in the clinic

Type 2 Diabetes

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CME Objective: To provide information about the screening and prevention, diagnosis, and treatment of type 2 diabetes.

The information contained herein should never be used as a substitute for clinical judgment.

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Diabetes is one of the most common illnesses encountered by internists. An estimated 23.6 million persons have diabetes in the United States, and only 17.9 million of these cases have been diagnosed (1). The incidence of diabetes is increasing because of the aging and changing ethnic mix of the population and because of worsening obesity. On the basis of current trends, the prevalence of diabetes is expected to nearly double by 2030 (2). Although diabetes care is improving by many measures, complications are still common, and diabetes remains the leading cause of visual loss, amputation, and end-stage renal disease in the United States (1). In addition, diabetes is a substantial risk factor for atherosclerotic disease, which is the leading cause of morbidity, mortality, and expenditures in persons with diabetes.

Screening and Prevention

Should we screen for type 2 diabetes?

Current data suggest that about 1 in 4 persons with diabetes are unaware of their disease (1). Diabetes has a fairly long asymptomatic phase, during which many patients will develop early disease complications. Some groups have therefore suggested screening for diabetes every 3 years in persons older than 45 years and in persons younger than 45 years who have diabetes risk factors (Box) (3).

There is no consensus on who should be screened for diabetes or how often. There is no direct evidence that screening improves health outcomes. Limited indirect evidence suggests that screening is unlikely to substantially improve outcomes or to be cost-effective when applied broadly (4, 5), and evidence-based guidelines focus on persons with particular risk for diabetes complications, in whom the diagnosis may alter management strategies (6).

Which patients are likely to benefit from diabetes screening?

Diabetes screening is most likely to improve outcomes in patients with risk factors for cardiovascular disease, particularly hypertension, because blood pressure treatment goals differ according to the presence of diabetes (7). The same may be true of persons with dyslipidemia, although studies on the benefits of screening in these patients are lacking.

Diabetes is more likely to be detected in those with risk factors for the disease (Box). However, beyond the increased prevalence of disease, little evidence supports improved clinical outcomes with screening in persons without hypertension, and thus recommendations are based largely on expert opinion.

Can type 2 diabetes be prevented?

Several high-quality randomized trials have shown that lifestyle changes in diet and exercise lead to substantial reductions in the incidence of type 2 diabetes in patients with "prediabetes." Prediabetes is defined as an impaired fasting glucose or impaired glucose tolerance that does not meet the diagnostic criteria for diabetes (Table 1). These dietary and exercise programs achieved modest weight loss (generally 5% to 7% of body weight) yet are markedly effective.

Risk Factors for Type 2 Diabetes

- Age >45 y
- First-degree relative with type 2 diabetes
- African-American, Hispanic, Asian, Pacific Islander, or Native-American ethnicity
- History of gestational diabetes or delivery of infant weighing ≥9 lbs
- The polycystic ovary syndrome
- Overweight, especially abdominal obesity
- Cardiovascular disease, hypertension, dyslipidemia, or other features of the metabolic syndrome

1. American Diabetes Association. Diabetes Statistics. 2007. Accessed at www.diabetes.org/diabetes-basics/diabetes-statistics/ on 20 January 2010.
2. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27:1047-53. [PMID: 15111519]
3. American Diabetes Association. Standards of medical care in diabetes---2010. Diabetes Care. 2010;33 Suppl 1:S11-61. [PMID: 20042772]
4. CDC Diabetes Cost-Effectiveness Study Group, Centers for Disease Control and Prevention. The cost-effectiveness of screening for type 2 diabetes. JAMA. 1998;280:1757-63. [PMID: 9842951]
5. Hofer TP, Vijan S, Hayward RA. Estimating the microvascular benefits of screening for type 2 diabetes. Int J Technol Assess Health Care. 2000; 16: 822-33.[PMID: 11028137]
6. U.S. Preventive Services Task Force. Screening for type 2 diabetes mellitus in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008;148:846-54. [PMID: 18519930]
7. Hoerger TJ, Harris R, Hicks KA, et al. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. Ann Intern Med. 2004;140:689-99. [PMID: 15126252]

Table 1. Diagnostic Criteria for Type 2 Diabetes*

Diagnosis	*Hemoglobin A_{1c} Level, %*	*Fasting Plasma Glucose†*	
		mmol/L	mg/dL
Prediabetes	6.0 to 6.4	5.55 to 6.94	100 to 125
Diabetes	≥6.5	≥7.0	≥126

** A random glucose of 11.1 mmol/L or greater (≥200 mg/dL), with classic diabetes symptoms, may be indicative of diabetes. However, the test should be confirmed by checking fasting glucose or hemoglobin A1c. If an oral glucose tolerance test is used, a 2-hour postglucose load level of 11.1 mmol/L or greater (≥200 mg/dL) is considered diagnostic of diabetes, whereas levels of 7.8 to 11.0 mmol/L (140 to 199 mg/dL) are diagnostic of impaired glucose tolerance.*

† Fasting is defined as no caloric intake for at least 8 h.

In a randomized, unblind, controlled trial of 522 overweight Finnish patients with impaired glucose tolerance (mean age, 55 years), an intervention aimed at a 5% reduction in weight decreased the incidence of newly diagnosed type 2 diabetes over 3 years from 23% to 11%. The intervention involved personal counseling sessions to encourage a reduction in total and saturated fat intake to less than 30% and 10% of energy consumed, respectively; an increase in fiber intake; and moderate exercise for at least 30 min/d (8).

The Diabetes Prevention Project, a randomized, controlled trial of 3234 U.S. patients with prediabetes (mean age, 51 years; mean body mass index, 34 kg/m^2), showed that a lifestyle modification program aimed at a 7% weight loss reduced the cumulative incidence of diabetes over 3 years from 29% to 14% compared with placebo (9). The 10-year follow-up showed persistence of the initial beneficial effect of the lifestyle changes. However, the incidence rates of diabetes in the lifestyle and placebo group were similar after the study, implying that the intervention must be maintained to see additional benefit (10).

In a randomized, controlled trial of 577 Chinese adults with impaired glucose tolerance randomly assigned to diet, exercise, both, or neither, the incidence of diabetes over 6 years was 68% among persons in the neither group, 44% in the diet group, 41% in the exercise group, and 46% in the both group. All 3 interventions showed statistically significant reductions in diabetes progression (11).

Some medications can prevent diabetes onset in patients with prediabetes.

In the medication group of the Diabetes Prevention Project, metformin (850 mg twice daily) reduced the cumulative incidence of diabetes from 29% to 22% over 3 years. This reduction was significant but smaller than that observed with lifestyle intervention (9). The 10-year follow-up again showed persistence of the initial beneficial effect, although the incidence rates in the metformin and placebo group were similar after the study period (10).

