type of diabetes in adults (>90 percent) and is characterized by hyperglycemia and variable degrees of insulin deficiency and resistance. The majority of patients with type 2 diabetes are asymptomatic, and hyperglycemia is noted on routine laboratory evaluation, prompting further testing. Classic symptoms of hyperglycemia include polyuria, polydipsia, nocturia, blurred vision, and, infrequently, weight loss. These symptoms are often noted only in retrospect after an elevated blood glucose value has been documented. (See 'Clinical presentation' above.)

- Type 1 diabetes is characterized by autoimmune destruction of the pancreatic beta cells, leading to absolute insulin deficiency. Diabetic ketoacidosis may be the initial presentation in approximately 25 percent of adults with newly diagnosed type 1 diabetes. Compared with children, the loss of insulin secretory capacity usually is less pronounced in adults with type 1 diabetes, and therefore, adults with type 1 diabetes typically have a longer symptomatic period (polyuria, polydipsia, weight loss, fatigue) prior to diagnosis than children. In some adults, the clinical presentation is similar to that of type 2 diabetes (ie, they are not initially insulin dependent), with autoimmune-mediated insulin deficiency developing later in the course of disease. (See 'Clinical presentation' above.)

- The diagnosis of diabetes mellitus is easily established when a patient presents with classic symptoms of hyperglycemia (thirst, polyuria, weight loss, blurry vision) and has a random plasma glucose value of 200 mg/dL (11.1 mmol/L) or higher.

  The diagnosis of diabetes in an asymptomatic individual can be established with the following criteria: fasting plasma glucose (FPG) values ≥126 mg/dL (7.0 mmol/L); two-hour, post-oral glucose tolerance test (OGTT) values of ≥200 mg/dL (11.1 mmol/L); and glycated hemoglobin (A1C) values ≥6.5 percent (48 mmol/mol) (table 1). In the absence of unequivocal symptomatic hyperglycemia, the diagnosis of diabetes must be confirmed on a subsequent day by repeat measurement, repeating the same test for confirmation. (See 'Diagnostic criteria' above.)

- According to American Diabetes Association (ADA) criteria, the diagnostic thresholds for categories of increased risk for diabetes are as follows (table 2) (see 'ADA criteria' above and 'A1C, FPG, and OGTT as predictors of diabetes' above):

  - Impaired fasting glucose (IFG) – FPG ≥100 to 125 mg/dL (5.6 to 6.9 mmol/L)

  - Impaired glucose tolerance (IGT) – Two-hour plasma glucose value during a 75 g OGTT≥140 to 199 mg/dL (7.8 to 11.0 mmol/L)

  - A1C – 5.7 to 6.4 percent (39 to 46 mmol/mol) (the International Expert Committee recommended 6.0 to 6.4 percent [42 to 46 mmol/mol])

- The etiologic classification of diabetes, including distinguishing type 2 from type 1 diabetes and monogenic diabetes (formerly referred to as maturity onset diabetes of the young [MODY]) from type 1 and type 2 diabetes, is reviewed elsewhere. (See "Classification of diabetes mellitus and genetic diabetic syndromes".)

- The evaluation and management of patients with diabetes is reviewed separately. (See "Overview of medical care in adults with diabetes mellitus" and "Initial management of blood glucose in adults with type 2 diabetes mellitus" and "Management of blood glucose in adults with type 1 diabetes mellitus".)



## REFERENCES

1. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20:1183.
2. Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003; 26:3160.
3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33 Suppl 1:S62.
4. Merger SR, Leslie RD, Boehm BO. The broad clinical phenotype of Type 1 diabetes at presentation. Diabet Med 2013; 30:170.

