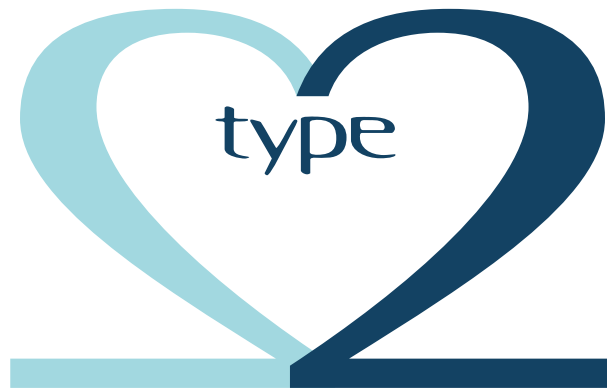


**The Council for the Advancement of Diabetes
Research and Education (CADRE) Presents**

Reducing Cardiovascular Risk in the Patient With Type 2 Diabetes



Proceedings From a Satellite Symposium Held in Conjunction With the AADE 32nd Annual Meeting and Exhibition

Reducing Cardiovascular Risk in Patients With Type 2 Diabetes: Strategies to Implement Medical Nutrition Therapy and Overcome Barriers to Insulin Use

As recently as a decade ago, the increased risk of cardiovascular disease (CVD) in patients with type 2 diabetes was considered at least partially attributable to diabetes-associated insulin resistance and high levels of circulating insulin. In recent years, however, increasing evidence suggests that insulin is not the culprit behind CVD. Many studies have shown a link between elevated glucose levels and CVD, and other results have suggested that the problem lies not strictly with high levels of circulating insulin, but rather with a mismatch between food intake and the timing of insulin availability. Recent studies have also demonstrated that insulin administration coupled with improved glucose control benefits the cardiovascular system in many ways.

One key to achieving these benefits is by mimicking as closely as possible the normal physiology of insulin release in response to food intake. This strategy, made possible by the introduction of insulin analogues, allows patients to lower their glucose to near-normal levels while minimizing their risk of hypoglycemia. Another essential element in effective management is medical nutrition therapy (MNT). MNT has been proven to reduce both low-density lipoprotein (LDL) cholesterol and blood pressure and should be part of any treatment plan no matter which medications are used to control glucose, cholesterol, or blood pressure.

This newsletter provides a summary of the proceedings of a joint symposium on this topic held on August 10, 2005, by the American Association of Diabetes Educators (AADE) and the Council for the Advancement of Diabetes Research and Education (CADRE). Regardless of whether or not you were able to attend our original presentation, we hope that this information will prove valuable for you and for your patients.

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Intensive Diabetes Control: Reaping the Benefits Promised by Clinical Trials

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Macrovascular complications are the major cause of mortality in individuals with type 2 diabetes (T2DM), accounting for approximately 65% of all deaths. Overall, patients with diabetes have a 2- to 4-fold greater risk of mortality due to cardiovascular disease (CVD) than those without diabetes. Studies have also suggested that diabetes should be considered a "coronary heart disease risk equivalent," implying that individuals with diabetes appear to have the same CVD risk as nondiabetic individuals with documented heart disease. Clearly, steps should be taken early on—even prior to T2DM onset—to prevent CVD.

Early CVD Risk in the Natural History of Diabetes

The risk for CVD in T2DM begins before blood glucose levels start to rise. The transition from prediabetes to diabetes is characterized by increasing insulin resistance requiring compensatory insulin secretion, with eventual β -cell failure, followed by rises in fasting and postprandial blood glucose levels. However, even prediabetic individuals are at risk for macrovascular complications. This was described by Hu and colleagues, who found in the Nurses' Health Study that baseline CVD risk for prediabetic women was significantly higher than for women who did not develop T2DM. This suggests that mechanisms are present in prediabetic states that promote the development of CVD well before the diagnosis

of diabetes is made.