In the randomized, double-blind, international Study to Prevent Non–Insulin-Dependent Diabetes Mellitus, which involved 1429 patients with impaired glucose tolerance, acarbose (100 mg 3 times daily) reduced the incidence of diabetes from 42% to 32% compared with placebo. The relative risk reduction over 3 years was 25% (12).

The DREAM (Diabetes Reduction Assessment With Ramiripril and Rosiglitazone Medication) trial randomly assigned 5269 adults without previous cardiovascular disease but with impaired fasting glucose, impaired glucose tolerance, or both to rosiglitazone, 8 mg/d, or placebo and to rosiglitazone, up to 15 mg/d, or placebo. After a median 3 years, 11.6% of patients who received rosiglitazone developed diabetes or died compared with 26.0% of patients who received placebo (hazard ratio, 0.40 [95% CI, 0.35 to 0.46]). Cardiovascular event rates were statistically similar in both groups (13).

The implications of disease prevention interventions on the effectiveness of diabetes screening programs have not been fully elucidated, but screening is generally needed to identify the high-risk prediabetes population. The best option is probably to consider screening persons who are at reasonably high-risk for the disease (Box) and to implement preventative measures in those who have prediabetes.

8. Tuomilehto J, Lindström J, Eriksson JG, et al; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344:1343-50. [PMID: 11333990]
9. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393-403. [PMID: 11832527]
10. Knowler WC, Fowler SE, Hamman RF, et al; Diabetes Prevention Program Research Group. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009;374:1677-86. [PMID: 19878986]
11. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care. 1997;20:537-44. [PMID: 9096977]
12. Chiasson JL, Josse RG, Gomis R, et al; STOP-NIDDM Trail Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet. 2002;359:2072-7. [PMID: 12086760]
13. Gerstein HC, Yusuf S, Bosch J, et al; DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006;368:1096-105. [PMID: 16997664]

Screening and Prevention... Little direct evidence shows clinical benefit from broad-based screening programs for type 2 diabetes. The most evidence-based approach is to screen persons with other cardiovascular risk factors (hypertension and perhaps dyslipidemia), because diabetes status alters the management goals in these patients. Diabetes can be prevented in patients with prediabetes with exercise and dietary programs aimed at modest weight loss. Medication may be indicated in those who cannot achieve lifestyle goals.

CLINICAL BOTTOM LINE

Diagnosis and Evaluation

What are the diagnostic criteria for type 2 diabetes in nonpregnant adults?

Clinicians should confirm the diagnosis of diabetes in persons with classic symptoms (polyuria, polydipsia, polyphagia, and weight loss) or evidence of diabetes complications (retinopathy, nephropathy, neuropathy, impotence, acanthosis nigricans, or frequent infections). Diabetes may be diagnosed by a fasting plasma glucose level of 7.0 mmol/L or greater (≥126 mg/dL), or when there are classic symptoms by a nonfasting glucose level greater than 11.1 mmol/L (>200 mg/dL); each should be confirmed on a different day. Impaired fasting glucose, or prediabetes, can be diagnosed in persons with fasting glucose levels of 5.6 to 6.9 mmol/L (100 to 125 mg/dL) (Table 1).

A hemoglobin A_{1c} level of 6.5% or greater is now recommended for the diagnosis of type 2 diabetes (3, 14), because of its ease of use (because no fasting is required) and reliability relative to fasting glucose measurement. The elevated hemoglobin A_{1c} value should be confirmed by repeat testing.

A hemoglobin A_{1c} level of 6.0% or greater may identify patients most likely to benefit from interventions aimed at preventing type 2 diabetes (for example, patients similar to those identified as having prediabetes by fasting glucose or glucose tolerance tests).

What should the initial evaluation of patients with newly diagnosed type 2 diabetes include?

Providers should conduct a detailed history and physical examination, including assessment of blood pressure and an inspection for possible diabetes complications, such as neurologic and foot examinations. Laboratory tests should assess levels of glucose control (hemoglobin A_{1c}), lipid profile, and nephropathy (urine microalbumin/creatinine ratio). At diagnosis, ophthalmologic assessment should be conducted to evaluate for retinopathy.

Diagnosis and Evaluation... Type 2 diabetes is common and should be considered when patients present with suggestive symptoms (for example, polyuria or polydipsia), signs (for example, acanthosis nigricans), or complications of disease (for example, retinopathy). The diagnosis of diabetes can be confirmed by a hemoglobin A_{1c} value of 6.5% or higher, or by fasting plasma glucose levels greater then 7.0 mmol/L (126 mg/dL) on 2 occasions at least 1 day apart. However, random plasma glucose levels and oral glucose tolerance testing can also be used to diagnose type 2 diabetes. Newly diagnosed patients should be examined for hypertension, as well as neurologic, ophthalmologic, and podiatric complications. The initial laboratory evaluation should include an assessment of glucose control, a lipid profile, and a urine microalbumin/creatinine ratio.

CLINICAL BOTTOM LINE

14. American Association of Clinical Endocrinologists/American College of Endocrinology. Statement on the Use of A_{1c} for the Diagnosis of Diabetes. Accessed at www.aace.com/pub/pdf/guidelines/AACEpositionA1cfeb2010.pdf on 4 February 2010.

What are the components of nondrug therapy for patients with type 2 diabetes?

Lifestyle changes, primarily diet and exercise, are the cornerstones for the management of type 2 diabetes and should be considered first-line therapy unless severe hyperglycemia requires immediate medication treatment. No one diet or exercise regimen applies to all patients with diabetes, and an individualized assessment should be used to develop a feasible strategy.

In a study of patients with newly diagnosed type 2 diabetes, diet initially improved hemoglobin A_{1c} levels by 2.25 percentage points. However, control deteriorated over time, and most patients eventually required drug therapy (15).

A meta-analysis of 14 randomized trials comparing exercise with no exercise in a total of 377 patients with type 2 diabetes showed that exercise significantly improved glycemic control, reduced visceral adipose tissue, and reduced plasma triglyceride levels even without weight loss (16).

What is the role of home glucose monitoring for patients with type 2 diabetes?

Home glucose monitoring lets patients and providers assess glucose control longitudinally. Home monitoring is part of the standard of care for patients using insulin therapy to allow sensible dose adjustments and to help determine whether symptoms are due to hyperglycemia or hypoglycemia. The optimum frequency of home monitoring has not been formally evaluated. The role of home glucose monitoring to guide oral therapy is less clear; a formal evidence review found no consistent benefits but was limited by poor-quality data with mixed intervention approaches and comparators (17).

