Nutritional strategies in the prevention and treatment of metabolic syndrome

Sabrina E. Feldeisen and Katherine L. Tucker

Abstract: The metabolic syndrome (MetS) is a clustering of metabolic abnormalities that increase the risk of developing atherosclerotic cardiovascular disease and type 2 diabetes. The exact etiology remains unclear, but it is known to be a complex interaction between genetic, metabolic, and environmental factors. Among environmental factors, dietary habits are of central importance in the prevention and treatment of this condition. However, there is currently no firm consensus on the most appropriate dietary recommendations. General recommendations include decreasing obesity, increasing physical activity, and consuming an anti-atherogenic diet, and have traditionally focused on low total fat intake. A major problem with the focus on low fat is that high-carbohydrate diets can contribute to increasing triglyceride and decreasing high-density lipoprotein (HDL) concentrations. Low-carbohydrate diets have been popular in recent years. However, such diets are typically higher in saturated fat and lower in fruits, vegetables, and whole grains than national dietary recommendations. More recently the quality of carbohydrate has been studied in relation to MetS, including a focus on dietary fiber and glycemic index. Similarly, there has been a move from limiting total fat to a focus on the quality of the fat, with evidence of beneficial effects of replacing some carbohydrate with monounsaturated fat. Other nutrients examined for possible importance include calcium, vitamin D, and magnesium. Together, the evidence suggests that the components of diet currently recommended as “healthy” are likely also protective against MetS, including low saturated and trans fat (rather than low total fat) and balanced carbohydrate intake rich in dietary fiber, as well as high fruit and vegetable intake (rather than low total carbohydrate); and the inclusion of low-fat dairy foods. Accelerating research on gene–diet interactions is likely to contribute interesting information that may lead to further individualized dietary guidance in the future.

Key words: metabolic syndrome, dietary recommendations, waist circumference, blood pressure, dietary pattern.
**Introduction**

The metabolic syndrome (MetS) is a clustering of metabolic abnormalities that increase the risk of developing atherosclerotic cardiovascular disease (Isomaa et al. 2001; Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2002; Lakka et al. 2002) and type 2 diabetes (Laaksonen et al. 2002; Grundy 2005). Individual components that define the MetS include atherogenic dyslipidemia, elevated blood pressure, elevated plasma glucose and (or) insulin resistance, abdominal obesity (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001, 2002) and, most recently recognized, a pro-inflammatory and prothrombotic state (Alberti et al. 2005; Alberti et al. 2006).

In response to a need for an internationally standardized definition of the MetS, the International Diabetes Federation (IDF) has recently proposed a definition for general use. They define the MetS as central obesity, classified by ethnic and sex-specific waist circumference cut-off points, plus 2 of the 4 following components: (i) elevated triglyceride concentration (≥1.7 mmol/L or ≥150 mg/dL), (ii) low high-density lipoprotein (HDL) cholesterol (<1.03 mmol/L or <40 mg/dL in males and <1.29 mmol/L or <50 mg/dL in females), (iii) elevated blood pressure (systolic BP ≥130 or diastolic BP ≥85 mmHg, or treatment of previously diagnosed hypertension), and (iv) elevated fasting plasma glucose (FPG ≥5.6 mmol/L or ≥100 mg/dL, or previously diagnosed type 2 diabetes) (Alberti et al. 2006). Additional components, currently recommended for research purposes, include pro-inflammatory and prothrombotic states (Alberti et al. 2006).

Data from the National Health and Nutrition Examination Survey (NHANES) 1999–2002 show that the age-adjusted prevalence of MetS in the US is approximately 39.1% (men 40.7 ± 1.6%; women 37.1 ± 1.3%), when defined by the IDF definition (Ford 2005). The increasing prevalence of MetS has been attributed to a variety of factors including obesity (Shirai 2004; Alberti et al. 2006), insulin resistance (Reaven 2002; Alberti et al. 2006), population aging, and physical inactivity (Alberti et al. 2006). The exact etiology of MetS remains unclear, but it is known to be a complex interaction between genetic, metabolic, and environmental factors (Gropp 2000; Wolever 2000; Lidfeldt et al. 2003). Among environmental factors, there is no doubt that dietary habits are of central importance in the prevention and treatment of this condition. However, there is no consensus on the most appropriate dietary recommendations for the prevention and treatment of MetS (Table 1). General recommendations include decreasing obesity, increasing physical activity and consuming an anti-atherogenic diet (Grundy et al. 2005). Specific recommendations by the IDF for primary management of the individual risk components include energy restriction, increased physical activity, reduction in total and saturated fat intake, increased fiber intake, and salt restriction (Alberti et al. 2006).