A Combination of Metabolic Factors Contribute to CVD Risk

Individuals with diabetes or prediabetes tend to have a clustering of metabolic abnormalities; this clustering has been referred to in the past as the metabolic syndrome, syndrome X, and, more recently, the cardiometabolic risk syndrome. The primary components of the syndrome include insulin resistance, hypertension, dyslipidemia, and obesity. The term cardiometabolic risk syndrome appropriately indicates the prognostic significance of these components, in that each individually confers risk for CVD. In combination, CVD risk increases as the number of components increases. Prevention of CVD events requires a multipronged approach, which includes

addressing all metabolic components, as well as modifying other major risk factors such as smoking.

Current Status of CVD Prevention in Diabetes

In spite of evidence-based guidelines generated by a host of medical organizations, it appears that we are still not doing very well at reaching blood glucose, blood pressure, and lipid goals. The National Health and Nutrition Examination (NHANES) III 1988-1994 and the NHANES 1999-2000 cohort data were compared for the control of CVD risk factors in US adults with diabetes. Based on targets of A1C <7%, blood pressure <130/80 mm Hg, and cholesterol <200 mg/dL, only 5% of all subjects had good control of all 3 risk factors in 1988-1994. By 1999-2000, only 7.3% demonstrated good control of all 3 risk factors, which is not a great improvement. Furthermore, even though NHANES analyses of mortality trends indicate that individuals without diabetes saw significant decreases in CVD mortality from the 1970s to the 1980s, men with diabetes had a much smaller decrease, while CVD mortality in women with diabetes actually rose by nearly 25%.

Why isn't CVD prevention improving in patients with diabetes? One reason may be that, as outlined above, CVD risk begins early, long before the presence of diabetes prompts medical evaluation. It is also likely that nontraditional risk factors, which are just now starting to be better understood, play a role.

The Role of Nontraditional Risk Factors in T2DM CVD Risk

Nontraditional risk factors may help to explain the increased risk for CVD in prediabetes and diabetes. One of these, endothelial cell dysfunction, is thought to be the earliest atherosclerotic lesion. The endothelium is an active organ that plays an important role at the interface between the bloodstream and internal organs, maintaining appropriate blood flow and tissue perfusion. Endothelial dysfunction appears to have prognostic value in predicting cardiovascular events in patients with CVD. This abnormality can be found very early in at-risk populations—long before the onset of CVD or diabetes. Other non-

traditional risk factors that have been associated with endothelial dysfunction, and which also appear to confer independent risk for CVD, include insulin resistance, inflammation, coagulopathy, and postprandial hyperglycemia. For example, elevated levels of C-reactive protein (CRP), a marker of inflammation, are associated with insulin resistance, T2DM, and CVD. Plasminogen activator inhibitor-1 (PAI-1), another nontraditional risk marker, is found at increased levels in the setting of insulin resistance.

The Benefits of Insulin Therapy

The beneficial effects of insulin therapy have been sullied by a long-standing misunderstanding—the concept that insulin is atherogenic. This derives from epidemiologic data relating elevated endogenous insulin levels with increased CVD risk and from a few observational studies suggesting a relationship between insulin therapy and CVD risk. However, these studies did not differentiate between the presence of elevated insulin levels (or the requirement for insulin treatment) and the presence of insulin resistance, which is now considered to be the major mediator of CVD risk. To further muddy the waters, in studies of both type 1 diabetes patients (Diabetes Control and Complications Trial [DCCT]) and T2DM patients (United Kingdom Prospective Diabetes Study [UKPDS]), intensive glucose control had a greater short-term impact on preventing microvascular than macrovascular complications.

However, several recent studies have shed a more positive light on the beneficial effects of insulin treatment. In the Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study, patients with diabetes who were hospitalized with acute myocardial infarction were given either standard treatment or standard treatment plus an insulin infusion followed by ≥ 3 months of multidose subcutaneous insulin. Those who received the insulin had a 28% relative reduction in 5-year mortality. A compelling recent piece of evidence comes from the 20-year follow-up of the DCCT, the Epidemiology of Diabetes Interventions and Complications (EDIC) trial. Subjects who received 6.5 years of early, intensive insulin therapy during

the DCCT have experienced subsequent CVD rates 42% lower than formerly conventionally treated participants ($P < 0.007$).