Patients are generally advised to monitor fasting and premeal glucose levels. However, postprandial measurement may be helpful in patients with elevated hemoglobin A_{1c} levels despite normal fasting levels. Some observational data suggest that postmeal glucose excursions may be tied to cardiovascular risk, leading some experts to recommend routine postprandial monitoring. However, no trials have shown that treating these excursions reduces cardiovascular risk.

What target for glycemic control should physicians aim for in patients with type 2 diabetes?

The optimum target for glycemic control is an area of mounting controversy. Most organizations and quality measurement groups advocate a target hemoglobin A_{1c} level of 7% or less for most patients, based on the results of the UKPDS (United Kingdom Prospective Diabetes

General Advice about Diet and Exercise for Patients with Type 2 Diabetes

Diet

- Stress the importance of moderation.
- Base calorie recommendations on the goal of achieving near-ideal body weight. A reasonable starting formula for weight maintenance is as follows: 10 calories per pound of current body weight, plus 20% for sedentary patients; 33% for those who engage in light physical activity; 50% for those who are moderately active; and 75% for heavily active patients.
- Weight loss will require caloric restriction below these levels. Reducing caloric intake by 15%–20% from maintenance levels is a reasonable goal to produce gradual weight loss.
- Advise patient to avoid saturated fats.
- Encourage regular meal schedule, particularly if patient is receiving insulin.
- Inform patient that frequent, small meals might aid in weight loss and control of blood glucose levels.
- Advise patient to choose complex carbohydrates (e.g., whole grains, cereals) over simple sugars (e.g., sweets).

Exercise

- Individualize exercise regimen, consider current level of activity, living situation, and comorbid conditions.
- Consider beginning with 15 min of low-impact aerobic exercise 3 times per week for patients who can exercise and gradually increasing the frequency and duration to 30–45 min of moderate aerobic activity 3–5 d per wk.
- Caution patients receiving drug therapy about hypoglycemia during and after exercise.

15. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837-53. [PMID: 9742976]
16. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2006;3:CD002968. [PMID: 16855995]

Study) (15). This randomized study of 3867 patients with newly diagnosed type 2 diabetes found that as compared with dietary measures alone, a more-intensive therapeutic approach aimed at achieving a lower hemoglobin A_{1c} level resulted in fewer microvascular complications over 10 years (particularly the need for retinal photocoagulation) but no clear benefit in cardiovascular outcomes. However, because the study enrolled patients with newly diagnosed mild disease, the results might not be generalizable to other patients with diabetes. In addition, by the end of the study, the mean hemoglobin A_{1c} level was 8% in the intensive-treatment group, making it difficult to firmly establish the hemoglobin A_{1c} target needed for a reduction in diabetes complications.

In a 20-year follow-up of a subset of patients after completion of the UKPDS study, the patients initially randomly assigned to intensive control had lower rates of myocardial infarction (16.8 vs. 19.6 per 1000 patient-years) and death (26.8 vs. 30.3 per 1000 patient-years), although differences in glycemic control were not maintained between groups (18).

This implies that early control may have a "memory" effect and may provide distant benefits, but also that significant benefits take many years to occur.

Some experts advocate more aggressive targets for glycemic control or treating to near-normal glucose levels when possible. Three trials recently evaluated this approach.

A study of 10 251 patients with type 2 diabetes (mean age, 62.2 years) randomly assigned participants to an intensive-treatment group with a target hemoglobin A_{1c} level less than 6.0% or to a more conventional targeted hemoglobin A_{1c} level of 7.0% to 7.9%. The achieved levels of control were 6.4% and 7.5%, respectively. After a mean follow-up of 3.5 years, the rate of cardiovascular end points (nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death) did not differ, but the trial was stopped due to a 22% increase in total mortality in the intensive-control group (5.0% vs. 4.0%; P = 0.04). Hypoglycemia and weight gain were more frequent in the intensive-control group (19).

A randomized study of 1791 veterans with previously treated diabetes (mean age, 60.4 years), compared an intensive-treatment approach aiming to lower hemoglobin A_{1c} level by 1.5% with standard therapy over a median of 5.6 years. Despite a median hemoglobin A_{1c} level of 6.9% in the intensive-treatment group compared with 8.4% in the control group, the rates of cardiovascular or total mortality, stroke, heart failure, need for vascular surgery, amputation, or microvascular events did not differ (20).

In a randomized study of 11 140 patients, an intensive-treatment group targeted a hemoglobin A_{1c} level of 6.5% or more and achieved a mean hemoglobin A_{1c} level of 6.5% over 5 years compared with 7.3% in a standard-treatment control group. The rate of nephropathy was reduced (4.1% vs. 5.2%; P = 0.006), but rates of cardiovascular events or mortality did not differ (21).

Interpretation and reconciliation of the results of the 4 major glucose-lowering trials is difficult. Moderate glucose control early in the disease course (for example, a mean hemoglobin A_{1c} level of 7% over the first 10 years, but with a worsening trend over that period) seems to eventually help to decrease cardiovascular events and mortality. Whether more aggressive control, at least in the short term, provides benefit or increases mortality is debated. It is unclear whether any specific subgroups of patients are harmed or receive benefit from more aggressive control. Current recommendations are to aim to control hemoglobin A_{1c} to less than 7% for patients with diabetes, particularly early in the course of disease. Glycemic targets, however, must be individualized by considering a patient's risk for hypoglycemia, comorbid conditions that limit life expectancy, and factors that may limit the safety of attempting aggressive glucose control.

When should the treatment of type 2 diabetes include drugs?

Once a hemoglobin A_{1c} goal is established, pharmacologic management should be instituted if diet

17. Weischen LM, Bloemendal E, Nijpels G, et al. Self-monitoring of blood glucose in patients with type 2 diabetes who are not using insulin. Cochrane Database Syst Rev. 2005; 18: CD0050060. [PMID 15846742]
18. Holman RR, Paul SK, Bethel MA, et al. Long-term follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359:1577-89. [PMID: 18784090].
19. Gerstein HC, Miller ME, Byington RP, et al. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358:2545-59. [PMID: 18539917]

and exercise do not achieve the goal. In general, initiation of pharmacologic therapy should not be delayed while awaiting the results of diet and exercise except in motivated and adherent patients. If diet and exercise have not accomplished the targeted reduction in glycemic values within approximately 6 weeks, pharmacologic therapy should be initiated (3, 14, 22). In addition, those with severe hyperglycemia or symptoms may require pharmacologic intervention immediately, although severe hyperglycemia is not clearly defined. In addition to lifestyle changes in diet and exercise, most patients should be treated with metformin.

How should physicians select therapies for a patient from among the many oral drugs available for type 2 diabetes?

Table 2 provides an overview of the classes of oral agents available to treat type 2 diabetes. Data are insufficient regarding the relative efficacy of many of the available oral therapies for type 2 diabetes at improving clinical end points.