This review aims to provide a summary of nutritional strategies for the prevention and treatment of MetS and its individual components. The intent is to focus on major aspects of diet and MetS based on recent evidence and trends in the literature, rather than to be exhaustive. Nutritional strategies specifically directed at the individual components of the syndrome will be mentioned briefly as well.

**General recommendations**

The primary approach for preventing and treating MetS includes consuming an overall healthy diet for weight reduction and long-term weight maintenance (Grundy et al. 2005; Lichtenstein et al. 2006). Widely accepted dietary recommendations by groups such as the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) and the American Heart Association (AHA) include moderate fat intake (25%–35% of energy), low saturated fat intake (<7% of total energy), avoidance of trans fat, limited cholesterol (<300 mg/d) and refined sugar intakes, and high intakes of fruits, vegetables, and whole grains (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2002; Lichtenstein et al. 2006). These recommendations derive from a traditional focus on lowering LDL cholesterol to reduce the risk of heart disease. For the MetS, however, triglyceride and HDL cholesterol concentrations are also important, requiring a more detailed examination of the recommendations.

**Macronutrient intakes**

**Low-fat diets**

Recommendations for weight loss and for MetS have traditionally focused on low total fat intakes. Several meta-analyses of the effectiveness of low-fat diets have shown positive weight loss results (Yu-Poth et al. 1999; Astrup et al. 2000). In an analysis of 16 trials, Astrup et al. (2000) found that reducing dietary fat without intentionally lowering energy intake did result in greater weight loss than with higher fat diets, especially for subjects that were more overweight. On the other hand, two reviews (Willett 2002; Pirrizzo et al. 2003) provide evidence that a low-fat diet may not be optimal for weight loss. Willett (2002) argues that short-term trials of low-fat diets noted only small changes in weight, and longer trials (1 y or more) showed little or no changes in body fatness. Additionally, there appeared to be no benefit of low-fat diets compared with other weight loss diets at 6, 12, or 18 months in 6 randomized controlled trials of overweight and obese individuals (Pirrizzo et al. 2003). In a recent randomized trial, postmenopausal women consuming a low-fat diet with high carbohydrate intake from vegetables, fruits, and grains did not gain weight over an average of 7.5 y of follow-up compared with women in the control group (Howard et al. 2006). The question, therefore, remains complex and it is likely that the quality of the entire...
dietary pattern is important rather than a focus on a single nutrient. Even with a benefit of low-fat diets on overall weight loss, more focus is needed on central adiposity, which is associated with insulin resistance and atherogenic dyslipidemia (Kwiterovich 2002) for those with MetS.

A major problem with the focus on low fat is that high-carbohydrate diets can contribute to increasing triglyceride and decreasing HDL concentrations (Krauss and Dreon 1995; Dreon et al. 1999; Reaven 2005), particularly as the low-fat recommendation may lead some individuals to consume more refined carbohydrates (Reaven 1997; Willett 1998). Excess carbohydrate consumption may be associated with the development of MetS. Studies using low-fat, high complex carbohydrate diets as recommended by the NCEP found reductions in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, but also in HDL cholesterol (Yu-Poth et al. 1999). Higher carbohydrate diets, particularly those in the refined form, have also been associated with elevated blood pressure (Esmailzadeh et al. 2005). An examination of cross-sectional data from NHANES III showed that high intake of carbohydrate (>60% energy intake) in men was associated with MetS (Zhu et al. 2004).

**Low-carbohydrate diets**

These observations have contributed to a recent focus on low-carbohydrate diets. There is some evidence of beneficial effects of low-carbohydrate diets on the risk of MetS (Volek and Feinman 2005). Low-carbohydrate diets typically consist of <100 g/d or <30% of total energy from carbohydrate (Bilsborough and Crowe 2003). In a randomized crossover study of 15 overweight men, a low-carbohydrate diet was more effective than a low-fat diet for decreasing MetS risk factors such as fasting serum triglycerides, the TAG–HDL cholesterol ratio, and fasting glucose and for improving the LDL subclass distribution (Sharman et al. 2004). A recent meta-analysis of 5 trials indicated that low-carbohydrate diets with no energy restriction produced weight loss similar to low-fat diets with energy restriction (Nordmann et al. 2006). The low-carbohydrate diets decreased triglyceride concentrations and increased HDL concentrations, whereas the low-fat diets showed improvements in LDL and total cholesterol concentrations. For MetS, the former profile is of greater importance, although the importance of LDL cholesterol to CVD risk cannot be ignored.