Conclusion

The processes that lead to CVD in diabetes begin years before diabetes onset. For this reason, all patients with diabetes should actually be treated as if they already have CVD. Because of the multifactorial nature of CVD in T2DM, and because both traditional and nontraditional risk factors play a role in its development, we must always consider our patients' full range of metabolic control needs when developing treatment plans. One important treatment modality is insulin. In spite of prior concerns that hyperinsulinemia and/or exogenous insulin might confer CVD risk, the true culprit is insulin resistance. Insulin treatment given to promote good metabolic control is clearly beneficial, both for its glucose-lowering and anti-inflammatory effects. Recent evidence actually suggests that insulin treatment may be associated with decreased CVD risk.

Recommended Reading

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Visit the CADRE Web site at www.cadre-diabetes.org to view William Cefalu's Question and Answer session and learn more about the role of insulin infusion therapy in acute myocardial infarction, if clinical benefits are associated with measuring lipid subfractions, and the benefits of targeting lower LDL cholesterol levels.



Patient Education: Addressing Multiple Risk Factors Through Medical Nutrition Therapy

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Medical nutrition therapy (MNT) is integral to both the treatment and prevention of diabetes and its related complications. Nutrition guidelines issued by the American Diabetes Association (ADA), the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) play an important role in the formulation of MNT recommendations for diabetes. These recommendations are presented in the following charts, which include descriptions of specific dietary and lifestyle modifications relevant to the management of diabetes through MNT. Recommendations from other leading organizations are also discussed. Research findings in support of each of these recommendations are provided, including the classification of major ADA nutrition guidelines according to an evidence-based grading system.

It is easy to become overwhelmed with the sheer number of MNT recommendations available. With these charts, I want to help translate available evidence into practicable, real-world recommendations and strategies that you can apply in your work with patients. Throughout this document, the need for patient education and involvement in the MNT process is stressed, along with an emphasis on the importance of setting realistic, individualized goals and treatment plans for each patient.

Recommendations for Daily Nutrition

Table 1 compares ADA and ATP III nutrition recommendations. The ADA uses a grading system consisting of 4 cate-

gories to characterize the level of evidence available in support of each recommendation. These include strong evidence (level A), some evidence (B), limited evidence (C), and expert consensus (D). Since the ADA incorporates its nutrition recommendations from several major organizations, including the NCEP, there are many similarities between ADA and ATP III guidelines. Some variance does exist, however. Although the ADA specifies that saturated fat intake should not exceed 10% of total calories for the general population, a reduced intake of 7% is indicated

Table 2. NCEP ATP III Guidelines Steps in TLC

First visit	<ul style="list-style-type: none"> • Introduce TLC diet with emphasis on reduced saturated fats and cholesterol • Initiate moderate physical activity • Consider referral to nutrition professional for MNT
Second visit (6 weeks later)	<ul style="list-style-type: none"> • Evaluate LDL-C response • If LDL-C goal is achieved, maintain current TLC intensity • If LDL-C goal is not achieved, increase TLC intensity, reinforce reduction in saturated fat and cholesterol, consider plant stanols/sterols and increased viscous fiber • Consider referral for MNT
Third visit (6 weeks later)	<ul style="list-style-type: none"> • Evaluate LDL-C response • If LDL-C goal is achieved, maintain current TLC intensity • If LDL-C goal is not achieved, continue TLC, consider drug therapy with LDL-C– lowering medication, initiate treatment for metabolic syndrome (if present) • Consider referral for MNT
Long-term follow-up	<ul style="list-style-type: none"> • Follow-up/monitoring visits every 4-6 months (year 1) • Follow-up/monitoring visits every 6-12 months (year 2 and thereafter) • More frequent visits recommended for patients on LDL-C–lowering medication