In the UKPDS, in patients who were more than 120% of ideal body weight, metformin was superior to sulfonylureas and insulin in reducing mortality, despite identical levels of glycemic control (23). Metformin also had lower rates of hypoglycemia and weight gain than insulin or sulfonylureas. Metformin should not be used in patients with severe renal insufficiency (glomerular filtration rate < 30 mL/min per 1.73 m^2), symptomatic heart failure, or severe liver disease, and must be stopped before radiologic procedures requiring intravenous contrast dye because of the risk for lactic acidosis.

In patients with contraindications or intolerance to metformin, the choice of oral agents should be based on patient preferences regarding potential side effects, efficacy, and cost. Although most drugs achieve similar

Table 2. Oral Medications for Type 2 Diabetes

Drug	*Initial Dose*	*Maximum Dose*	*Usual Dose*
Biguanide			
Metformin	500 mg bid or 850 mg/d	2550 mg/d	500–1000 mg bid
Metformin XR	500 mg/d	2000 mg/d	1500–2000 mg/d
Sulfonylurea			
Glimepiride	1–2 mg/d	8 mg/d	4 mg/d
Glipizide	2.5–5 mg/d	40 mg/d	10–20 mg/d (or bid)
Glipizide SR	5 mg/d	20 mg/d	5–20 mg/d (or bid)
Glyburide	2.5–5 mg/d	20 mg/d	5–20 mg/d (or bid)
Glyburide micronized	0.75–3 mg/d	12 mg/d	3–12 mg/d (or bid)
Thiozolidinedione			
Pioglitazone	15–30 mg/d	45 mg/d	15–45 mg/d
Rosiglitazone	4 mg/d (or bid)	8 mg/d	4–8 mg/d (or bid)
α-Glucosidase inhibitors			
Acarbose	25 mg tid	100 mg tid	25–100 mg tid
Miglitol	25 mg tid	100 mg tid	25–100 mg tid
Meglitinides			
Repaglinide	0.5 mg before meals	4 mg before meals (16 mg/d). Wait ≥7 d between dose increases)	0.5–4 mg before meals
Netaglinide	120 mg tid before meals (60 mg tid if near glycemic goals)	120 mg tid before meals	60–120 mg tid before meals
Dipeptidyl peptidase IV inhibitor			
Sitagliptin	100 mg/d	100 mg/d	100 mg/d
Saxagliptin	2.5 mg/d	5 mg/d	5 mg/d

20. Duckworth W, Abraira C, Moritz T, et al; VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2009;360:129-39. [PMID: 19092145]
21. Patel A, MacMahon S, Chalmers J, et al; ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358:2560-72. [PMID: 18539916]

glycemic control, differences in mechanism, tolerability, and the timing of administration may help to individualize care. For example, nonsulfonylurea insulin secretagogues (nateglinine, replaglinide) and the α-glucosidase inhibitors (acarbose, miglitol) can be administered before meals and may therefore be useful to patients with irregular mealtimes (for example, truck drivers).

Most patients with diabetes have worsening glycemic control over time and will require more than one agent to maintain adequate glycemic control. Increasing the dose of existing oral agents is generally the first step, although the response from dose escalation, particularly with metformin and sulfonylureas, is limited. Patients therefore often require the addition of a second oral agent. Although data showing the effect of various drug combinations on glycemic control are available, few studies have assessed clinical end points. Several combination formulations are available and may provide advantages in convenience or cost for some patients. Sulfonylureas and thiozolidinediones may each cause hypoglycemia; thiozolidinediones may also cause weight gain. Patients should be warned about these possibilities and educated to recognize and treat hypoglycemia.

When should physicians consider insulin therapy for patients with type 2 diabetes?

Patients who do not achieve adequate glycemic control with oral medications, whether alone or in combination, are candidates for insulin therapy. The Box lists other indications.

Many insulin formulations are available, differing primarily in their onset of action and duration (Table 3). No single regimen has been established as superior (24). Most patients achieve a 1- to 2-percentage point decrease in hemoglobin A_{1c} level after starting insulin (25, 26). When intensive glycemic control is planned, fasting glucose values of less than 6.7 mmol/L (<120 mg/dL) are reasonable. The primary risks of insulin are hypoglycemia and weight gain, and patients must be warned about these possibilities and educated to recognize and treat hypoglycemia (15).

When insulin therapy begins, most patients can be treated with a once daily injection. Patients without hypoglycemia can often be treated with a single bedtime dose of neutral protamine Hagedorn (NPH) in combination with an oral agent. In patients who have normal fasting glucose or high-risk for hypoglycemia, glargine or detemir may be a preferred first choice. Starting doses of insulin are typically 0.1 to 0.2 U/kg. If the hemoglobin A_{1c} remains above goal despite normal fasting glucose levels, prandial insulin may be considered.

A combination of an insulin and an oral agent (typically either NPH or glargine with metformin) can be effective and can limit insulin dose to once daily at bedtime, which is often more acceptable to patients (27). Some patients need twice-daily insulin to achieve glycemic targets, but more-frequent injections have not been shown to substantially improve control in most patients with type 2 diabetes.

What other options are available if control is inadequate on traditional oral drugs or insulin?

Two newer injectable agents and 1 newer oral agent are available for control of blood glucose in type 2 diabetes.

Other Indications for Insulin Therapy in Patients With Type 2 Diabetes

- New diagnosis with severe, symptomatic hyperglycemia
- Hospitalization, where frequent changes in diet and such procedures as contrast imaging studies make oral agents relatively unsafe
- Pregnancy, where insulin is considered the standard of care (although recent studies suggest that some oral agents also are safe to use)
- Intolerance of oral medications

22. AACE Diabetes Mellitus Clinical Practice Guidelines Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. Endocr Pract. 2007;13 Suppl 1:1-68. [PMID: 17613449]
23. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet. 1998;352:854-65. [PMID: 9742977]
24. Yki-Järvinen H, Kauppila M, Kujansuu E, et al. Comparison of insulin regimens in patients with non-insulin-dependent diabetes mellitus. N Engl J Med. 1992;327:1426-33. [PMID: 1406860]

Table 3. Onset and Mechanisms of Action of Various Types of Insulin*

Currently Available Insulin Preparations†	*Pharmacodynamic Characteristic*		
	Onset	*Peak*	*Duration*
Insulin class			
Rapid-acting (insulin analogues lispro, aspart, glulisine)	≤30 min	0.5–3 h	3–5 h
Short-acting (human regular)	0.5–1 h	2–5 h	Up to 12 h
Intermediate-acting (human NPH)	1.5–4 h	4–12 h	Up to 24 h
Long-acting (insulin analogues glargine, detemir)	0.8–4 h	Relatively peakless	Up to 24 h
Human insulin mixtures			
70% NPH/30% regular	0.5–2 h	2–12 h	Up to 24 h
50% NPH/50% regular	0.5–2 h	2–5 h	Up to 24 h
Analogue mixtures			
75% lispro protamine/25% lispro	<15 min	1–2 h	Up to 24 h
50% lispro protamine/50% lispro	<15 min	1–2 h	Up to 24 h
70% aspart protamine/30% aspart	10–20 min	1–4 h	Up to 24 h

NPH = Neutral protamine Hagedorn.

** The time course of action of each insulin may vary among persons or at different times in the same person. Because of this variation, the time periods indicated here should be considered general guidelines only. Inhaled insulin powder (Exubera, Pfizer) has been omitted because it has been withdrawn from the market.*

† Preperations vary within class. Please see package inserts for specific pharmacodynamic data.

‡ Blood glucose–lowering effect.

Pramlintide is a synthetic form of the pancreatic hormone amylin. Pramlintide requires preprandial dosing, making it somewhat less convenient than other agents for many patients with diabetes. Pramlintide is typically started at a dose of 60 mg subcutaneously before meals, and increased to 120 mg if it is tolerated. The dose of short-acting insulins should be decreased by 50% before starting pramlintide to minimize the risk for hypoglycemia. Blood sugar should be checked before and after meals and at bedtime; when pramlintide dose is stabilized, insulin dosing should be optimized. The most common side effects are nausea and hypoglycemia, which may require a dose reduction or discontinuation.

Exenatide is an incretin mimetic, which acts through glucagon-like peptide 1, a naturally occurring hormone involved in glucose homeostasis. Exanatide has many effects, including enhanced glucose-dependent insulin secretion; delayed gastric emptying; and, in many patients, decreased appetite and weight loss. Exenatide should be considered in persons receiving oral agents who have not achieved glycemic goals. It is not approved by the U.S. Food and Drug Administration for combination with insulin, although some studies suggest it is effective in this setting (28, 29). The primary risks of exenatide are gastrointestinal effects, notably nausea and vomiting, and possibly increased risk for pancreatitis.

Exenatide should be started at 5 μg subcutaneously twice daily. Patients taking sulfonylureas should have their dose reduced to avoid hypoglycemia; a change in metformin dose is not necessary. The dose of exenatide can be increased to 10 μg twice daily in persons who tolerate the drug.

25. Buse JB, Wolffenbuttel BH, Herman WH, et al. DURAbility of basal versus lispro mix 75/25 insulin efficacy (DURABLE) trial 24-week results: safety and efficacy of insulin lispro mix 75/25 versus insulin glargine added to oral antihyperglycemic drugs in patients with type 2 diabetes. Diabetes Care. 2009;32:1007-13. [PMID: 19336625]
26. Hayward RA, Manning WG, Kaplan SH, et al. Starting insulin therapy in patients with type 2 diabetes: effectiveness, complications, and resource utilization. JAMA. 1997;278:1663-9. [PMID: 9388085]

Sitagliptin is an oral dipeptidyl peptidase-IV (DPP-IV) inhibitor that also works through the incretin and glucagon-like peptide 1 pathway. Sitagliptin is dosed at 100 mg/d. It can be used alone or in combination with other oral drugs, particularly metformin. The main side effects of sitagliptin are nausea, diarrhea, headache, and upper respiratory symptoms. It may also increase the risk for pancreatitis.

Saxagliptin is a newly approved oral DPP-IV inhibitor. It is dosed at 2.5 to 5 mg/d, with the lower dose preferred in persons with renal insufficiency or those on other drugs that strongly inhibit cytochrome P450 3A4/5. The most common side effects are headache, upper respiratory symptoms, and urinary tract infections.

What novel therapeutic options are on the horizon for patients with type 2 diabetes?

Several additional DPP-IV inhibitors are being developed, including one (vildagliptin) that has been approved for use in the European Union. Liraglutide, a long-acting injectable glucagon-like peptide 1 analogue, was recently approved by the U.S. Food and Drug Administration. It is similar to exenatide but is approved for once-daily injection. Exenatide is currently being reviewed for once-weekly injection.

Besides glycemic control, what other clinical interventions reduce complications of type 2 diabetes?

Hypertension is a major risk factor for diabetes complications, and blood pressure control may be the most important treatment to reduce complications in patients with diabetes. Patients with diabetes and hypertension should receive aggressive therapy aimed at maintaining a blood pressure of less than 135/80 mm Hg (30–32). The best choice of agents for blood pressure control has not been defined. A combination of a thiazide diuretics and either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin-receptor blocker (ARB) may be preferred treatment in many patients with diabetes and hypertension. Both ACE inhibitors and ARBs prevent the progression of microalbuminuria in patients with type 2 diabetes. Other agents should be added as needed to achieve blood pressure goals (30).

Treatment of dyslipidemia is also a priority in patients with diabetes. For primary prevention, evidence suggests that nearly all patients with diabetes who are older than 40 years benefit from statin therapy, regardless of initial level of low-density lipoprotein (LDL) cholesterol. Optimum LDL cholesterol targets, however, have not been established, and moderate dosing of statins is recommended (33, 34). For secondary prevention, statin use should be encouraged in all patients without contraindication. Optimum LDL targets have not been established; some evidence suggests that higher-dose statin therapy (for example, simvastatin, 80 mg, or atorvastatin, 80 mg) may be more effective than lower-dose statin therapy in patients with existing coronary artery disease (35, 36).

Aspirin therapy is generally recommended for patients with type 2 diabetes (3), although its benefit in preventing progression of cardiovascular disease in patients with diabetes is unclear. A recent randomized, controlled study of aspirin use in patients with type 1 or 2 diabetes found no evidence to support the use of aspirin for the primary prevention of cardiovascular events (37). Patients with a history of heart disease and no contraindication should take aspirin, 75 to 325 mg/d.

Retinal examinations reduce the incidence of vision loss in patients with type 2 diabetes. Examination frequency for patients without high-risk retinal lesions may range

27. Yki-Järvinen H, Ryysy L, Nikkilä K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial. Ann Intern Med. 1999;130:389-96. [PMID: 10068412]
28. Sheffield CA, Kane MP, Busch RS, et al. Safety and efficacy of exenatide in combination with insulin in patients with type 2 diabetes mellitus. Endocr Pract. 2008;14:285-92. [PMID: 18463034]
29. Yoon NM, Cavaghan MK, Brunelle RL, et al. Exenatide added to insulin therapy: a retrospective review of clinical practice over two years in an academic endocrinology outpatient setting. Clin Ther. 2009;31:1511-23. [PMID: 19695400]
30. Vijan S, Hayward RA. Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care. Ann Intern Med. 2003;138:593-602. [PMID: 12667032]

from 1 to 3 years, depending on underlying risk (34). Measurement of urine microalbumin/creatinine ratio helps to guide the use of ACE inhibitors or ARBs in persons with nephropathy and to reduce the risk for progression to end-stage renal disease. Neuropathy screening and foot care are essential in reducing the risk for amputation. Painful neuropathy is uncommon in type 2 diabetes but can be treated with many agents.

How frequently should physician see patients with type 2 diabetes, and what should physicians include in follow-up visits?

No direct evidence examines the ideal frequency of visits for patients with type 2 diabetes. Expert opinion and the recommended frequency of monitoring hemoglobin A_{1c} levels suggest that quarterly visits are reasonable; for patients with stable disease, this can be reduced to every 6 months (3). Table 5 lists components of follow-up.

When should generalist physicians consult specialists to care for patients with type 2 diabetes?

Meta-analyses have found that diabetes education by a certified educator is effective in improving many key domains in diabetes care, including glycemic control, although the durability of these effects is not clear.

Endocrinology consultation is helpful when there are questions about diagnosis or when glycemic management has become difficult (for example, in patients with highly labile blood glucose levels). Patients who are pregnant or contemplating pregnancy should be referred to assist with glucose control, because poor glucose control is associated with adverse fetal outcomes.

Ophthalmologic examination, whether by ophthalmology,

Table 4. Antihypertensive Agents in Type 2 Diabetes*

Antihypertensive Agent	*Notes*	*Advantages*	*Disadvantages*
ACE inhibitors	ADA and ACP advocate as first-line agent	Cardioprotective Renoprotective	Caution with advanced renal failure
ARBs	ADA and ACP advocate as second-line agent	Cardioprotective Renoprotective	Expensive Caution with advanced renal failure
β-Blockers	Use in patients with known CAD	Cardioprotective Most are inexpensive	Can mask hypoglycemia May be associated with weight gain and metabolic abnomalities
Thiazide diuretics	Often used in combination with other agents to achieve blood pressure targets. ACP advocates as first-line age.	May reduce CHF Inexpensive Cardioprotective	May elevate blood glucose levels
α-Blockers	Use only if target blood pressure cannot be reached with other agents	Can help alleviate symptoms of benign prostatic hypertrophy	Do not protect against CHF. Generally must be used with other agent
Calcium-channel blockers	Use if target blood pressure cannot be reached with ACE inhibitors, ARBs, and thiazides	Some evidence suggests this class is cardioprotective	Appear to offer less cardioprotection than other antihypertensive agents

**ACE = angiotensin-converting enzyme; ACP = American College of Physicians; ADA = American Diabetes Association; ARB = angiotensin-receptor blocker; CAD = coronary artery disease; CHF = congestive heart failure.*

31. Snow V, Weiss KB, Mottur-Wilson C; Clinical Efficacy Subcommittee of the American College of Physicians. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. Ann Intern Med 2003; 138: 587-92.[PMID: 12667031]
32. Holman RR, Paul SK, Bethel MA, et al. Long-term follow-up after tight control of blood pressure in type 2 diabetes. N Engl J Med. 2008;359:1565-76. [PMID: 18784091]
33. Vijan S, Hayward RA; American College of Physicians. Pharmacologic lipid-lowering therapy in type 2 diabetes mellitus: background paper for the American College of Physicians. Ann Intern Med. 2004;140:650-8. [PMID: 15096337]
34. Snow V, Aronson MD, Hornbake ER, et al; Clinical Efficacy Subcommittee of the American College of Physicians. Lipid control in the management of type 2 diabetes mellitus: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2004; 140: 644-9. [PMID: 15096336]
35. LaRosa JC, Grundy SM, Waters DD, et al; Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005;352:1425-35. [PMID: 15755765]
36. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004; 350: 1495-504. [PMID: 15007110]

Table 5. Components of Follow-up Care for Type 2 Diabetes

Issue	*Actions*	*How Often?*
Glycemic control	Ask about diet, exercise, results of home monitoring, and medications. Adjust medications.	Each visit (at least quarterly)
	Check hemoglobin A1c values	Quarterly
Weight control	Weigh patient. Ask about diet and exercise.	Each visit
Cardiovascular complications	Ask about diet, smoking, and cardiac events in family members	Each visit
	Measure blood pressure, examine heart and peripheral pulses. Adjust antihypertensive therapies as needed	Each visit
	Measure lipid levels and adjust therapy as needed	Annually, or more frequently to monitor therapy
	Consider performing other cardiac testing	If patient has symptoms; has abnormal findings on examination or electrocardiography; or is sedentary and >35 y of age and plans vigorous exercise (the gradual adoption of a progressively increasing exercise regimen is probably preferable).
Vision complications	Ask about visual acuity, central vision loss, and eye pain	At least annually; each visit once problem exists
	Have specialist conduct eye examination	At least annually in high-risk patients, otherwise every 2-3 years; each visit once problem exists.
Neurologic complications	Ask about burning, tingling, numbness in extremities	At least annually; each visit once problem exists
	Conduct neurologic examination with monofilament testing	At least annually; each visit once problem exists
Nephrologic complications	Measure electrolytes, blood urea nitrogen, and creatinine; test urine for microalbuminuria	At least annually; more frequently once problem exists
Infectious complications	Ask about infections, including skin, dental, foot, genitourinary	Each visit
	Examine for periodontal disease, skin infection, and foot infection	Each visit
Patient education	Advocate diet, exercise, monitoring, and medication adherence	Each visit

optometry, or through retinal photography, should be conducted every 1 to 3 years depending on previous examination results and the degree of glycemic control (38). Other conditions (for example, known retinopathy, glaucoma, cataracts) may require more frequent examination.

Nephrology evaluation is prudent in patients whose glomerular filtration rate has decreased to less than 45 mL/min per 1.73 m^2, or in whom the origin of renal insufficiency is unclear. Patients with hyperkalemia, acidemia, or difficult-to-control blood pressure may also benefit.

Podiatry evaluation is helpful for management of lesions, such as calluses or deformities, which require intervention to reduce the risk for foot ulcers and amputation.

When should patients with type 2 diabetes be hospitalized?

Some patients with severe, symptomatic hyperglycemia may require hospitalization, particularly at the time of diagnosis. Diabetic ketoacidosis or hyperosmolar coma requires hospitalization for management. Diabetes complications, including cellulites in need of intravenous antibiotic therapy, may require hospitalization.

Treatment... Diet and exercise are the cornerstones for achieving glycemic control in patients with type 2 diabetes, and clinicians should stress the importance of lifestyle modification regardless of whether patients also require pharmacologic therapy. Metformin is superior to sulfonylureas and insulin in reducing mortality and should be considered in patients without contraindications or intolerance to metformin. However, data comparing the many other oral and insulin-based therapies are limited, and clinicians should consider effectiveness, potential side effects, comorbid conditions, costs, and patient preferences when selecting treatment regimens for glycemic control. The optimum target for glycemic control in patients with type 2 diabetes is debated; a hemoglobin A_{1c} level less than 7% is recommended but must be individualized according to risks, particularly hypoglycemia, and factors which may limit benefits, such as short life expectancy or other factors that may limit the achievability of tight control. In addition to glycemic control, patients with type 2 diabetes should be treated for dyslipidemia and should receive therapy aimed at maintaining a blood pressure of less than 135/80 mm Hg.

CLINICAL BOTTOM LINE

Current Standards of Diabetes Care

Eye Examination
- Percentage of patients who received a retinal or dilated eye examination by an eye care professional (optometrist or ophthalmologist) during the reporting year or during the previous year if a patient is at low risk for retinopathy.
- A patient is considered low-risk if all 3 of the following criteria are met: the patient is not taking insulin, the patient has a hemoglobin A_{1c} level <8.0%; and the patient had no evidence of retinopathy in the past year.

Hemoglobin A_{1c} Management
- Percentage of patients with diabetes with one or more hemoglobin A_{1c} test(s) conducted during the measurement year.

Hemoglobin A_{1c} Management Control
- Percentage of patients with diabetes whose most recent hemoglobin A_{1c} level was >9.0% (poor control).

Lipid Measurement
- Percentage of patients with diabetes with ≥1 low-density lipoprotein (LDL) cholesterol level test (or all component tests).

LDL Cholesterol Level
- Percentage of patients with diabetes with most recent LDL cholesterol level less than 2.59 mmol/L (<100 mg/dL) or less than 3.37 mmol/L (<130 mg/dL).

Blood Pressure Management
- Percentage of patients with diabetes who had their blood pressure documented in the past year as less than 140/90 mm Hg.

Practice Improvement

What measures do U.S. stakeholders use to evaluate the quality of care for patients with type 2 diabetes?

The Ambulatory Care Quality Alliance recommends several measures of diabetes care. Note that these do not perfectly align with clinical targets. The Box describes the current standards of care, which are widely endorsed.

Note that the clinical targets for blood glucose and blood pressure are specifically designed to identify poor control rather than optimum control. These are not necessarily clinical targets but instead acknowledge several issues, such as variation in populations treated by physicians, issues of measurement reliability, and the achievability of clinical goals.

What do professional organizations recommend regarding the care of patients with type 2 diabetes?

Several profession associations publish guidelines for diabetes care. Note that these do not always agree on all aspects and that the nature of the organization inevitably influences recommendations. Many guidelines for diabetes can be found at the National Guideline Clearinghouse

37. Belch J, MacCuish A, Campbell I, et al; Prevention of Progression of Arterial Disease and Diabetes Study Group. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. BMJ. 2008;337:a1840. [PMID: 18927173]

38. Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA. 2000;283:889-96. [PMID: 10685713]
39. Qaseem A, Vijan S, Snow V, et al; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Glycemic control and type 2 diabetes mellitus: the optimal hemoglobin A1c targets. A guidance statement from the American College of Physicians. Ann Intern Med. 2007;147:417-22. [PMID: 17876024

(www.guidelines.gov). The following organizations are 3 of the most commonly cited sources.

American College of Physicians (ACP)

The ACP conducted systematic reviews of the evidence to construct guidelines on the management of hypertension and lipids in type 2 diabetes (30–34). In addition, the ACP reviewed and rated existing guidelines for glycemic control and developed an assessment of the best existing guidelines on the topic (39). Guidelines are available at www.acponline.org/clinical_information/guidelines/.

American Diabetes Association (ADA)

The ADA releases diabetes standards of care yearly. The standards are broad and encompass most relevant areas of diabetes screening, prevention, and management. Complete guidelines are available at http://care.diabetesjournals.org/content/33/Supplement_1/S11.full.

American Association of Clinical Endocrinologists (AACE)

The AACE last updated their guidelines in 2007. They are available at www.aace.com/pub/pdf/guidelines/DMGuidelines2007.pdf.

in the clinic

Tool Kit

Type 2 Diabetes

PIER Modules

www.pier.acponline.org

Access the PIER module on type 2 diabetes. PIER modules provide evidence-based, updated information on current diagnosis and treatment in an electronic format designed for rapid access at the point of care.

Patient Information

www.annals.org/intheclinic/toolkit-diabetes.html

Access the Patient Information material that appears on the following pages for duplication and distribution to patients.

http://diabetes.niddk.nih.gov/dm/pubs/type2_ES/index.htm (English)

http://diabetes.niddk.nih.gov/dm/pubs/type2_ES/index.htm#Spanish (Spanish)

Access information for patients by the National Institute of Diabetes and Digestive and Kidney Diseases: Type 2 Diabetes: What You Need to Know

www.nlm.nih.gov/medlineplus/diabetes.html

Access MEDLINE Plus information about diabetes for patients, including an interactive tutorial available in both English and Spanish.

Clinical Guidelines

www.aace.com/pub/pdf/guidelines/DMGuidelines2007.pdf

Guidelines from the American Association of Clinical Endocrinologists guidelines, released in 2007, on the management of diabetes mellitus.

www.bmj.com/cgi/content/extract/336/7656/1306

Guidelines from The National Institute for Health and Clinical Excellence for the United Kingdom's National Health Service, updated in 2008, on management of diabetes type 2.

http://diabetes.acponline.org/

Access the ACP Diabetes Portal for clinical information, management tools, and patient information regarding diabetes care.

Diagnostic Tests and Criteria

http://pier.acponline.org/physicians/public/d296/tables/d296-t1.html

List of screening and diagnostic tests for diabetes mellitus from the American College of Physicians.

Quality Measures

www.qualitymeasures.ahrq.gov/search/searchresults.aspx?Type=3&txtSearch=diabetes&num=20

Access information on National Quality Measures Clearinghouse relating to diabetes.

http://pier.acponline.org/qualitym/t002.html

Access quality measures related to diabetes from the Centers for Medicare & Medicaid Services Physician Quality Reporting Initiative (PQRI).

THINGS YOU SHOULD KNOW ABOUT TYPE 2 DIABETES

What is type 2 diabetes?

- In type 2 diabetes, a hormone called insulin cannot adequately control the use of sugar from food. So, sugar builds up in the blood.
- If type 2 diabetes is not controlled, complications may include vision loss, kidney damage, and poor circulation and nerve damage that can lead to infections, foot ulcers, and potentially amputation. Nerve damage may also lead to digestive problems.
- Type 2 diabetes is sometimes called non–insulin-dependent diabetes mellitus or adult-onset diabetes.