5. Karjalainen J, Salmela P, Ilonen J, et al. A comparison of childhood and adult type I diabetes mellitus. N Engl J Med 1989; 320:881.
6. American Diabetes Association. 2. Classification and Diagnosis of Diabetes. Diabetes Care 2017; 40:S11.
7. Selvin E, Crainiceanu CM, Brancati FL, Coresh J. Short-term variability in measures of glycemia and implications for the classification of diabetes. Arch Intern Med 2007; 167:1545.
8. Carson AP, Reynolds K, Fonseca VA, Muntner P. Comparison of A1C and fasting glucose criteria to diagnose diabetes among U.S. adults. Diabetes Care 2010; 33:95.
9. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. Diabetes Care 2010; 33:562.
10. Malkani S, Mordes JP. Implications of using hemoglobin A1C for diagnosing diabetes mellitus. Am J Med 2011; 124:395.
11. http://www.who.int/diabetes/publications/report-hba1c_2011.pdf (Accessed on June 07, 2011).
12. http://whqlibdoc.who.int/publications/2006/9241594934_eng.pdf (Accessed on December 22, 2011).
13. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009; 32:1327.
14. Nathan DM, Davidson MB, DeFronzo RA, et al. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care 2007; 30:753.
15. Chiang JL, Kirkman MS, Laffel LM, et al. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. Diabetes Care 2014; 37:2034.
16. Peters AL, Davidson MB, Schriger DL, Hasselblad V. A clinical approach for the diagnosis of diabetes mellitus: an analysis using glycosylated hemoglobin levels. Meta-analysis Research Group on the Diagnosis of Diabetes Using Glycated Hemoglobin Levels. JAMA 1996; 276:1246.
17. Rohlfing CL, Little RR, Wiedmeyer HM, et al. Use of GHb (HbA1c) in screening for undiagnosed diabetes in the U.S. population. Diabetes Care 2000; 23:187.
18. Buell C, Kermah D, Davidson MB. Utility of A1C for diabetes screening in the 1999 2004 NHANES population. Diabetes Care 2007; 30:2233.
19. Bennett CM, Guo M, Dharmage SC. HbA(1c) as a screening tool for detection of Type 2 diabetes: a systematic review. Diabet Med 2007; 24:333.
20. Nathan DM, Kuenen J, Borg R, et al. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008; 31:1473.
21. Sabanayagam C, Liew G, Tai ES, et al. Relationship between glycated haemoglobin and microvascular complications: is there a natural cut-off point for the diagnosis of diabetes? Diabetologia 2009; 52:1279.
22. Miyazaki M, Kubo M, Kiyohara Y, et al. Comparison of diagnostic methods for diabetes mellitus based on prevalence of retinopathy in a Japanese population: the Hisayama Study. Diabetologia 2004; 47:1411.
23. Massin P, Lange C, Tichet J, et al. Hemoglobin A1c and fasting plasma glucose levels as predictors of retinopathy at 10 years: the French DESIR study. Arch Ophthalmol 2011; 129:188.
24. Cheng YJ, Gregg EW, Geiss LS, et al. Association of A1C and fasting plasma glucose levels with diabetic retinopathy prevalence in the U.S. population: Implications for diabetes diagnostic thresholds. Diabetes Care 2009; 32:2027.
25. Ashraf H, Boroumand MA, Amirzadegan A, et al. Hemoglobin A1C in non-diabetic patients: an independent predictor of coronary artery disease and its severity. Diabetes Res Clin Pract 2013; 102:225.

26. Huang Y, Cai X, Mai W, et al. Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis. BMJ 2016; 355:i5953.
27. Emerging Risk Factors Collaboration, Di Angelantonio E, Gao P, et al. Glycated hemoglobin measurement and prediction of cardiovascular disease. JAMA 2014; 311:1225.
28. Ishihara M, Inoue I, Kawagoe T, et al. Is admission hyperglycaemia in non-diabetic patients with acute myocardial infarction a surrogate for previously undiagnosed abnormal glucose tolerance? Eur Heart J 2006; 27:2413.
29. McAllister DA, Hughes KA, Lone N, et al. Stress hyperglycaemia in hospitalised patients and their 3-year risk of diabetes: a Scottish retrospective cohort study. PLoS Med 2014; 11:e1001708.
30. MacIntyre EJ, Majumdar SR, Gamble JM, et al. Stress hyperglycemia and newly diagnosed diabetes in 2124 patients hospitalized with pneumonia. Am J Med 2012; 125:1036.e17.