when low-density lipoprotein (LDL) cholesterol levels exceed 100 mg/dL, which is consistent with the standard ATP III recommendation. To lower LDL cholesterol levels and achieve concurrent weight loss, the ADA recommends that saturated fat intake be reduced. If weight loss is not desired, saturated fat should be replaced with carbohydrates or monounsaturated fat. According to the ADA, dietary cholesterol intake should be <300 mg/day unless LDL cholesterol levels are high, in which case daily intake should not exceed 200 mg/day. The ATP III recommends this lower level of intake as a general standard. The ADA and ATP III are consistent regarding polyunsaturated fat, protein, and plant stanols/sterols recommendations. The ADA also reports that when monounsaturated fat replaces carbohydrates in a weight-maintaining diet, postprandial glucose and plasma triglyceride levels may improve, but fasting plasma glucose (FPG) and A1C levels may not (B).

Use a Stepwise Approach to Lower Cholesterol Levels

The successful implementation of ATP III recommendations for lowering LDL cholesterol requires a phased approach (Table 2). This allows for a stepwise introduction to therapeutic lifestyle changes (TLC) and periodic assessment of LDL cholesterol response and patient status. Referral to a nutritionist or certified diabetes educator (CDE) for MNT

Table 1. ADA and ATP III Nutrition Recommendations

NUTRIENT	ADA	ATP III TLC DIET
Saturated fat	<10% of calories (A) <7% of calories if LDL-C >100 (A)	<7% of calories
Polyunsaturated fat (PUFA)	<10% of calories (B)	<10% of calories
Monounsaturated fat (MUFA)	MUFA plus carbohydrates provide 60%-70% of calories (D)	<20% of calories
Transunsaturated fat	Minimize (A)	
Total fat		25%-35% of calories
Cholesterol	<300 mg/day (A) <200 mg/day if LDL-C >100 (A)	<200 mg/day
Carbohydrate	MUFA plus carbohydrates provide 60%-70% of calories (D)	50%-60% of calories
Total fiber	Encourage (B)	20-30 g/day
Soluble fiber		10-25 g/day
Protein	15%-20% of calories if normal renal function (B)	15% of calories
Plant stanols/sterols	2 g/day (B)	2 g/day

LDL-C = low-density lipoprotein cholesterol (mg/dL).
TLC = therapeutic lifestyle changes.

guidance is advised. Professionals involved in implementing TLC should place an emphasis on patient empowerment and education. In addition, new dietary and physical activity recommendations should be introduced gradually, to prevent patient “burn out.” This approach improves compliance and encourages patients to be active participants in the TLC process. Studies have shown that patients who are involved in managing their chronic disease have more successful outcomes.

Reduce Cholesterol Through MNT

ATP III recommendations for lowering LDL cholesterol include reduced intake of saturated fats and cholesterol, weight loss, and the addition of viscous fiber and plant sterols/stanols to the diet. Reductions in LDL cholesterol levels possible with individual ATP III dietary modifications

Dietary Component	Dietary Change	Approximate LDL-C Reduction
Saturated fat	<7% of calories	8%-10%
Dietary cholesterol	<200 mg/day	3%-5%
Weight reduction	Lose 10 pounds	5%-8%
Viscous fiber	5-10 g/day	3%-5%
Sterols/stanols	2 g/day	6%-15%
Cumulative estimate		20%-30%

have been estimated based upon available literature (Table 3). Although clinical trial data are not yet available, it is believed that a cumulative LDL cholesterol-lowering effect of 20% to 30% could be achieved when these therapeutic options are combined. As a result of this cumulative LDL cholesterol response, MNT has the potential to produce LDL cholesterol reductions comparable to those achieved with standard doses of statin drugs.

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI 18.5-24.9 kg/m ²)	5-20 mm Hg/ 22-lb weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables and low-fat dairy products, with reduced total fat and saturated fat content	8-14 mm Hg
Dietary sodium Reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2-8 mm Hg
Physical activity	Engage in regular aerobic exercise such as brisk walking at least 30 minutes/day, most days of the week	4-9 mm Hg
Moderate alcohol consumption	Men: No more than 2 drinks/day (eg, 24 oz beer, 10 oz wine or 3 oz 80-proof whiskey) Women: No more than 1 drink/day	2-4 mm Hg

BMI = body mass index.
BP = blood pressure.
DASH = Dietary Approaches to Stop Hypertension.