High-protein, low-carbohydrate diets have been shown to reduce weight and positively affect certain blood lipoproteins (Foster et al. 2003; Stern et al. 2004; Nordmann et al. 2006). A clinical trial of 63 obese men and women found that a low-carbohydrate diet produced greater weight loss than a conventional diet (high-carbohydrate, low-fat, low energy) after 6 months (Foster et al. 2003). However, subjects tended to regain the weight after 1 y, and this study had a high attrition rate.

Low-carbohydrate diets, including the Atkins diet, have been popular in recent years. However, such diets are typically higher in saturated fat and lower in fruits, vegetables, and whole grains than national dietary recommendations (Grundy et al. 2005). Low-carbohydrate diets such as the Atkins and Zone diets have shown some benefits for initial weight loss, and they may improve some cardiovascular risk factors over short periods of time (Brehm et al. 2003; Foster et al. 2003; Samaha et al. 2003; Nordmann et al. 2006). Data on long term effects, however, are inadequate owing to poor adherence rates observed in trials assessing low-carbohydrate, high-protein diets (Foster et al. 2003; Samaha et al. 2003; Dansinger et al. 2005). One study found that a modified low-carbohydrate diet that was higher in complex carbohydrates, protein, and monounsaturated fats led to more weight loss than a low-fat, high-carbohydrate diet following the NCEP guidelines (Aude et al. 2004). Another,

### Table 1. Dietary recommendations and components of MetS.

<table>
<thead>
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<th>Metabolic components</th>
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<td>HDL cholesterol</td>
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<td>Low saturated and trans fat, and cholesterol</td>
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<td>High fruit, vegetable, whole grains, and dietary fiber</td>
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<td>Low to moderate alcohol intake</td>
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*Demographic approaches to stop hypertension.
† High-density lipoprotein.
comparing a high-carbohydrate, high-fiber diet to a high-fat Atkins diet and a high-protein Zone diet, saw weight loss and reduction in triglyceride concentrations in all 3 (McAuley et al. 2005). However, participants consuming the high-fat and high-protein diets lost significantly more weight and significantly reduced fasting triglyceride concentrations more than those following the high-carbohydrate, high-fiber diet.

**Carbohydrate quality**

The quality of carbohydrate has been studied in relation to MetS. The glycemic index (GI), which is used to quantify the effect of carbohydrate-rich foods on postprandial glucose and insulin response, may provide more insight into the relationship between dietary carbohydrate and the MetS. In the Framingham Offspring study, the relative risk of MetS was 1.41 (1.04–1.91) for individuals in the highest quintile of glycemic index compared with the lowest quintile after adjusting for dietary fiber (McKeown et al. 2004). The combination of a low-glycemic, low-fat, high-protein diet has been shown to result in a better overall lipoprotein profile relative to an AHA phase I diet in a short-term intervention (Dumesnil et al. 2001). A review by Davy and Melby (2003) provides evidence of potential beneficial effects of low-fat, high-carbohydrate diets rich in dietary fiber on MetS.

The use of whole grains contributes to a lower glycemic index while providing fiber and additional nutrients. Several studies provide evidence of a protective effect of whole grains on the prevalence of MetS (McKeown et al. 2004; Esmailzadeh et al. 2005; Sahyoun et al. 2006). However, other studies have found no association with whole grains (Yoo et al. 2004) and further research is needed.

**Type of dietary fat**

Riccardi et al. (2004) emphasize that total fat intake may not be as important for individuals with MetS as dietary fat composition. The type of fatty acids consumed (saturated, polyunsaturated, monounsaturated, or trans fat) may have greater implications for MetS and its components. For example, saturated fat plays a role in atherogenic dyslipidemia, but may also be important for insulin resistance (Riccardi et al. 2004). A review by Grundy et al. (2002) supports these recommendations by providing evidence of the importance of a diet low in saturated and trans fat for managing LDL-cholesterol, further noting the potential beneficial effects of replacing some carbohydrate with monounsaturated fat for triglyceride concentrations. A high-fat diet (40% of energy) that is high in monounsaturated fatty acids and low in saturated fatty acids has been shown to reduce total and LDL cholesterol, similar to the effects of a low-fat, high-carbohydrate diet (Grundy 1986). In addition, the high monounsaturated fat diet did not lower HDL cholesterol or increase triglyceride concentrations, as seen with a low-fat, high-carbohydrate diet. Other studies have found similar favorable changes in blood lipids with a high monounsaturated fatty acid diet (Mensink et al. 1989; Ginsberg et al. 1990; Appel et al. 2005).

