Approach to Treatment of the Patient with Metabolic Syndrome: Lifestyle Therapy

Neil J. Stone, MD*, and David Saxon, BA

The National Cholesterol Education Program’s Adult Treatment Panel III definition of the metabolic syndrome identifies those at high risk for diabetes mellitus and/or a cardiac event by clustering a number of easily measured clinical findings, including abdominal obesity, elevated plasma levels of triglycerides, low plasma levels of high-density lipoprotein cholesterol, elevated fasting blood glucose, and elevated blood pressure. The presence of ≥3 of these 5 risk factors justifies a diagnosis of the metabolic syndrome. This article focuses on root causes of the syndrome (atherogenic diet, sedentary lifestyle, and overweight/obesity) and highlights recent studies that demonstrate the effectiveness of therapeutic lifestyle changes in improving or preventing the components of the metabolic syndrome. We offer a practical approach with a focus that embraces not only patients, but also physicians and healthcare professionals as well as the larger healthcare system. © 2005 Elsevier Inc. All rights reserved. (Am J Cardiol 2005;96[suppl]:15E–21E)

The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) offered an evidence-based approach to management of the patient with high plasma levels of cholesterol.1 Due to the strong causal relation between elevated plasma values for low-density lipoprotein (LDL) cholesterol and coronary artery disease (CAD), the primary focus of the ATP III algorithm was on LDL cholesterol. Knowledge of LDL cholesterol plasma level alone, however, is not enough to describe individual risk for CAD. Risk factors increase the likelihood of CAD at every level of LDL cholesterol, and individuals with multiple or severe risk factors are found to have CAD at low plasma levels of LDL cholesterol. An important syndrome of multiple metabolic risk factors, the metabolic syndrome was operationally defined in the ATP III report by requiring ≥3 of 5 easily measured clinical and laboratory parameters.2 The components and the diagnostic criteria for the metabolic syndrome are given in Table 1.

Subsequent to the ATP III report, studies have shown that metabolic syndrome enhances the risk of CHD, not only in those with elevated plasma levels of LDL cholesterol, but also in those with average or below-average levels.3,4 Even individuals with 1 or 2 risk factors of the metabolic syndrome are at increased risk. Moreover, presence of the metabolic syndrome predicts CAD risk more strongly than each of the individual risk factors does alone. This accentuated CAD risk likely involves not only the dyslipidemia (high plasma levels of triglycerides and low plasma levels of high-density lipoprotein [HDL] cholesterol), hypertension, and hyperglycemia, but also other clinically unmeasured risk factors such as prothrombotic (eg, fibrinogen, plasminogen activator inhibitor–1) and proinflammatory (eg, ultrasensitive C-reactive protein) markers. Whereas each risk factor can be dealt with individually, the initial therapeutic approach to the metabolic syndrome should focus on reversing its root causes of atherogenic diet, sedentary lifestyle, and overweight or obesity. This article reviews those studies that have focused on what ATP III called therapeutic lifestyle change as the nonpharmacologic approach to management of the metabolic syndrome.

Atherogenic Diet

Currently, the diet of the United States is characterized by being high in calories, saturated fat, and dietary cholesterol. Because of the key role of saturated fat intake in raising plasma cholesterol levels and eventual CAD death rates,5 national organizations have recommended a restriction in saturated fat intake for several decades. For many years, the NCEP and the American Heart Association (AHA) advocated an intake of <7% of energy as saturated fats and <30% of total energy as fat. In the 2001 ATP III report, total fat was allowed to range from 25% to 35% of total energy because it was recognized that some groups may benefit from a higher intake of unsaturated fat and less carbohydrate. Willet and Leibel6 reviewed randomized dietary trials lasting ≥1 year and concluded that fat consumption had little, if any, effect on body fatness. They also noted that the substantial decline in total dietary fat was associated with an increase, not a decrease in the prevalence of obesity.

To treat the metabolic syndrome, a diet should lower saturated fat intake but also promote weight loss. A review of popular American diets shows that regardless of whether
Table 1
Adult Treatment Panel III guidelines: lifestyle and metabolic risk factors associated with the metabolic syndrome

<table>
<thead>
<tr>
<th>Lifestyle risk factors</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Atherogenic diet</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td></td>
</tr>
<tr>
<td>Metabolic risk factors</td>
<td></td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt;1.03 mmol/L (&lt;40 mg/dL)</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;1.29 mmol/L (&lt;50 mg/dL)*</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥1.69 mmol/L (≥150 mg/dL)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥130/≥85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥6.11 mmol/L (≥110 mg/dL)*</td>
</tr>
</tbody>
</table>

* 40 mg/dL is only about the 15th percentile for women; in the United States, the mean value for women is about 55 mg/dL.

The American Diabetes Association recently changed the definition of impaired fasting glucose from ≥110 mg/dL to ≥100 mg/dL.

Carbohydrate intake is high or low, short-term weight loss is possible. However, there is no compelling evidence supporting long-term weight loss with low-carbohydrate diets, despite their popularity. Shortly after the publication of this meta-analysis, 2 studies compared carbohydrate-restricted diets against standard advice (not the ATP III diet) (Table 2). The study by Samaha and colleagues had a high dropout rate (only 79 of 132 subjects completed the study), but its results indicated that people assigned to the low-carbohydrate diet as compared with a low-fat diet lost more weight, had a greater decrease in plasma triglyceride levels, and exhibited improved insulin sensitivity. At 1-year follow-up, the low-carbohydrate group showed a number of positive metabolic changes, including a greater decrease in plasma levels of triglycerides as well as a lesser decrease in plasma HDL cholesterol and, for the small group of participants with diabetes (n = 54), improved hemoglobin A1c levels.

The study by Foster and associates assigned subjects to a low-carbohydrate, high-protein, high-fat (Atkins) diet or a low-calorie, high-carbohydrate, low-fat (conventional) diet. Weight-loss results were encouraging for the Atkins-like diet at 3-month and 6-month follow-ups; however, after 12 months, the difference in weight loss between the 2 groups was insignificant (p = 0.26). This lack of success with weight loss is problematic, owing to the putative long-term consequences of low-carbohydrate diets, including hypercalciuria and the effects of a high-protein diet on the kidneys.

A low-energy regimen that appeared to promote dietary adherence consisted of moderate fat intake (35% of energy) that emphasized sources of monounsaturated fats. Mccmanus and colleagues randomized 101 men and women to either the Mediterranean-style diet that had unsaturated oils, peanut butter, and nuts or to a low-fat diet with 20% of energy as fat. All subjects in this randomized trial were instructed to consume between 1,200 and 1,500 daily calories that were low in saturated fat and cholesterol. Weight-loss was modest but more sustained in the moderate-fat diet group. Drop-out rates over the course of the 18-month trial were lower in the moderate-fat, low-energy group than in the low-fat, low-energy group.

Although the promise for weight loss and improved risk factor profile is touted for very-low-fat diets, an ongoing concern is that only a highly selected group of subjects participate in available clinical trials, limiting the ability to generalize the findings to the broader population. Ornish and colleagues examined the effects of a very-low-fat diet on a small group of patients with CAD. Patients were randomized to an AHA diet or to a multiple risk factor reduction program that included exercise, stress management, and smoking cessation and a diet that offered <10% of total calories as fat. As expected, dietary cholesterol and saturated fat intake were very low. At the end of the first year, the intervention group had lost 10 kg (22.2 lb) of weight and had convincing improvements in clinical angina and angiographic progression in contrast with the control group. This weight loss was maintained at 5 years. In addition, in 440 subjects who had both CAD and multiple metabolic risk factors, the Ornish program resulted in significant weight loss and improved risk factor profiles.

Despite the favorable results in the small numbers of studies to date, there have been concerns regarding adherence rates in study subjects with a dietary fat restriction of <25% of calories. Moreover, certain patients, especially those with the metabolic syndrome, can exhibit lower HDL cholesterol and higher triglyceride plasma levels or their lipid profiles can shift from large LDL particles to smaller, dense LDL particles with such low-fat diets.

Exercise

Exercise is a key component of effective treatment of the metabolic syndrome. It can improve the plasma lipid profile as well as other risk factors and provide the added bonus of increased fitness. It has been noted that sedentary lifestyles exact a heavy medical and economic toll in our society. The US Behavioral Risk Factor Surveillance System defined sedentary lifestyle as “one in which demanding physical activity does not exceed 20-minute sessions or when such activity occurs fewer than 3 times per week.” Most importantly, great benefits accrue to the persons who can go from sedentary to fit. Blair and colleagues found that men who maintained or improved adequate physical fitness were less likely to die of any cause or of cardiovascular disease during follow-up than were persistently unfit men. Indeed, their observational cohort study of 19,173 men aged 20 to 83 years, from the Aerobics Center Longitudinal Study, not only confirmed that obesity and the metabolic syndrome are associated with an increased risk of cardiovascular disease mortality and all-cause mortality, but their data also argued
Table 2
Informative randomized, controlled studies ≥1 year in duration examining weight-loss diets or lifestyle programs

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions</th>
<th>Duration (yr)</th>
<th>Subjects</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N</td>
<td>Women (%)</td>
</tr>
<tr>
<td>Samaha et al8</td>
<td>Low carbohydrate diet: &lt;30 g/day</td>
<td>1</td>
<td>132 (79 completed)</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Conventional diet: restrict caloric intake by 500 calories/day with &lt;30% fat</td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>calories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foster et al10</td>
<td>Low carbohydrate diet: 4-phase program*</td>
<td>1</td>
<td>63 (37 completed)</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>Conventional diet: 60% carbohydrates, 25% fat, 15% protein; low-calorie</td>
<td></td>
<td></td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>(women, &lt;1,500/day; men, 1,500–1,800/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPP25</td>
<td>Placebo</td>
<td>2.8 (mean)</td>
<td>3,234 with IGT</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>Metformin (850 mg bid)</td>
<td></td>
<td></td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Life-style intervention: goals = 7% weight loss and exercise 150 min/wk</td>
<td></td>
<td></td>
<td>68</td>
</tr>
<tr>
<td>Finnish Diabetes Prevention</td>
<td>Control</td>
<td>3.2 (mean)</td>
<td>522 with IGT</td>
<td>67</td>
</tr>
<tr>
<td>Study26</td>
<td>Life-style intervention: reduce weight, total and saturated fat intakes;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>increase fiber intake and exercise</td>
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</tbody>
</table>

BMI = body mass index; DM = progression to diabetes mellitus; HDL-C = high-density lipoprotein cholesterol; IGT = impaired glucose tolerance; MS = metabolic syndrome; TG = triglycerides; Wt = weight.
that these risks were largely explained by cardiorespiratory fitness.\textsuperscript{21} The same appears to hold true for women. Among 936 women enrolled in the National Heart, Lung, and Blood Institute–sponsored Women’s Ischemia Syndrome Evaluation (WISE) prospective cohort study, higher self-reported physical fitness scores were shown to be an important consideration in predicting good CAD outcomes.\textsuperscript{22} In these women, who underwent coronary angiography for suspected ischemia, higher self-reported physical fitness scores were independently associated with fewer CAD risk factors, less angiographic coronary disease, and a lower risk for adverse cardiovascular events.

How does exercise-induced weight loss compare with that obtained through diet? Ross and associates\textsuperscript{23} found that exercise-induced weight loss and diet-induced weight loss provide similar reductions in abdominal obesity, visceral fat, and insulin resistance. Two reasons to include exercise are the improvements in fitness (vide supra) and the fact that exercise without dieting was found to reduce abdominal fat while effectively maintaining body weight.

Finally, exercise can normalize the elevated triglyceride and lowered HDL cholesterol plasma levels seen in the metabolic syndrome. In the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study,\textsuperscript{24} the effect of exercise training after 20 weeks was only beneficial in subjects with baseline plasma levels high in triglycerides and low in HDL cholesterol (as may be seen in the metabolic syndrome) in contrast to its lack of effect on isolated low levels of HDL cholesterol.

**Lifestyle-Change Programs**

Three studies, the Diabetes Prevention Program,\textsuperscript{25} the Finnish Diabetes Prevention Study,\textsuperscript{26} and the Da Qing Trial,\textsuperscript{27} have illuminated the benefits of therapeutic lifestyle change in individuals with impaired glucose tolerance (IGT). In the Diabetes Prevention Program,\textsuperscript{25} 3,234 obese subjects with IGT but without type 2 diabetes mellitus were randomized to regimens of metformin, lifestyle modification, or placebo. The lifestyle-modification group had goals of 7% weight loss and 150 minutes of physical activity per week. This intervention resulted in a 58% reduction in the incidence of type 2 diabetes when compared with placebo and was significantly more effective than metformin (31% reduction versus placebo). The Finnish Diabetes Prevention Study\textsuperscript{26} consisted of 522 men and women with IGT who were randomized to either lifestyle intervention or placebo. Subjects in the intervention group received individualized counseling aimed at reducing both weight and intake of total and saturated fats while increasing fiber consumption and physical activity. After a mean follow-up of 3.2 years, the lifestyle-modification group achieved a greater weight loss and a 58% reduction in the incidence of type 2 diabetes (p <0.001) with the greatest benefit for those who exercised the most.

The Da Qing Trial\textsuperscript{27} consisted of 577 men and women with IGT. The cumulative incidence of diabetes at 6 years was 67.7% (59.8% to 75.2%) in the control group versus 43.8% (35.5% to 52.3%) in the diet group, 41.1% (33.4% to 49.4%) in the exercise group, and 46.0% (37.3% to 54.7%) in the diet-plus-exercise group. Taken together, these studies provide strong evidence for lifestyle recommendations in those with IGT.

Another important use for lifestyle intervention is in prevention of weight gain, especially in high-risk groups such as perimenopausal women. A 5-year randomized clinical trial known as the Women’s Healthy Lifestyle Project\textsuperscript{28} assigned 535 healthy, premenopausal women aged 44 to 50 years to either a lifestyle-intervention group receiving a 5-year behavioral, dietary, and physical activity program or to an assessment-only control group. The lifestyle-intervention group was given modest weight-loss goals (5 to 15 lb [2.25 to 6.75 kg]); a low-calorie, 25% total fat, 7% saturated fat eating pattern; and an increase in energy expenditure per week. After 4.5 years, significantly more subjects in the lifestyle-intervention group (55%) were at or below baseline weight contrasted with control subjects (26%), and beneficial effects on mean weight change and waist circumference were seen. Participants in the lifestyle-intervention group were consistently more physically active and reported eating fewer calories and less fat than controls.

Other periods that may be appropriate for weight-gain prevention include the ages between 25 and 35 years; the year following successful weight loss; and during interventions that often result in weight gain, such as smoking cessation, use of steroids for disease control, and use of certain antidiabetic, antidepressant, or antipsychotic medications. Wing\textsuperscript{29} suggested that such weight-gain prevention efforts include exercise, changes in quality and quantity of food consumed, behavior modification, and some degree of therapist contact.

**How Are These Goals Accomplished?**

One approach to the hurdles of implementation in clinical practice is to consider 3 elements of the problem:

- **The patient:** How to overcome internal and external barriers to adhering to the diet and exercise prescription
- **The physician/healthcare provider:** How to determine the level of patient motivation and how to prescribe an appropriate diet and exercise regimen
- **The system:** How to use a multidisciplinary approach using an array of healthcare professionals to translate the physician’s orders into the patient’s acquisition of the proper knowledge and skills for needed change.

**The patient:** For each patient, there are internal and external hurdles to lifestyle change. A crucial internal barrier is lack of motivation. Thus, an important first step a
physician can take is to query patients on their desire to change. Manson and colleagues adapted the stages-of-change model for weight loss and physical activity. They suggested that the stages for the intended behaviors of weight loss and increased physical activity are (1) precontemplation, in which desired behaviors are not occurring and the patient does not intend to initiate them; (2) contemplation, in which desired behaviors are not occurring and the patient intends to initiate them; (3) preparation, in which the patient is exploring options; (4) action, in which the patient has begun lifestyle modification and engaged in it for <6 months; and (5) maintenance, in which the patient has engaged in lifestyle modification for ≥6 months.

One way to initiate this discussion is to ask the patient to rate their willingness to change on a scale of 1 to 10, with 10 indicating certainty and lower numbers less certainty that behavioral change will occur. For those in precontemplation, it is useful to provide an empowering comment such as the statement, “I have patients like you who have successfully changed; let me know when you are ready to change.”