Manage Hypertension With Lifestyle Change

The JNC 7 guidelines for the prevention and management of hypertension recommend lifestyle modifications including weight loss, adoption of the DASH eating plan, dietary sodium reduction, exercise, and moderation of alcohol intake (Table 4). Implementation of these JNC 7 recommendations has been shown to reduce blood pressure and decrease the risk of cardiovascular disease (CVD), leading to a lower incidence of stroke, myocardial infarction, heart failure, and kidney disease. In addition, these lifestyle modifications may be used to replace or enhance the efficacy of antihypertensive medications. For example, the results of one study showed that a diet consisting of the DASH eating plan combined with reduced sodium intake (1600 mg/day) was comparable to single drug therapy for hypertension management.

Increase Fiber Intake

Fiber, an indigestible complex carbohydrate, is associated with a variety of health benefits including reduced CVD risk. The ADA recommends daily fiber consumption of at least 20 to 35 g. Sources include both insoluble (eg, whole-grain breads, cereals, fruits, vegetables) and soluble fibers (eg, oats, barley, soy nuts, artichoke). It is estimated that the typical American only consumes 17 g of fiber daily, so it is reasonable to estimate that most patients will require an increase of at least 5 to 10 g/day. This is the equivalent of adding a daily bowl of oatmeal, 3 servings of fruits and vegetables, and a daily serving of beans to one's diet (Table 5). Fiber supplementation (eg, Metamucil®) can also be a useful way to increase fiber intake.

Increase Omega-3 Fatty Acid Intake

The polyunsaturated fats known as omega-3 fatty acids are essential parts of a balanced diet. Marine life and plants are the 2 sources of these fatty acids (Table 6). Marine sources offer eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), while plant sources such as flaxseed are rich in alpha-linolenic acid. The average American consumes about 160 mg/day of omega-3 fatty acids, with plants being the primary source.

Flaxseed is a rich source of alpha-linolenic acid and lignin and can help meet dietary needs for both omega-3 fatty acids and fiber (Table 7). The seeds have a nutty flavor, can be used whole or ground, and can be sprinkled on a variety of foods (soups, cereals, yogurt, salads) or used as a substitute for shortening or eggs when cooking. Grinding will help release more of the omega-3 oils than chewing. A coffee grinder works well for this. One tablespoon of ground flaxseed provides 1800 mg of omega-3 fatty acids and 2.2 g of fiber. Grinding the seeds releases the oils, making

Fiber-Containing Foods	Grams of Soluble Fiber
1.5 cups cooked oatmeal	3
1 medium fruit	1-2
1 cup cooked vegetables	2
1 cup (100 g) cooked legumes	2-3

Type	Omega-3 Fatty Acid	Sources
Marine	Eicosapentaenoic acid (EPA) Docosahexaenoic acid (DHA)	Salmon, tuna, mackerel, herring, sardines
Plant	Alpha-linolenic acid	Flaxseed, canola, walnuts

them available for absorption. A tablespoon of flaxseed oil contains 8000 mg of omega-3 fatty acids but is higher in

	Calories	Omega-3 Fats	Fiber
1 tbsp ground flaxseed	36	1800 mg	2.2 g
1 tbsp flax oil	124	8000 mg	0 g

calories than flaxseed and does not provide fiber. There are no definitive guidelines regarding how much flaxseed is recommended; however, several research studies have found benefits associated with 1 to 3 tablespoons daily of ground flaxseed or flax oil.