Who is most likely to get type 2 diabetes?

- Overweight or inactive people
- People older than 45 years
- People with a family history of type 2 diabetes
- Women who had diabetes when they were pregnant.
- African Americans, Latinos, Native Americans, Asian Americans, Native Hawaiians, and other Pacific Islanders

How is type 2 diabetes diagnosed?

- Your doctor may suspect diabetes if you have symptoms such as increased thirst, urination, and fatigue. A diagnosis of diabetes is made with blood tests that measure whether the glucose in your blood is too high. Sometimes the blood testing is done after fasting or after you eat food with sugar.

How is type 2 diabetes treated?

- Type 2 diabetes is a long-term condition. Treatment is focused on lowering high levels of blood glucose. Long-term goals are to prevent diabetes-related complications.
- The primary treatment is regular exercise and a healthful diet. If diet and exercise are not effective enough, medications may be used to lower blood sugar levels.
- Patients may practice regular self-testing to check blood sugar levels at home. This allows them to monitor how well diet, exercise, and any diabetes medications are working.

How is type 2 diabetes different from type 1 diabetes?

- In type 1 diabetes, the pancreas (where insulin is made) is attacked by the body itself. These patients need to take insulin. Not all patients with type 2 diabetes need insulin.

What are some symptoms of type 2 diabetes?

- Dry mouth, increased thirst, hunger, or urination
- Blurred vision, or numbness of the hands or feet
- Unexplained weight loss or fatigue
- Impotence
- Dark, velvety looking skin in the armpit or back of the neck

For More Information

American College of Physicians Foundation: HEALTH TiPS: Diabetes
www.acpfoundation.org/files/ht/diab_en.pdf

American Diabetes Association: Diabetes Basics
www.diabetes.org/diabetes-basics/type-2/

National Institute of Diabetes and Digestive and Kidney Diseases: Type 2 Diabetes: What You Need to Know
http://diabetes.niddk.nih.gov/dm/pubs/type2_ES/index.htm (English)
http://diabetes.niddk.nih.gov/dm/pubs/type2_ES/index.htm#Spanish (Spanish)

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Patient Information

CME Questions

MKSAP
MEDICAL KNOWLEDGE Self-Assessment Program

1. A 72-year-old man comes to the office for a follow-up evaluation. He has had type 2 diabetes mellitus for 13 years. Over the past 5 years, his hemoglobin A1c value has slowly increased to 9.8%, and his fasting blood glucose levels at home have frequently exceeded 10.0 mmol/L (180 mg/dL). He has adhered to recommended lifestyle changes. The patient is currently on metformin, 1000 mg twice daily, and extended-release glipizide, 20 mg/d. He has hypertension treated with candesartan and hydrochlorothiazide and hyperlipidemia treated with atorvastatin.

   Results of physical examination are normal.

   Which is the best next step in therapy?

   A. Add insulin glargine
   B. Add pioglitazone
   C. Add sitagliptin
   D. Double his dose of glipizide

2. A 68-year-old woman is reevaluated after laboratory studies show a fasting plasma glucose level of 6.3 mmol/L (113 mg/dL). She has a maternal family history of type 2 diabetes mellitus.

   On physical examination, blood pressure is 142/88 mm Hg and body mass index is 29 kg/m2. Other vital signs and examination findings are normal.

   She undergoes an oral glucose tolerance test, during which her 2-hour plasma glucose level increases to 7.5 mmol/L (135 mg/dL).

   Her hemoglobin A1c level is 5.8%, her low-density lipoprotein cholesterol level is 2.85 mmol/L (110 mg/dL), her high-density lipoprotein cholesterol level is 1.24 mmol/L (48 mg/dL), and her triglyceride level is 1.94 mmol/L (172 mg/dL).

   Which is the most appropriate treatment recommendation to control her glucose level?

   A. Acarbose administration
   B. Diet and exercise
   C. Metformin administration
   D. Ramipril administration
   E. Rosiglitazone administration

3. An 83-year-old woman who has had type 2 diabetes mellitus for 25 years comes to the office for routine care. She also has a history of hypertension, dyslipidemia, and coronary artery disease. Her current antihyperglycemic regimen includes glipizide, pioglitazone, and insulin glargine, 24 U at bedtime. Fasting blood glucose levels at home range between 6.11 and 8.33 mmol/L (110 and 150 mg/dL), and her most recent hemoglobin A1c value was 7.2%. Other medications include metoprolol, lisinopril, and simvastatin.

   Physical examination shows a blood pressure of 108/72 mm Hg, a pulse rate of 76/min, and a respiration rate of 16 beats/min. Background retinopathy, a left femoral bruit, and mild loss of light-touch sensation in the feet are noted.

   Results of laboratory studies show a low-density lipoprotein cholesterol level of 1.7 mmol/L (65 mg/dL).

   Which is the most appropriate treatment for this patient?

   A. Add exenatide to her regimen
   B. Add metformin to her regimen
   C. Continue her current regimen
   D. Stop pioglitazone treatment

4. A 48-year-old man comes to the office after lunch for a routine physical examination. The patient is asymptomatic but overweight, with a body mass index of 29.2 kg/m2. Although he has no pertinent personal medical history, he has a strong family history of diabetes mellitus. He currently takes no medications.

   Results of physical examination are normal.

   Results of routine laboratory studies show a random plasma glucose level of 8.77 mmol/L (158 mg/dL).

   Which term best describes his current glycemic status?

   A. Impaired fasting glucose
   B. Impaired glucose tolerance
   C. The metabolic syndrome
   D. Type 2 diabetes mellitus
   E. Noncategorizable

5. An obese 44-year-old woman is evaluated for persistent hyperglycemia. For the past 3 months, she has followed a strict regimen of diet and exercise in an attempt to control her hyperglycemia. Home blood glucose monitoring has shown preprandial levels between 6.66 and 8.88 mmol/L (120 and 160 mg/dL) and occasional postprandial levels exceeding 11.1 mmol/L (>200 mg/dL). She has a history of hypertension and hyperlipidemia. Current medications include lisinopril, hydrochlorothiazide, and pravastatin.

   Vital signs and physical examination findings are normal, except for a body mass index of 30 kg/m2.

   The serum creatinine level is 70.7 µmol/L (0.8 mg/dL), and the urine is negative for microalbuminuria.

   Which is the most appropriate next step in treatment to improve her glycemic control?

   A. Continue the diet and exercise for an additional 3 months
   B. Begin exenatide
   C. Begin glimepiride
   D. Begin metformin
   E. Begin pioglitazone

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP, accessed at http://www.acponline.org/products_services/mksap/15/?pr31). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.