Consumption of long-chain omega-3 fatty acids, present in oily fish, is beneficial for reducing risk of CVD (Kris-Etherton et al. 2002) and may be beneficial for those with MetS through a reduction of plasma triglyceride concentrations (Harris 1997; Farmer et al. 2001; Rivellese et al. 2003) and atherogenic small, dense, lipoprotein particles (Carpentier et al. 2006). However, these fatty acids may also increase LDL cholesterol (Harris 1997; Farmer et al. 2001; Rivellese et al. 2003). A review of the effects of omega-3 polyunsaturated fatty acids in persons with type 2 diabetes (Nettleton and Katz 2005) and a more recent review of omega-3 fatty acids and MetS (Carpentier et al. 2006) suggest potential benefits including lower triglyceride concentrations, increased HDL cholesterol concentrations, improved endothelial function, and lower blood pressure, weighed against modest increases in LDL cholesterol. Omega-3 fatty acids may also play a role in reducing inflammation, platelet, and leukocyte activation, (Carpentier et al. 2006) and potentially insulin resistance (Nettleton and Katz 2005). A review by Calder (2006) describes direct (e.g., by inhibiting arachidonic acid metabolism) and indirect (e.g., by modifying inflammatory gene expression) mechanisms by which omega-3 polyunsaturated fatty acids may result in anti-inflammatory effects. This may have important implications for MetS, as inflammatory and prothrombotic states have been recently associated with the syndrome (Dandona et al. 2005; Calder 2006). Additional information regarding dietary factors and inflammation are discussed below.

**Alcohol**

The relationship between alcohol intake and MetS remains controversial (Goude et al. 2002; Djousse et al. 2004; Yoon et al. 2004; Fan et al. 2006). In a cross-sectional study, moderate alcohol consumption of all types was associated with a lower prevalence of MetS in a U-shaped relation in men and a dose-dependent relation in women (Djousse et al. 2004). For specific types of alcohol, wine appears to be protective against the prevalence of MetS in women (Rosell et al. 2003), but this may be due to an overall healthier lifestyle associated with wine use, rather than from the wine consumption itself (Djousse et al. 2004). In contrast, intake of spirits has been shown to be associated with a less favorable metabolic profile in both men and women (Rosell et al. 2003). Data from the Korean National Health and Nutrition Examination Survey indicate a 29% and 20% lower prevalence of MetS for men and women, respectively, who consumed 1 to 14.9 g/d of alcohol compared with those who consumed no alcohol, but with increasing alcohol intake, the risk of MetS and its components increased (Yoon et al. 2004). Recent evidence indicates that lifetime alcohol consumption may be associated with greater risk of MetS (Fan et al. 2006). It appears that heavy alcohol intake is associated with risk, and remains unclear as to whether low to moderate alcohol consumption is protective against MetS. More prospective studies are needed to elucidate this relationship.

**Micronutrients**

**Calcium and vitamin D**

Higher intake of calcium (total, dietary, and supplemental) has been associated with a lower prevalence of MetS. Liu et al. (2005) found a protective effect of increasing quintiles of total calcium intake on the prevalence of MetS.
after adjusting for smoking status, exercise, alcohol intake, multivitamin use, and parental history of myocardial infarction before age 60 y. Total and supplemental vitamin D was not associated with the prevalence of MetS in this study. However, other studies have found that inadequate levels of vitamin D are associated with MetS (Boucher et al. 1998; Chiu et al. 2004; Ford et al. 2005).

The major source of calcium and vitamin D in the US population is dairy products, and several studies suggest that dairy consumption may be protective of MetS (Pereira et al. 2002; Azadbakht et al. 2005b; Liu et al. 2005). The Women’s Health Study, including 10 066 women aged 45 y, reported a protective effect of both calcium intake and dairy products on MetS (Liu et al. 2005). However, it has been noted that high dairy intake tends to be associated with higher consumption of fiber, fruits, vegetables, and whole grains, and that the observed protective association may be driven by an improved overall dietary pattern (Azadbakht et al. 2005b). The Coronary Artery Risk Development in Young Adults (CARDIA) study, a population-based 10 y prospective study, found that overweight individuals in the highest category of dairy consumption were 72% less likely (OR, 0.28 (0.14–0.58)) to develop insulin resistance syndrome relative to those with the lowest dairy intake (Pereira et al. 2002). In contrast, one study found that older women who never drank milk had a lower prevalence of the MetS than those who drank milk (OR = 0.55; 0.33–0.94) after adjusting for age (Lawlor et al. 2005). Subjects who never drank milk had lower BMI, mean homeostasis model assessment (HOMA) scores and triglyceride concentrations, and higher HDL concentrations than those who did drink milk. However, the actual amount of milk consumed was not assessed in this study.