Source	Amount (oz)
White tuna	4
Sardines	2-3
Chum or sockeye salmon	4.5
Pink, chinook, or Atlantic salmon	2-3
Atlantic cod	12
Catfish	20
Scallops	17

Preparation: Fish should be baked or broiled in order to maintain omega-3 levels.

reduction in all-cause mortality in male myocardial infarction survivors who had a 200 to 400 g increase per week of fatty fish in their diets. Similarly, the GISSI-Prevention Study reported a 20% reduction in all-cause mortality and a 45% reduction in sudden death in coronary heart disease (CHD) patients given 850 mg/day of omega-3 fatty acids. Therefore, the American Heart Association (AHA) recommends that individuals without CHD eat fatty fish at least 2 times a week as well as increase intake of foods rich in alpha-linolenic acid. Individuals with CHD should consume a combined EPA/DHA total of ~1000 mg/day. Table 8 shows fish-based sources for obtaining 1000 mg/day of EPA/DHA. Supplementation can also be used; omega-3 supplements should be refrigerated and taken in the evening. Consumers should read labels to determine the dosage required to obtain 1000 mg/day of combined EPA and DHA. Owing to the triglyceride-lowering effects of omega-3, individuals with hypertriglyceridemia should try to consume 2 to 4 g/day of EPA/DHA.

A number of studies have explored the benefits of omega-3 fatty acids. Two randomized controlled trials of interest are the Diet and Reinforcement Trial (DART) and the GISSI-Prevention Study. DART reported a 29%

Fish	Recommended Limits for Children, Pregnant Women, Nursing Mothers, Women Who May Become Pregnant
Shark, swordfish, king mackerel, tilefish	Do not eat
Canned white albacore, tuna steaks	≤6 oz/week
All other fish*	≤12 oz/week

* Low levels of methylmercury are found in shrimp, canned light tuna, salmon, pollock, catfish, cod.

Avoid Mercury Exposure

Due to the presence of methylmercury in almost all fish and shellfish, the US Food and Drug Administration (FDA) and US Environmental Protection Agency recommend that children, pregnant women, nursing mothers, and women who may become pregnant restrict their intake of certain fish (Table 9). Using these guidelines, the dietary benefits of fish and shellfish can still be realized while exposure to methylmercury is limited. The FDA has also set specific guidelines for all other adults on intake of certain fish high in methylmercury.

Increase Soy Protein Intake

The combined results of 38 controlled clinical studies showed substantial cholesterol reductions associated with increased soy intake. Research supports a daily consumption of ≥25 g soy protein (Table 10). This is the equivalent of adding a 4 oz serving of tofu and 1/2 cup of soy nuts in one's daily diet.

Benefits of Nuts, Cinnamon, and Dark Chocolate

Nuts and peanuts are rich in unsaturated fats, fiber, magnesium, vitamins, minerals, and antioxidants (Table 11). The Nurses' Health Study has found that the regular consumption of macadamia nuts, walnuts, peanuts, peanut butter, or almonds has been associated with a decreased risk of type 2 diabetes mellitus (T2DM) and CHD. However, due to the high fat content of nuts and peanut butter, it is recommended that they be substituted for refined grains and meats in the diet.

Recent studies also indicate that cinnamon and dark chocolate may provide significant health benefits. In one

Soy Product	Protein (g)	Benefits	Beneficial Components
1 cup green soy beans	22	9% reduction in total cholesterol 12.9% reduction in LDL-C 10.5% reduction in triglycerides	Isoflavones Saponins Fiber Phytic acid
½ cup soy nuts	17		
1 cup soy milk	7		
4 oz tofu	9		
¼ cup miso	16		
½ cup tempeh	16		

Table 11. Benefits of Nuts, Cinnamon, and Dark Chocolate

	Benefits	Recommendations
Nuts Macadamia Walnuts Almonds Peanuts Peanut butter	Shown to decrease T2DM and CHD risk	Substitute nuts for refined grains or meats
Cinnamon	One study showed reductions in mean serum glucose (18%-29%), triglycerides (23%-30%), and LDL-C (7%-27%)	A wide range of intake may be beneficial; ≤1 g daily is likely to be beneficial
Dark Chocolate	One study showed reductions in mean 24-hour blood pressure (-11.9/-8.5 mm Hg), insulin resistance, and LDL-C (-15.5 mg/dL)	No current recommendations available; however, daily intake of flavonol-rich dark chocolate may provide cardiovascular benefit