Topic 1812 Version 25.0

## GRAPHICS

### ADA criteria for the diagnosis of diabetes

| |
|---|
| 1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* |
| **OR** |
| 2. FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least eight hours.* |
| **OR** |
| 3. Two-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75-gram anhydrous glucose dissolved in water.* |
| **OR** |
| 4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L). |

ADA: American Diabetes Association; A1C: glycated hemoglobin; NGSP: National Glycohemoglobin Standardization Program; DCCT: Diabetes Control and Complications Trial; FPG: fasting plasma glucose; OGTT: oral glucose tolerance test.
* In the absence of unequivocal hyperglycemia, criteria 1 to 3 should be confirmed by repeat testing.



Graphic 61853 Version 13.0

## Categories of increased risk for diabetes (prediabetes)*

| |
|---|
| FPG 100 to 125 mg/dL (5.6 to 6.9 mmol/L) (IFG) |
| Two-hour post-load glucose on the 75 g OGTT 140 to 199 mg/dL (7.8 to 11.0 mmol/L) (IGT) |
| A1C 5.7 to 6.4% (39 to 46 mmol/mol) |

FPG: fasting plasma glucose; IFG: impaired fasting glucose; OGTT: oral glucose tolerance test; IGT: impaired glucose tolerance; A1C: glycated hemoglobin.
* For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range.



Graphic 82479 Version 13.0

## Etiologic classification of diabetes mellitus

| |
|---|
| **Type 1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)** |
| A. Immune-mediated |
| B. Idiopathic |
| **Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)** |
| **Other specific types** |
| A. Genetic defects of beta cell function |
| 1. Chromosome 12, HNF-1-alpha (MODY3) |
| 2. Chromosome 7, glucokinase (MODY2) |
| 3. Chromosome 20, HNF-4-alpha (MODY1) |
| 4. Chromosome 13, insulin promoter factor-1 (IPF-1; MODY4) |
| 5. Chromosome 17, HNF-1-beta (MODY5) |
| 6. Chromosome 2, NeuroD1 (MODY6) |
| 7. Mitochondrial DNA |
| 8. Others |
| B. Genetic defects in insulin action |
| 1. Type A insulin resistance |
| 2. Leprechaunism |
| 3. Rabson-Mendenhall syndrome |
| 4. Lipoatrophic diabetes |
| 5. Others |
| C. Diseases of the exocrine pancreas |
| 1. Pancreatitis |
| 2. Trauma/pancreatectomy |
| 3. Neoplasia |
| 4. Cystic fibrosis |
| 5. Hemochromatosis |
| 6. Fibrocalculous pancreatopathy |
| 7. Others |
| D. Endocrinopathies |
| 1. Acromegaly |
| 2. Cushing's syndrome |
| 3. Glucagonoma |
| 4. Pheochromocytoma |
| 5. Hyperthyroidism |
| 6. Somatostatinoma |
| 7. Aldosteronoma |
| 8. Others |
| E. Drug or chemical induced |
| 1. Vacor |
| 2. Pentamidine |
| 3. Nicotinic acid |
| 4. Glucocorticoids |
| 5. Thyroid hormone |
| 6. Diazoxide |
| 7. Beta-adrenergic agonists |
| 8. Thiazides |
| 9. Dilantin |
| 10. Alpha interferon |
| 11. Others |

| |
|---|
| F. Infections |
| 1. Congenital rubella |
| 2. Cytomegalovirus |
| 3. Others |
| G. Uncommon forms of immune-mediated diabetes |
| 1. "Stiff man" syndrome |
| 2. Anti-insulin receptor antibodies |
| 3. Others |
| H. Other genetic syndromes sometimes associated with diabetes |
| 1. Down syndrome |
| 2. Klinefelter syndrome |
| 3. Turner syndrome |
| 4. Wolfram syndrome |
| 5. Friederich's ataxia |
| 6. Huntington's chorea |
| 7. Laurence-Moon-Biedl syndrome |
| 8. Myotonic dystrophy |
| 9. Porphyria |
| 10. Prader-Willi syndrome |
| 11. Others |
| **Gestational diabetes mellitus** |
| Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient. |



Graphic 59403 Version 4.0

## Contributor Disclosures

**David K McCulloch, MD** Nothing to disclose **David M Nathan, MD** Research Support: Abbott [Diabetes (point-of-care A1C assay)]. **Joseph I Wolfsdorf, MB, BCh** Nothing to disclose **Jean E Mulder, MD** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy