

Tight Control of Type 1 Diabetes: Recommendations for Patients

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Tight control of blood glucose levels and risk factors for cardiovascular disease (e.g., hypertension, hypercholesterolemia) can substantially reduce the incidence of microvascular and macrovascular complications from type 1 diabetes. Physicians play an important role in helping patients make essential lifestyle changes to reduce the risk of these complications. Key recommendations that family physicians can give patients to optimize their outcomes include: take control of daily decisions regarding your health, focus on preventing and controlling risk factors for cardiovascular disease, tightly control your blood glucose level, be cognizant of potentially inaccurate blood glucose test results, use physiologic insulin replacement regimens, and learn how to manage and prevent hypoglycemia. (*Am Fam Physician* 2006;74:971-8, 983-4. Copyright © 2006 American Academy of Family Physicians.)

► Patient information:

A handout on type 1 diabetes, written by the authors of this article, is provided on page 983.

Randomized clinical trials¹⁻⁵ have demonstrated that tight control of blood glucose levels reduces the risk of microvascular and macrovascular complications in patients with type 1 diabetes; this is not true for patients with type 2 diabetes. Although many patients with type 1 diabetes may benefit from tightly controlling their blood glucose levels,³ few do so.⁶ The Diabetes Control and Complications Trial (DCCT)⁴ showed that, compared with conventional therapy, intensive therapy significantly reduced the risk of retinopathy progression (4.7 versus 1.2 per 100 patient-years, number needed to treat [NNT] = three for 10 years) and clinical neuropathy (9.8 versus 3.1 per 100 patient-years, NNT = 1.5 for 10 years). In a long-term follow-up study,⁴ the likelihood that a patient would experience a cardiovascular event was significantly lower in the intensive treatment group (0.38 versus 0.80 events per 100 patient-years). Thus, intensive therapy prevented one cardiovascular event for every 25 patients treated over a 10-year period in this relatively young group of patients.⁴ Intensive therapy is not without risk, however. The risk of severe hypoglycemia and subsequent coma or seizure was significantly higher in the intensive therapy group (16.3 versus 5.4 per 100 patient-years).³

Recommendations for Patients

Physicians may provide patients with the following recommendations to help them tightly control their diabetes; a few of the recommendations may not be appropriate for patients with type 2 diabetes, even those who use insulin. *Table 1*^{1-5,7-26} includes tips for controlling blood glucose levels and minimizing complications. These tips are consistent with consensus guidelines from the American Diabetes Association (ADA) and others (these tips are informed by my experience practicing tight control of type 1 diabetes for 50 years -S.H.).

TAKE CONTROL OF YOUR HEALTH

Tight control of type 1 diabetes requires patients to independently make daily decisions about diet, exercise, and insulin intake. Family physicians can encourage patients to proactively control their disease by teaching them how to properly adjust their insulin dosages and adopt lifestyle changes to reduce the risk of complications. Physician encouragement can effectively help patients change their behaviors.⁷

One randomized clinical trial⁸ on immediate and delayed patient education and empowerment programs showed that

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation (advice for patients with type 1 diabetes)</i>	<i>Evidence rating</i>	<i>References</i>	<i>Comments</i>
Adopt multiple strategies to prevent the complications of type 1 diabetes.	A	9, 10	Reduced mortality with decreased blood pressure and lipids
Exercise regularly.	B	16, 17	Cohort studies
Test blood glucose level frequently and at critical times.	A	1-3	Randomized controlled trials
Use an ultralong-acting insulin once daily and a rapid-acting insulin before each meal.	C	19-22, 24	Less hypoglycemia; other outcomes not proved
Learn the signs and symptoms of hypoglycemia and how to manage the condition.	C	23	Expert opinion

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 906 or <http://www.aafp.org/afpsort.xml>.

95 percent of patients who participated in the programs reportedly changed their diet, exercise regimen, and/or frequency of blood glucose testing. A1C levels, measured after patients completed the education programs, were more improved in patients who received immediate education compared with patients who received delayed education (-0.72 versus -0.04 percent, $P = .05$).

ADOPT MULTIPLE STRATEGIES TO PREVENT COMPLICATIONS

Tight glycemic control can significantly reduce the risk of microvascular complications from type 1 diabetes. For example, a reduction in A1C from 10 to 7 percent is associated with a reduction in the risk of retinopathy from 0.5 to 0.1 percent.^{27,28}

Patients can reduce their risk of cardiovascular disease (CVD) by learning to prevent and control other major risk factors (e.g., high cholesterol, hypertension).^{9,10,29-32} Patients who smoke should quit to reduce the risk of CVD and microvascular complications. Family physicians should screen for these risk factors and help patients modify their lifestyles to reduce risks. Patients should keep their low-density lipoprotein (LDL) cholesterol level at less than 100 mg per dL (2.60 mmol per L),³³ with a therapeutic option of less than 70 mg per dL (1.80 mmol per L) for high-risk patients (e.g., those with known CVD).³⁴ Patients should maintain blood pressure levels of less than 130/80 mm Hg.³⁵ A daily aspirin regimen lowers coronary heart disease risk by 20 to 25 percent.³⁶

Closely monitoring and treating patients with retinopathy reduces progression of microvascular complications. Diabetic retinopathy can be treated, and³⁷ tight glycemic control reduces its progression.³ The ADA recommends that patients receive dilated eye examinations at least annually starting three to five years after the onset of type 1 diabetes.²⁵

Early nephropathy can be detected by screening for microalbuminuria. Hypertension control,³⁷ tight blood glucose control,³ and the use of angiotensin-converting

TABLE 1

Twenty Tips for Patients to Help Tightly Control Their Type 1 Diabetes

- Take control of your health.^{7,8}
- Adopt multiple strategies to prevent the complications of type 1 diabetes.^{9,10}
- Eat a heart-healthy diet.¹¹⁻¹³
- Maintain a healthy weight.^{14,15}
- Exercise regularly.^{16,17}
- Meet your blood glucose goals as closely as possible.¹⁻⁵
- Test blood glucose level frequently and at critical times.¹⁻³
- Be wary of potentially inaccurate blood glucose readings.¹⁸
- Use a rapid-acting insulin before each meal.¹⁹⁻²²
- Carry rapid-acting insulin syringes or pens.²³
- Take ultralong-acting insulin once per day.²⁴
- Know the onset, peak, and duration of your insulins.²³
- Learn the signs and symptoms of hypoglycemia and how to manage the condition.²³
- Always carry a source of sugar.²³
- Teach those in your life about hypoglycemia.^{23,25}
- Keep glucagon at home.^{23,25}
- Wear a medical alert bracelet or necklace.²³
- Recognize effects of stress on blood glucose levels and manage your stress level.²³
- Limit alcohol consumption to moderate amounts.^{15,26}
- Lead a normal life.²³

Information from references 1 through 5 and 7 through 26.

enzyme (ACE) inhibitors (regardless of blood pressure)³⁸ reduce the risk of progression.

EAT A HEART-HEALTHY DIET

Hypercholesterolemia and hypertension increase the risk of CVD, retinopathy, and nephropathy.^{39,40} Approximately 90 percent of adults develop hypertension⁴¹; patients with diabetes generally develop the condition earlier in life.⁴² More than 70 percent of American adults develop elevated cholesterol levels.¹¹ These risk factors are largely preventable, however.^{40,41}

Patients should follow a heart-healthy diet to reduce blood pressure and cholesterol levels. Specifically, patients should limit their daily fat intake to 30 percent or less of calories, with less than 7 percent from saturated fat; limit their sodium intake to 1,500 mg or less per day; and eat at least 3 oz of whole grains, 2 cups of fruit, and 3 cups of vegetables per day.¹¹⁻¹³ Patients should only eat sweets in moderation. To slow the rapidly rising blood glucose levels caused by sweets, patients should eat them with other foods when possible and use rapid-acting insulin.²⁵ Bedtime and other snacks are largely unnecessary to raise blood glucose levels if a patient uses insulin, but they may be necessary if the patient's blood glucose level is low.

MAINTAIN A HEALTHY WEIGHT

The DCCT¹⁴ demonstrated that tight control of blood glucose levels can cause weight gain and even obesity. Weight gain causes an increase in blood pressure, LDL cholesterol levels, and triglyceride levels and causes a decrease in high-density lipoprotein (HDL) cholesterol levels.¹⁵ Weight gain also can lead to insulin resistance and can make glycemic control more difficult. Men should maintain a waist size of 40 in (102 cm) or less, and women should maintain a waist size of 35 in (88.9 cm) or less.³³ Patients should be reminded that food portion control and lower caloric intake plus regular physical activity are critical to avoid weight gain.

EXERCISE REGULARLY

Regular physical activity is especially important for patients with diabetes, because

inactivity in these patients is associated with a two times higher risk of CVD.¹⁶ Exercise improves glucose and HDL cholesterol levels, decreases stress, and helps normalize weight.¹⁷ However, less than 20 percent of Americans get sufficient exercise.³²

Patients should exercise for 30 to 60 minutes daily at an intensity of at least a brisk walk,¹⁷ and they should be counseled on how to accommodate exercise's effect on blood glucose levels. Before exercise, patients can reduce their insulin dose or consume extra carbohydrates proportionate to the intensity and duration of their physical activities. Physicians should tell patients that insulin is absorbed and peaks faster during exercise, especially when injected into the leg.

MEET YOUR BLOOD GLUCOSE GOALS AS CLOSELY AS POSSIBLE

It is important for physicians to provide patients with blood glucose goals. The ADA intensive treatment goals for blood glucose and A1C levels, which are similar to those established by the DCCT Research Group, are highlighted in *Table 2*.²⁵ To achieve these goals, patients may need counseling on how to appropriately balance their caloric intake, physical activity, and insulin doses throughout the day. This balance requires patients to learn how food, physical activity, and insulin affect their blood glucose levels. Blood glucose control also requires patients to start with basal insulin and use an insulin bolus at mealtime to mimic normal physiologic insulin levels. Physicians may refer a patient to a certified diabetes educator at the time of

TABLE 2
ADA Recommendations for Blood Glucose and A1C Goals

Measurement	Goal
Preprandial blood glucose	90 to 130 mg per dL (5.0 to 7.2 mmol per L)
Postprandial blood glucose	Less than 180 mg per dL (10.0 mmol per L)
A1C level	Less than 7 percent

ADA = American Diabetes Association.

Adapted with permission from American Diabetes Association. *Clinical practice recommendations 2005. Diabetes Care 2005;(28 suppl 1):S22.*

diagnosis or if the patient is unable to meet his or her glycemic goals.

FREQUENTLY TEST BLOOD GLUCOSE LEVELS

Patients should assess fingertip blood glucose levels at least three times daily.⁴³ In addition, patients should test their blood glucose levels before and after exercising, before driving, and when they are uncertain if their blood glucose is at an appropriate level. Bedtime testing is especially important because nocturnal symptoms may go unnoticed, causing severe hypoglycemia. If a patient's blood glucose level drops below 100 mg per dL (5.6 mmol per L), he or she should eat a small snack.

Meters that measure glucose from a site other than the fingertip usually are reliable; however, nonfingertip testing 60 minutes after meals and after exercise has been shown to be less reliable than fingertip testing.⁴⁴ Therefore, the fingertip remains the recommended test site.

Continuous glucose monitoring systems can detect the frequency and severity of unrecognized hypoglycemic episodes; these systems are effective but expensive. A controlled crossover trial⁴⁵ showed that patients using continuous glucose monitoring systems had significantly lower A1C levels compared with control patients (-0.39 versus -0.1 percent).

BE WARY OF POTENTIALLY INACCURATE BLOOD GLUCOSE READINGS

Patients should be aware that inaccurate blood glucose readings potentially can occur because of faulty equipment or improper testing techniques. One study¹⁸ concluded that faulty meters or test strips could provide grossly inaccurate readings. Patients can use a control solution to check the accuracy of their meters if they believe their equipment is not functioning properly. Physicians should suspect an inaccurate reading if a home blood glucose test is inconsistent with A1C testing. When an unexpectedly high or low reading occurs, patients should assess the

presence or absence of symptoms before taking extra insulin or sugar.

USE RAPID-ACTING INSULIN BEFORE EACH MEAL

Rapid-acting insulin (e.g., lispro [Humalog], aspart [NovoLog], glulisine [Apidra]), taken shortly before eating, can effectively control postprandial blood glucose levels.^{19-22,46} With a peak activity of about one hour, which is similar to normal postprandial blood glucose levels, rapid-acting insulin is more physiologic than regular insulin. The use of rapid-acting insulin is associated with fewer postprandial hypoglycemic episodes compared with regular insulin (about 3 versus 4 percent over six to 12 months). Studies have not yet demonstrated that rapid-acting insulin improves other clinical outcomes compared with regular insulin; therefore, other than the decreased risk of hypoglycemia from using insulin analogues instead of regular insulin, regular insulin can be substituted if cost is an issue.

Patients may benefit from instruction on how to count carbohydrates to accurately determine how much insulin to take. Patients typically need 1 unit of insulin per 10 to 15 g of carbohydrates. If the patient's blood glucose rises above the recommended level, a supplemental dose should be taken to restore the level to 100 mg per dL. One unit of short-acting insulin typically reduces blood glucose levels 20 to 60 mg per dL (1.1 to 3.3 mmol per L), depending on insulin sensitivity; the level of reduction can be estimated by dividing 1,800 by the daily insulin dosage.⁴⁷

ALWAYS CARRY RAPID-ACTING INSULIN SYRINGES OR PENS

Patients should always carry rapid-acting insulin to accommodate flexible meal and snack times or in case additional doses are needed.²³ Repeated use of plastic syringes does not increase the risk of infection if the needle is recapped after each use.⁴⁸ Patients may choose to carry insulin pens, although they cost more than syringes. Some highly motivated patients may prefer an insulin pump, which is more difficult to use, for optimal physiologic insulin replacement. Pumps cost more than syringes or pens.

Patients with type 1 diabetes should use an insulin bolus at mealtime plus a long-acting insulin to mimic normal physiologic insulin levels.

USE GLARGINE ONCE DAILY IF YOU DO NOT USE AN INSULIN PUMP

Patients who do not use insulin pumps may consider using glargine (Lantus) as their basal insulin (typically 16 to 24 units). If a patient does not use basal insulin, blood glucose levels can become unstable during the night and between short-acting insulin doses. Glargine slowly releases insulin over 24 hours, causing more physiologic basal insulin levels. Insulin pumps create the same effect,⁴⁹ maintaining stable blood glucose levels between meals.

Glargine is absorbed more consistently than intermediate-acting insulins and has no peak action time, reducing the risk of hypoglycemia. A study²⁴ that compared glargine insulin with insulin isophane suspension (neutral protamine Hagedorn) in patients with type 1 diabetes showed that symptomatic hypoglycemia was less common in patients who used glargine (39.9 versus 49.2 percent over one month, $P = .02$).²⁴ Data are lacking regarding the effect of glargine on other clinical outcomes (e.g., macrovascular complications, mortality) in patients with type 1 diabetes compared with other long-acting insulins.

KNOW THE ONSET, PEAK, AND DURATION OF YOUR INSULINS

Patients should know how rapidly their insulins take effect, when they peak, and how long they are active (*Table 3*¹⁸). Each type of insulin has distinct advantages and disadvantages. Rapid-acting insulin controls postprandial blood glucose more effectively than regular insulin; however, too much rapid-acting insulin can cause a rapid onset of hypoglycemia, giving the patient less time to recognize the symptoms.

Intermediate-acting insulin remains active longer than other insulins but has a slower onset, its peak action is not related to mealtimes, and it can cause hypoglycemia if eating is delayed or if physical activity is increased. Because intermediate-acting insulin peaks many hours after it is administered, patients must eat meals at set intervals to avoid hypoglycemia. The disadvantages of intermediate-acting insulin outweigh the advantages of tight blood glucose control.

LEARN THE SIGNS AND SYMPTOMS OF HYPOGLYCEMIA AND HOW TO MANAGE THE CONDITION

Soon after diabetes is diagnosed, patients with hypoglycemia typically experience adrenergic symptoms (e.g., shakiness, palpitations, nervousness, unexplained diaphoresis, hunger). After many years, especially if a patient experiences recurrent hypoglycemia, neuroglycopenic symptoms (e.g., fatigue, slow speech or movement, confusion, irrationality, irritability, weakness, blurred vision, pallor, twitching, headache) predominate. Symptoms of hypoglycemia can be as subtle as slight fatigue or as dramatic as a feeling of imminent collapse.

Hypoglycemia normally does not require hospitalization. Patients instead should immediately eat or drink something that contains sugar; overtreatment can cause an

TABLE 3
Onset, Peak, Duration, and Cost of Insulins

Type of insulin	Onset	Peak (hours)	Duration (hours)	Cost*
Rapid-acting				
Aspart (NovoLog)	5 minutes	1 to 2	3 to 4	\$84
Lispro (Humalog)	5 minutes	1 to 2	3 to 4	78
Lispro pen	5 minutes	1 to 2	3 to 4	31 (3 ml)
Regular insulin injection	15 minutes	3 to 4	6 to 8	46
Intermediate-acting				
Insulin isophane suspension (neutral protamine Hagedorn)	1 hour	6 to 8	12	35
Insulin zinc suspension (Lente)	1 hour	6 to 8	12	33
Long-acting				
Glargine	1 hour	None	24	75
Glargine pen†	1 hour	None	24	30 (3 ml)

*—Estimated cost to the pharmacist for one 10-mL vial based on average wholesale prices in Red book. Montvale, N.J.: Medical Economics Data, 2006. Cost to the patient will be higher, depending on prescription filling fee.

†—The authors do not recommend glargine pens because the insulin cartridges are sold separately from the device that holds them, this device only is available in physician offices and not in pharmacies, and the devices are difficult to use.

Adapted from Havas S, Mayfield J. *Self-control: a physician's guide to blood glucose monitoring in the management of diabetes*. Leawood, Kan: American Academy of Family Physicians, 2004.

ongoing cycle of hyperglycemia, followed by hypoglycemia. Four to 8 oz of juice or soda is recommended for initial treatment of hypoglycemia, followed by a fingertip blood glucose test 15 to 20 minutes later to assess the need for further treatment.

Physicians should assure patients that hypoglycemia is an anticipated complication of tight glycaemic control despite the best precautions.³ Patients can be taught to recognize and treat early symptoms of hypoglycemia and to learn from each episode (e.g., how to reduce the chances of recurrence). Severe hypoglycemia can be fatal.

Fortunately, the availability of more physiologic long- and rapid-acting insulins has reduced the incidence of severe hypoglycemia. Patients with frequent hypoglycemia and those who are less aware of hypoglycemic symptoms should raise their short-term blood glucose goals to improve hypoglycemia awareness.

ALWAYS CARRY A SOURCE OF SUGAR

Because food is not always readily available, it is important for patients to carry a source of sugar (e.g., a vial of sugar, glucose tablets, candy) with them in case they become hypoglycemic, particularly if they are tightly controlling their blood glucose levels.

EDUCATE THOSE IN YOUR LIFE ABOUT HYPOGLYCEMIA

The patient or physician can teach persons who have frequent contact with the patient about the symptoms of hypoglycemia, how to treat the condition, how to overcome the patient's occasional hypoglycemia-induced confusion, and the importance of remaining calm during an episode. If the patient needs assistance, they should simply provide him or her with a source of sugar. Patients usually recover quickly; if not, additional sugar can be given.

KEEP GLUCAGON AT HOME

If extreme hypoglycemia inhibits a patient from eating or drinking safely, a single injection of glucagon (1 mg intravenously or subcutaneously) typically will restore consciousness within five to 10 minutes.

WEAR A MEDICAL ALERT BRACELET OR NECKLACE

A medical alert bracelet or necklace stating that the patient has diabetes can alert others that hypoglycemia may be causing unusual behavior, seizure, or coma. This may help the patient receive appropriate treatment faster. Patients can purchase medical identification bracelets or necklaces online.

MANAGE STRESS LEVELS

Physical and psychological stress can cause counterregulatory hormone (e.g., cortisol, epinephrine) elevations, which increase insulin resistance and gluconeogenesis. Depression has been associated with a significant increase in glycaemic control difficulties.⁵⁰

Patients may not recognize symptoms of hypoglycemia if they are distracted by stress. Patients should increase the frequency of blood glucose testing if they are stressed and should adjust their insulin and food intake accordingly. Physical stress (e.g., infection) also can cause blood glucose levels to rise.

LIMIT ALCOHOL CONSUMPTION

Excessive alcohol consumption increases the incidence of hypertension and stroke^{12,26} and inhibits the liver from releasing glucose, exacerbating hypoglycemia. Patients should limit alcohol consumption to one to two drinks per day and focus on maintaining a normal blood glucose level when drinking alcohol.

LEAD A NORMAL LIFE

Patients with diabetes should be reassured that they can do virtually anything those without diabetes can do as long as they maintain glycaemic control. Family physicians can significantly influence their patients' outlooks on living with diabetes by educating them and encouraging them to take control of their health.

Helping Patients Apply Recommendations

The previous recommendations focus on the key educational messages that patients with diabetes need to know. Taking the time to explain these recommendations, instead of simply providing written materials, may ben-

efit patients. These discussions can increase patients' satisfaction and understanding and benefit their future health. For patient education programs, newsletters, and journals on type 1 diabetes, go to the ADA Web site at <http://www.diabetes.org>.

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REFERENCES

1. Wang PH, Lau J, Chalmers TC. Meta-analysis of effects of intensive blood-glucose control on late complications of type 1 diabetes. *Lancet* 1993;341:1306-9.
2. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med* 1993;329:304-9.
3. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-86.
4. The Diabetes Control and Complications Trial Research Group. Effect of intensive diabetes management on macrovascular events and risk factors in the Diabetes Control and Complications Trial. *Am J Cardiol* 1995;75:894-903.
5. Nathan DM, Lachin J, Cleary P, Orchard T, Brillonn DJ, Backlund JY, et al., for the Epidemiology of Diabetes Interventions and Complications Research Group. Diabetes Control and Complications Trial. Intensive diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. *N Engl J Med* 2003;348:2294-303.
6. Wisdom K, Fryzek JP, Havstad SL, Anderson RM, Dreiling MC, Tilley BC. Comparison of laboratory test frequency and test results between African-Americans and Caucasians with diabetes: opportunity for improvement. Findings from a large urban health maintenance organization. *Diabetes Care* 1997;20:971-7.
7. Brown SA. Interventions to promote diabetes self-management: state of the science. *Diabetes Educ* 1999;25(6 suppl):S52-61.
8. Anderson RM, Funnell MM, Butler PM, Arnold MS, Fitzgerald JT, Feste CC. Patient empowerment. Results of a randomized controlled trial. *Diabetes Care* 1995;18:943-9.
9. ALLHAT officers and coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). [Published corrections appear in *JAMA* 2003;289:178; *JAMA* 2004;291:2196] *JAMA* 2002;288:2981-97.
10. Collins R, Armitage J, Parish S, Sleight P, Peto R, for the Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 2003;361:2005-16.
11. Carleton RA, Dwyer J, Finberg L, Flora J, Goodman DS, Grundy SM, et al. Report of the Expert Panel on Population Strategies for Blood Cholesterol Reduction. A statement from the National Cholesterol Education Program, National Heart, Lung, and Blood Institute, National Institutes of Health. *Circulation* 1991;83:2154-232.
12. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, et al., for the National High Blood Pressure Education Program Coordinating Committee. Primary prevention of hypertension: clinical and public health advisory from the National High Blood Pressure Education Program. *JAMA* 2002;288:1882-8.
13. U.S. Department of Health and Human Services. U.S. Department of Agriculture. Dietary guidelines for Americans 2005. Accessed Nov. 15, 2005, at: <http://www.healthierus.gov/dietaryguidelines/>.
14. Influence of intensive diabetes treatment on body weight and composition of adults with type 1 diabetes in the Diabetes Control and Complications Trial. *Diabetes Care*. 2001;24:1711-21.
15. Purnell JQ, Hokanson JE, Marcovina SM, Steffes MW, Cleary PA, Brunzell JD. Effect of excessive weight gain with intensive therapy of type 1 diabetes on lipid levels and blood pressure: results from the DCCT. Diabetes Control and Complications Trial. [Published correction appears in *JAMA* 1998;280:1484] *JAMA* 1998;280:140-6.
16. Moy CS, Songer TJ, LaPorte RE, Dorman JS, Kriska AM, Orchard TJ, et al. Insulin-dependent diabetes mellitus, physical activity, and death. *Am J Epidemiol* 1993;137:74-81.
17. U.S. Office of the Surgeon General. Physical activity and health: report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
18. Havas S, Mayfield J. Self-control: a physician's guide to blood glucose monitoring in the management of diabetes. Leawood, Kan.: American Academy of Family Physicians, 2004:1-24.
19. Anderson JH Jr, Brunelle RL, Koivisto VA, Pftzner A, Trautmann ME, Vignati L, et al., for the Multicenter Insulin Lispro Study Group. Reduction of postprandial hypergly-