A population-based cross-sectional study in Tehranian adults reported that those in the highest quartile of dairy consumption showed a lower prevalence of high waist circumference, hypertension, and MetS, with p < 0.001–0.02 (Azadbakht et al. 2005b). The population-based prospective Malmo Diet and Cancer Study found that milk fat based food patterns showed a protective effect against hyperinsulinemia in women with an odds ratio of 0.66 (0.48, 0.91) and suggested protective effects against dyslipidemia and hyperglycemia with odds ratios of 0.70 (0.47–1.03) and 0.74 (0.47–1.15), respectively (Wirfalt et al. 2001). Another commonly cited study conducted in France found that dairy products were inversely associated with MetS and its components among men (Mennen et al. 2000). However, data on fruit and vegetables were not collected, and confounding by these foods cannot be ruled out.

Magnesium

Magnesium appears to be important for glucose metabolism and insulin homeostasis and may play a role in mediating other risk factors of MetS (Barbagallo and Dominguez 2006). Magnesium is found in many whole foods, including dark green leafy vegetables, whole grains, some fruits, nuts, seeds, legumes, and soy products. Few studies have examined the association between magnesium and MetS. Cross-sectional studies have reported inverse associations between dietary (Song et al. 2005) and serum magnesium levels (Guerrero-Romero and Rodriguez-Moran 2002) and MetS or with fasting insulin levels in overweight women (Song et al. 2004).

One longitudinal study showed a greater risk of incident type 2 diabetes with low magnesium intake (Lopez-Ridaura et al. 2004). Another study found a 31% reduced risk of incident MetS in young adults with the highest versus the lowest quartile of magnesium intake (He et al. 2006). Magnesium intake was also inversely associated with fasting glucose concentration, waist circumference, and HDL cholesterol in this study, after adjusting for potential confounders. When adjusted for calcium and potassium, however, associations were attenuated, due to collinearity of intake. Therefore, it remains unclear which of these minerals was of greatest importance. Intervention trials can be informative in this case, but few studies are available for MetS. A meta-analysis of magnesium supplementation and blood pressure reported a dose-dependent effect of magnesium indicating reductions of 4.3 mmHg systolic blood pressure and 2.3 mmHg diastolic blood pressure for each increase of 10 mmol/d magnesium (Jee et al. 2002).

Dietary patterns

Together, the data described above suggest that the components of diet currently recommended as healthy are likely protective against MetS. Looking at the total diet together, descriptions of “healthy dietary patterns” have emerged from prospective studies using cluster and factor analysis. These are typically characterized by higher intakes of fruits, vegetables, reduced-fat dairy products, and whole grains (Hu et al. 2000; Newby et al. 2003; Newby and Tucker 2004). Dietary pattern analysis can address the complex interactions between nutrients, collinearity between nutrients, and dietary recommendations (Newby and Tucker 2004). A cross-sectional study identified a healthy dietary pattern using principal component analysis that was found to be protective of risk factors for MetS such as fasting glucose and central obesity in a UK-based cohort (Williams et al. 2000).

Dietary patterns characterized by highly processed cereals with a high glycemic index are associated with an increased risk of MetS. Baxter et al. (2006) states in a recent review that there appears to be no single dietary component that is associated with MetS, but rather it is associated with an overall dietary pattern. Food patterns that are dominated by higher fiber intake have been associated with more favorable risk factors for MetS, whereas patterns higher in refined grains, cheese, cake and alcoholic beverages have been associated with more adverse effects (Wirfalt et al. 2001).

In a cross-sectional study of Tehranian adults, a higher dietary diversity score, used as an indicator of overall diet and quality of diet, was inversely associated with MetS (Azadbakht et al. 2005a). This diversity score was associated with relatively higher intakes of fiber, fruit, vegetables, vegetable oil, and dairy and lower meat and cholesterol intake. Although those with a higher diversity score also consumed more energy and tended to be more obese, it was thought that the increased energy intake may be from foods that are part of a healthy dietary pattern that may reduce some of the risk factors for MetS (Azadbakht et al. 2005a). In the Framingham Offspring Spouse study, an “empty calorie” dietary pattern characterized by a higher consumption of fat,
energy and sweetened beverages, and lower dietary fiber and vegetable intake, was associated with the highest prevalence of MetS and with low HDL levels in obese women and with dyslipidemia in all women (Sonnenberg et al. 2005).