study of patients with T2DM, it was found that cinnamon at 1, 3, or 6 mg daily was associated with significant decreases in glucose levels, triglycerides, LDL cholesterol, and total cholesterol. These benefits were sustained for a 20-day period beyond the length of the study, leading the authors to conclude that cinnamon intake of ≤1 g daily could be helpful. Another crossover study conducted in hypertensive patients indicated that daily consumption of 100 g of flavonol-rich dark chocolate significantly decreased 24-hour blood pressure, insulin resistance, and LDL cholesterol. It is important to note that for these benefits to be exerted, chocolate must be high in flavonols; chocolates with the highest flavonol levels are dark (ie, bitter or semi-sweet, not milk, chocolate). European chocolates, as opposed to American, tend to have higher flavonol levels.

The Portfolio Diet: Putting the Recommendations Into Practice

The Portfolio Diet is based on the NCEP ATP III, AHA, and FDA recommendations for reduction of serum cholesterol through dietary modifications. By prescribing a meal pattern consisting of combined, increased intake of plant sterols (1-1.2 g/1000 kcal), viscous fibers (8.3-9.8 g/1000 kcal), soy protein (16.2-21.4 g/1000 kcal), and almonds

(14 g/1000 kcal) alongside a low-saturated fat and low-cholesterol diet, studies have shown that the Portfolio Diet can achieve cholesterol reductions comparable to those observed with initial therapeutic doses of first-generation statins. The Portfolio Diet may also be used in combination with statins to reduce their dosage levels.

Engage in Regular Physical Activity

Regular physical activity provides significant benefits to individuals with T2DM (Table 12). These benefits include increased insulin sensitivity, improved glycemic control, and decreased CVD risk. In addition, a Centers for Disease Control and Prevention (CDC) study found that walking at least 2 hours each week significantly reduces mortality rates for adults with diabetes regardless of age, BMI, diabetes duration, or comorbid conditions. According to this study, CVD and all-cause mortality rates for individuals with diabetes who walked a minimum of 2 hours per week were reduced by 34% and 39%,

respectively, compared with inactive adults. Those who walked 3 to 4 hours per week experienced the lowest mortality rates, corresponding to a 54% reduction compared with inactive individuals. Moderate intensity walking was associated with the largest reduction in mortality rates. The study concluded that 1 death per year could be prevented for every 61 people who followed a regular exercise program consisting of at least 2 hours of walking each week.

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Table 12. Physical Activity

Exercise habits of adults ≥18 years of age in the United States (1997-1998):

- 31% engage in no regular activity
- 38% engage in less activity than recommended
- <25% walk at least 30 minutes/day

CDC research examining relationship of walking to mortality among US adults with diabetes:

- Prospective cohort study of 2896 adults over 8 years
- Mortality rates for those who walked at least 2 hours/week compared with inactive individuals
 - 39% lower all-cause mortality rate among walkers
 - 34% lower CVD mortality rate among walkers
 - Lowest mortality rates for those who walked 3 to 4 hours/week
 - Lowest mortality rates for moderate-intensity walking
- Study showed 1 death per year may be prevented for every 61 people who walk at least 2 hours/week

Visit the CADRE Web site at www.cadre-diabetes.org to view Melinda Maryniuk's Question and Answer session and learn more about plant stanol and sterol supplements, as well as whether taking vitamin E or other antioxidant supplements can reduce CVD risk.

Overcoming Barriers to Intensive Insulin Administration

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The prevalence of type 2 diabetes (T2DM) in the United States has tripled in the last 30 years. Today, approximately 18.3 million Americans have diabetes and over 40 million have pre-diabetes. T2DM is characterized by both insulin resistance and progressive β -cell dysfunction. Multiple studies have documented the long-term benefits of tight glycemic control. Owing to this, increased focus has turned to strategies that will improve blood glucose control without exposing patients to hypoglycemia or other adverse events.