- emia and frequency of hypoglycemia in IDDM patients on insulin-analog treatment. *Diabetes* 1997;46:265-70.
20. Brunelle BL, Llewelyn J, Anderson JH Jr, Gale EA, Koivisto VA. Meta-analysis of the effect of insulin lispro on severe hypoglycemia in patients with type 1 diabetes. *Diabetes Care* 1998; 21:1726-31.
 21. Home PD, Lindholm A, Hylleberg B, Round P, for the UK Insulin Aspart Study Group. Improved glycemic control with insulin aspart: a multicenter randomized double-blind crossover trial in type 1 diabetic patients. *Diabetes Care* 1998;21:1904-9.
 22. Danne T, Becker RH, Heise T, Bittner C, Frick AD, Rave K. Pharmacokinetics, prandial glucose control, and safety of insulin glulisine in children and adolescents with type 1 diabetes. *Diabetes Care* 2005;28:2100-5.
 23. Havas S. Educational guidelines for achieving tight control and minimizing complications of type 1 diabetes. *Am Fam Physician* 1999;60:1985-92, 1997-8.
 24. Ratner RE, Hirsch IB, Neifing JL, Garg SK, Mecca TE, Wilson CA, for the U.S. Study Group of Insulin Glargine in Type 1 Diabetes. Less hypoglycemia with insulin glargine in intensive insulin therapy for type 1 diabetes. *Diabetes Care* 2000;23:639-43.
 25. American Diabetes Association. Clinical practice recommendations 2005. *Diabetes Care* 2005; 28 (suppl 1): S1-79.
 26. 10th special report to the U.S. Congress on alcohol and health: highlights from current research from the Secretary of Health and Human Services. Rockville, Md.: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism, 2000:463.
 27. The absence of a glycemic threshold for the development of long-term complications: the perspective of the Diabetes Control and Complications Trial. *Diabetes* 1996;45:1289-98.
 28. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. *Diabetes* 1995;44:968-83.
 29. Fields LE, Burt VL, Cutler JA, Hughes J, Roccella EJ, Sorlie P. The burden of adult hypertension in the United States 1999 to 2000: a rising tide. *Hypertension* 2004;44:398-404.
 30. Ford ES, Mokdad AH, Giles WH, Mensah GA. Serum total cholesterol concentrations and awareness, treatment, and control of hypercholesterolemia among U.S. adults: findings from the National Health and Nutrition Examination Survey, 1999 to 2000. *Circulation* 2003;107:2185-9.
 31. Malarcher AM, Ford ES, Nelson DE, Chrismon JH, Mowery P, Merritt RK, et al. Trends in cigarette smoking and physicians' advice to quit smoking among people with diabetes in the U.S. *Diabetes Care* 1995;18:694-7.
 32. Ford ES, Herman WH. Leisure-time physical activity patterns in the U.S. diabetic population. Findings from the 1990 national health interview survey—health promotion and disease prevention supplement. *Diabetes Care* 1995;18:27-33.
 33. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
 34. Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, et al.; National Heart, Lung, and Blood Institute; American College of Cardiology Foundation; American Heart Association. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. [Published correction appears in *Circulation* 2004;110:763] *Circulation* 2004;110:227-39.
 35. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-52.
 36. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. [Published correction appears in *BMJ* 1994;308:1540] *BMJ* 1994;308:81-106.
 37. The Diabetic Retinopathy Study Research Group. Indications for photocoagulation treatment of diabetic retinopathy: diabetic retinopathy study report no. 14. *Int Ophthalmol Clin* 1987;27:239-53.
 38. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD, for the Collaborative Study Group. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. [Published correction appears in *N Engl J Med* 1993;330:152] *N Engl J Med* 1993;329:1456-62.
 39. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA* 1979;241:2035-8.
 40. Ferris FL III, Chew EY, Hoogwerf BJ, for the Early Treatment Diabetic Retinopathy Study Research Group. Serum lipids and diabetic retinopathy. *Diabetes Care* 1996;19:1291-3.
 41. Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, et al. Residual lifetime risk for developing hypertension in middle-aged women and men. The Framingham heart study. *JAMA* 2002;287:1003-10.
 42. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease: an update. [Published correction appears in *Hypertension* 2001;37:1350] *Hypertension* 2001;37:1053-9.
 43. Karter AJ, Ackerson LM, Darbinian JA, D'Agostino RB Jr, Ferrara A, Liu J, et al. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente diabetes registry. *Am J Med* 2001;111:1-9.
 44. Bina DM, Anderson RL, Johnson ML, Bergenstal RM, Kendall DM. Clinical impact of prandial state, exercise, and site preparation on the equivalence of alternative-site blood glucose testing. *Diabetes Care* 2003;26:981-5.
 45. Klonoff DC. Continuous glucose monitoring: roadmap for 21st century diabetes therapy. *Diabetes Care* 2005;28:1231-9.
 46. Hirsch IB. Insulin analogues. *N Engl J Med* 2005;352:174-83.
 47. Multiple-component insulin regimens. In: Klingensmith, Georgeanna J, eds. *Intensive Diabetes Management*. 3rd ed. Alexandria, Va.: American Diabetes Association, 2003.
 48. Collins BJ, Richardson SG, Spence BK, Hunter J, Nelson JK. Safety of reusing disposable plastic insulin syringes. *Lancet* 1983;1:559-61.
 49. Home PD, Ashwell SG. An overview of insulin glargine. *Diabetes Metab Res Rev* 2002;18(suppl 3):S57-63.
 50. Van Tilburg MA, McCaskill CC, Lane JD, Edwards CL, Bethel A, Feinglos MN, et al. Depressed mood is a factor in glycemic control in type 1 diabetes. *Psychosom Med* 2001;63:551-5.