A 2 y intervention study using a low-calorie diet based on NCEP ATP III recommendations including low-fat, high-carbohydrate, and high dietary fiber successfully reduced MetS in 37% of obese subjects, especially in those who had greater than 10% weight loss (Muzio et al. 2005). Additionally, there were no adverse effects on blood glucose, triglycerides, or HDL cholesterol. This indicates that weight loss programs following an overall healthy diet can be beneficial for reducing the prevalence of MetS.

It appears that diets characterized by low total and saturated fat intake and higher fruit, vegetable, whole grain, and low-fat dairy intake are protective against MetS and its individual components. The dietary approaches to stop hypertension (DASH) diet, characterized by high fruit and vegetable intake, low-fat dairy products, whole grains, poultry, fish, and nuts and low saturated and total fat, meats, sweets, and sugar drinks, significantly reduced components of the MetS compared with controls in men and women (Azadbakht et al. 2005c). Positive results were seen for systolic blood pressure, body mass, fasting blood glucose, triglycerides, and HDL cholesterol. The favorable changes in the metabolic components remained after adjusting for weight loss. It is suggested that the dietary composition of the DASH diet (dietary fiber, vitamins, minerals, and phytochemicals (Most et al. 2004)) may drive the protective associations seen in this study (Azadbakht et al. 2005c).

There is considerable evidence that a Mediterranean dietary pattern may have beneficial effects on cardiovascular disease risk (de Lorgeril et al. 1999; Singh et al. 2002), MetS (Esposito et al. 2004), and all-cause mortality (Trichopoulou et al. 2003). While there are variations in the Mediterranean diet between countries and regions, this dietary pattern is characterized by high intake of fruit, vegetables, whole grains, beans, nuts, and olive oil (Kris-Etherton et al. 2001). Dairy products, fish, poultry, eggs, and wine are typically consumed in low to moderate amounts and a large proportion of energy intake from dietary fat is in the form of monounsaturated fats. A recent review by Serra-Majem et al. (2006) revealed the need for more clinical and observational trials to make concrete recommendations regarding MetS and the Mediterranean diet, as most of the research is based on observational epidemiological studies. However, one trial of 180 men and women, randomized to consume a Mediterranean diet or to follow a prudent diet, found an approximately 50% reduction in the prevalence of MetS with the Mediterranean diet owing to significant decreases in waist circumference, blood pressure, plasma glucose, total cholesterol, and triglyceride concentrations, and a significant increase in HDL in the intervention group (Esposito et al. 2004).

**Individual risk factors for MetS**

**Central obesity**

For the MetS, central adiposity is of primary interest. Central adiposity, specifically visceral adiposity, has been shown to be significantly associated with all components of MetS (Carr et al. 2004). It has been shown that adiposity in obese individuals is associated with insulin resistance (Grundy et al. 2005) and in abnormal inflammatory responses (Grundy et al. 2005; Calder 2006), which are both related to MetS. The importance of waist circumference as a measure of central adiposity has recently been emphasized as one of the major components of MetS (Alberti et al. 2006; Katzmarzyk et al. 2006). Waist circumference has been reported to be most specifically associated with cardiovascular risk (Dobbelsteyn et al. 2001), as well as other components of MetS including blood pressure, fasting glucose, and lipid profiles (Zhu et al. 2005). Waist circumference has been shown to be a better measure of central adiposity (Misra et al. 2005) and has been more highly correlated than BMI with the components of MetS (Zhu et al. 2005).

Weight loss is a primary intervention recommended for the prevention and treatment of MetS. A recent randomized, controlled, trial of 70 premenopausal women found that increased physical activity and consumption of a low-energy diet lead to significant reductions in body mass, BMI, waist circumference, total fat mass, trunk fat mass, and insulin and leptin levels (Lofgren et al. 2005). Of interest is the fact that 7 out of 8 participants who had MetS prior to the intervention no longer had it after the intervention. Aude et al. (2004) compared an NCEP diet to a modified low-carbohydrate diet (lower in total carbohydrates, higher in protein, monounsaturated fat, and complex carbohydrates) and found that weight loss was significantly greater on the modified low-carbohydrate diet than on the NCEP diet after 12 weeks. Further, a significant reduction in the waist-to-hip ratio was observed only within the modified low-carbohydrate diet group and not between the groups. Dietary patterns identified from cluster or factor analysis have shown that healthy patterns are associated with lower BMI and waist circumference (Newby et al. 2003; Newby and Tucker 2004).