It may be useful to point out that many people finally are ready to change after a serious cardiac event occurs either to themselves or to a close relative, a friend, a coworker, or even a national figure. When motivation is the result of such events, it is consistent with the Health Belief Model that perception that drug therapy is easier and, in all cases, more effective.

The ATP III report noted several external barriers to lifestyle modification for patients:

- Increased consumption of foods prepared away from home
- Lack of time to both eat right and exercise
- Lack of third-party reimbursement for nutritional counseling
- Lack of adequate strategies for referral to registered dietitians and exercise trainers
- Perception that drug therapy is easier and, in all cases, more effective.

Good examples of these points have recently appeared in the literature. For example, the Coronary Artery Risk Development in Young Adults (CARDIA) study examined dietary habits and metabolic parameters in 3,031 young adults (aged 18 to 30 years at enrollment). During the 15-year study, subjects who visited fast-food restaurants more than twice per week both at baseline and follow-up gained an extra 4.5 kg (9.9 lb) of body weight and exhibited a significant 2-fold greater increase in insulin resistance compared with individuals who visited fast-food restaurants infrequently. A way to remove an external barrier is with home exercise equipment. In a small, carefully conducted study in obese women, multiple short bouts of exercise with home equipment improved long-term weight and fat loss compared with the same regimen without home exercise equipment.

To prevent childhood obesity, the limiting of children’s television, videotape, and video game use holds great promise as a population-based approach.

The physician/healthcare provider: ATP III commented on survey data showing that many physicians had little confidence in the patient’s ability to adhere to dietary change. This may reflect several factors. One important concern that can be easily remedied is the lack of availability of a brief, validated dietary assessment tool. ATP III included a detailed dietary questionnaire in their full report. This can be filled out by the patient before the visit and serve as a useful source of dietary information for the physician and the healthcare team. A simpler tool that provides useful feedback is the use of a diet diary that the patient brings to the visit. Asking the patient to identify areas that can be improved can be a valuable learning experience or at least indicate areas where professional guidance with a dietitian can be useful. Also, physicians can provide suggestions for patients to incorporate more physical activity into their daily lives.

Physicians concerned about improving adherence should also be aware of the findings of the Obesity Guidelines panel that reviewed 36 randomized clinical trial reports to determine potential benefits of behavioral therapy. Key findings from these studies to improve adherence include multimodal strategies; more frequent contact with the healthcare team; greater intensity of intervention, especially initially; and setting achievable goals from the outset.

The system: ATP III noted that the use of a multidisciplinary team in the management of patients with high plasma cholesterol levels, and especially in individuals with the metabolic syndrome, was an important factor in the successful implementation of their recommendations. ATP III recommended the use of nurses, dietitians, nurse practitioners, pharmacists, and health educators whenever possible. Alternatively, referral to commercial weight-loss programs can be considered, but a systematic review noted that “with the exception of 1 trial of Weight Watchers, the evidence to support the use of the major commercial and self-help weight-loss programs is suboptimal.” Of interest, a small study showed that a combination of a commercial program (Weight Watchers) and individualized counseling proved to be the best for achieving weight loss in obese women with breast cancer.

Although smoking cessation counseling per se is beyond the scope of this article, it is worth noting that the effectiveness of the Agency for Health Care Policy and Research clinical practice recommendations of “ask, advise, assist, and arrange” to facilitate quitting smoking can be improved with appropriate individual and team feedback. It may be appropriate for clinics and private practices periodically to
review how they are doing with counseling efforts for weight control, better diet, exercise, and smoking cessation.

Conclusion

Several determinants of the metabolic syndrome, especially in young adults, are fatness, fitness, and lifestyle. We believe that clinics or practices that focus not only on the patient, but also on the providers and the system will manage the metabolic syndrome most effectively. We reemphasize that the benefits of either preventing weight gain during vulnerable periods in the life cycle or encouraging and supporting small amounts of weight loss brought about by lifestyle changes are crucial. Losing weight over the short term is not a comprehensive enough goal for patients with the metabolic syndrome, and thus neither they nor healthcare providers should be satisfied with short-term improvements. How to accomplish long-term improvement in features of the metabolic syndrome by means of lifestyle changes—in a cost-effective manner that extends to the entire population—remains an important challenge.

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