To reach and maintain blood glucose target levels, clinicians must implement more intensive treatment regimens than have generally been used. Traditionally, patients with newly diagnosed T2DM have been managed in a stepwise fashion beginning with lifestyle changes that emphasize diet and exercise. Oral antihyperglycemic monotherapy is added when these changes are no longer adequate to maintain normoglycemia. This is followed by polytherapy with 2 or even 3 oral agents, and finally, insulin therapy is added. Although considered the standard of care, the stepwise approach has historically resulted in

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extended periods of poor glycemic control. This is because, in order to be effective, this model requires diligent monitoring and a transition to more intensive therapies when glycemic control begins to wane. However, the A1C action point at which therapeutic change is implemented has typically been set at >8%, not >7%. In a retrospective analysis of 7208 patients who undertook stepwise therapy, Brown and colleagues found that, between diagnosis and starting insulin, the average patient accumulated nearly 5 cumulative years of A1C levels >8.0% and about 10 years of A1C >7.0%.

The news isn't all bad, however. Against this backdrop of poor glycemic control, results from several studies demonstrate that more intensive therapy, including earlier, targeted use of insulin, can help reverse this trend. Exogenous insulin preserves and improves β -cell function, helps to restore normal insulin sensitivity, and improves the efficacy of oral medications.

In spite of insulin's safety and efficacy, patients are reluctant, for many reasons, to start insulin therapy. They are concerned about lifestyle changes and restrictions, social embarrassment, painful injections, and the association of insulin with worsening health. These concerns must be addressed by clinicians, who often have their own barriers to implementing insulin. The Diabetes Attitudes, Wishes, and Needs (DAWN) study found that 40% of health care providers preferred to delay starting insulin until absolutely necessary. Both

physicians and patients worry about weight gain and hypoglycemia associated with insulin use. Primary care physicians, who treat the majority of T2DM patients, often lack the experience and support they need—that is, access to diabetes educators, nurses, and dietitians—to successfully manage insulin regimens.

To overcome these obstacles, physicians must abandon the old stepwise model for a more physiologic and aggressive treatment approach. Because individualized insulin regimens are complicated to implement, when possible, providers should collaborate with support staff trained to educate and help manage T2DM patients. One good initial approach involves discussing at diagnosis goals for blood glucose and the concept of insulin as a valuable and routine diabetes medication. This will also facilitate addressing patients' fears and concerns early in their disease. In some cases, short-term insulin used to control severe hyperglycemia post-diagnosis can provide rapid glycemic control and be used as a tool to allay concerns about its later use.

Simple insulin regimens can also pave the way to intensive insulin use long before it becomes a "last resort." For example, adding a single bedtime, or basal, dose of long-acting glargine or NPH to an oral regimen can enhance the efficacy of oral agents, preserve β -cell function, and lower A1C. Physicians can easily adjust and titrate basal dosing, and patients are required to perform only 1 additional check of fasting glucose. The Treat-to-Target Trial has demonstrated that nighttime insulin added to oral agent therapy leads to

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A1C levels <7% in a majority of previously uncontrolled patients.

As patients become more comfortable with the demands of insulin therapy

and additional self-monitoring, they could move to a basal-bolus insulin regimen. This requires the addition of a short-acting insulin analogue, such as insulin lispro or aspart, before meals. The basal-bolus regimen most closely mimics the body's natural insulin response. The basal dose provides a steady plasma insulin level for approximately 24 hours, while the bolus doses exhibit a rapid physiologic peak to address deficient first-phase postprandial insulin secretion. Although 3 additional shots a day seems like a major burden, insulin pumps and pens can increase the ease and convenience of injections, and patients are often pleased to learn they have more control over when they can eat.

Regardless of the timing of insulin's introduction, it is incumbent on the provider to consistently discuss insulin use as an eventuality. Patients should be encouraged to learn more about insulin delivery methods and the drug's mechanism of action and should be educated regarding newer analogues, which provide for more flexible delivery options, as well as

decreased adverse event profiles. All patient education should be provided in a positive and affirming environment, with emphasis placed on the health and quality-of-life benefits associated with insulin replacement.

Recommended Reading

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Visit the CADRE Web site at www.cadre-diabetes.org to view Roberta McDuffie's Question and Answer session and learn more about current research on oral agent use in prediabetes.