Dietary patterns do not always relate similarly to BMI and to central adiposity. One prospective study showed that a healthy dietary pattern characterized by high fruit, vegetable, low-fat dairy, and whole grain and low red and processed meats, soda, and fast foods was associated with smaller gains in BMI and waist circumference relative to others, but that a pattern high in refined carbohydrates (white bread) was associated with the largest gains in waist circumference, whereas a “meat” pattern was associated with the largest gains in BMI (Newby et al. 2003). In the multi-ethnic insulin resistance atherosclerosis study (IRAS 1992–1994), a dark bread pattern derived from cluster analysis was associated with the highest fiber intake relative to total energy and with lower waist circumference (Liese et al. 2004). This is consistent with findings from other studies, where higher dietary fiber patterns have been related to less central obesity (Wirfalt et al. 2001). In the IRAS, the highest intake of beer, which emerged within the white bread group, was associated with central and total obesity, whereas the wine group was associated with low adiposity; this indicates that alcohol intake is associated with other health characteristics that need to be accounted for to examine alcohol intake alone (Liese et al. 2004).

Similar to these findings, a high intake of refined grains was positively associated with an increase in 6 y change in
waist circumference among women after adjusting for BMI, whereas potatoes were protective against gain in waist circumference for men (Halkjaer et al. 2004). This study measured diet with food factor scores and examined intakes of 10 food or beverage groups in relation to 6 y changes in waist circumference. Beer and spirits intake was associated with increases in waist circumference in women only. Tea and coffee appeared to be associated with increases in waist circumference; however, the relationship was weakened when adjusted for BMI (Halkjaer et al. 2004). Another prospective study examining dietary intake in relation to 9 y waist gain indicated that changes in trans fat intake but not total fat intake were related to increases in waist gain, whereas changes in fiber intake were protective (Koh-Banerjee et al. 2003).

**Blood pressure**

Dietary approaches have been the focus and primary action for lowering blood pressure and preventing hypertension (Appel et al. 1997). Changes in lifestyle behaviors by modifying dietary intake can lead to weight reduction, decreased sodium intake, and decreased alcohol intake, all factors that are beneficial and recommended for reducing blood pressure (Chobanian et al. 2003; Champagne 2006). A systematic review of prospective studies and clinical trials with 2 years or more of follow-up concluded that, in overweight and (or) obese adults, every 10 kg of weight loss was associated with a 6.0 mmHg decrease in systolic blood pressure and a 4.6 mmHg decrease in diastolic blood pressure, although changes in blood pressure were greater after initial weight loss than they were over longer time periods (Aucott et al. 2005). Newer evidence indicates that monounsaturated fats, but not omega-3 fatty acids, may play a role in reducing blood pressure, specifically diastolic blood pressure (Rasmussen et al. 2006).

Blood pressure management can be attained through healthful dietary patterns such as the DASH trial diet (Appel et al. 1997; Sacks et al. 2001). In an 11-week clinical trial, the DASH diet lowered systolic blood pressure by 5.5 mmHg more and diastolic blood pressure by 3.0 mmHg more than a control diet (Appel et al. 1997). The control diet represented the average consumption of macronutrients and dietary fiber in the US and approximated the 25th percentile of US consumption for potassium, magnesium, and calcium. Greater reductions in blood pressure on a DASH diet have been observed for individuals with hypertension than those who are normotensive (Appel et al. 1997; Lopes et al. 2003). However, the DASH diet has been shown to be beneficial for participants without hypertension, indicating the potential for preventing hypertension (Lopes et al. 2003). The potential benefits of the DASH diet on blood pressure may occur through an increase in antioxidant capacity and reduction in oxidative stress related to hyperlipidemia in obese hypertensive participants (Lopes et al. 2003).

There is convincing evidence that a reduction of dietary sodium intake lowers blood pressure (Cutler et al. 1997; Sacks et al. 2001; He and MacGregor 2002; He et al. 2005). In a meta-analysis by He and MacGregor (2002), a reduction of 6 g (100 mmol/d) of dietary salt per day predicted a significant decrease in systolic and diastolic blood pressure in hypertensive and normotensive individuals by 7.11/3.88 mmHg and 3.57/1.66 mmHg, respectively. The Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends a DASH diet and a decrease in dietary sodium intake to 2.4 g (100 mmol) for improved blood pressure (Chobanian et al. 2003). Sacks et al. (2001) provided evidence that a reduction in dietary sodium intake in combination with a DASH diet resulted in greater effects than either intervention alone. The effects of the 2 dietary interventions, however, did not appear to be fully additive.

The DASH diet recommends foods that are good sources of calcium, potassium, and magnesium (Appel et al. 1997). Several studies, but not all, have shown that dairy intake and dietary calcium are inversely associated with blood pressure (Ruidavets et al. 2006). A recent meta-analysis of 40 randomized controlled trials concluded that supplemental calcium is important in the reduction of systolic and diastolic blood pressure (van Mierlo et al. 2006). Although some studies have shown a significant relationship between systolic blood pressure and high dairy intake (Ruidavets et al. 2006), others have found significant but weak differences (≤1–3 mmHg) in adjusted systolic and diastolic blood pressure after adjusting for potential confounders between the highest and lowest dairy calcium intakes (Jorde and Bonaa 2000).

More consistent findings have been seen for the inverse association between potassium and systolic and diastolic blood pressure (Kotchen and McCarron 1998; He and MacGregor 1999; Hajjar et al. 2001). Data from NHANES III included 17030 individuals age 20 y or older and found that higher intakes of potassium were negatively associated with systolic and diastolic blood pressure (Hajjar et al. 2001). Data regarding magnesium intake are less consistent, but some studies have also shown an inverse association between magnesium intake and blood pressure (Mizushima et al. 1998).

A recent systematic review of randomized controlled trials concluded that a healthy diet with decreased alcohol and sodium intakes was significantly associated with a reduction in mean systolic and diastolic blood pressure, but there was no support for a protective relationship with the use of calcium, magnesium, or potassium supplements (Dickinson et al. 2006). The JNC recommends that alcohol intake be limited to no more than 2 drinks (30 mL of ethanol) per day in most men and 1 drink (15 mL of ethanol) per day in women and lighter-weight persons (Chobanian et al. 2003). A review (Beilin and Puddey 2006) and a meta-analysis (Xin et al. 2001) suggest reductions in systolic and diastolic blood pressure with decreasing alcohol consumption. Further, a randomized crossover trial indicated that moderate alcohol consumption increased blood pressure in normotensive men regardless of the type of alcoholic beverage (Zilkens et al. 2005). The data regarding alcohol consumption and blood pressure remain inconsistent (Cushman et al. 1998), but suggest that limiting alcohol intake is likely to be beneficial for blood pressure.

**Insulin resistance**

Insulin resistance occurs when tissues cannot respond optimally to normal circulating concentrations of insulin, which results in a decrease in the amount of glucose that...
get into the muscle and adipose tissue (Le Marchand-Brustel et al. 2003). Insulin resistance has been called the “pathogenic link” underlying MetS and may be influenced by different dietary factors (Riccardi et al. 2004). Individuals with insulin resistance, especially those who are overweight or obese, can benefit from weight loss (Reaven 2005).

In a recent review, Reaven (2005) concludes that there is little evidence regarding a low-fat, high-carbohydrate diet for improving insulin sensitivity and that this dietary pattern may actually increase concentrations of glucose and insulin in those with insulin resistance. However, diets rich in whole grains, especially cereal fiber, are associated with lower fasting insulin concentrations (McKeown et al. 2004). Observational studies have not consistently shown an association between total carbohydrate intake (McKeown et al. 2004; Lau et al. 2005) or simple sugar intake (Daly 2003; Lau et al. 2005) and insulin resistance.

There is evidence that higher intake of dietary fiber is associated with lower fasting insulin levels (Marshall et al. 1997; Ludwig et al. 1999), and inversely associated with measures of insulin resistance (McKeown et al. 2004; Lau et al. 2005) and improved insulin sensitivity (Liese et al. 2005). A review by McKeown (2004) found improved insulin sensitivity with diets high in whole-grain foods, that may be mediated by magnesium and dietary fiber found in the whole grains. Cluster analysis has shown that a dietary pattern with high intakes of white bread, meats, and fats was associated with the worst insulin sensitivity relative to other dietary patterns (Liese et al. 2004). In the same study, the dark bread group and the wine group were associated with the more desirable levels of insulin sensitivity. There also appears to be a relationship between low magnesium status, MetS (Guerrero-Romero and Rodriguez-Moran 2002), and increased fasting insulin levels (Ma et al. 1995).

The role of dietary fats and MetS through impaired insulin sensitivity or insulin resistance has been recently reviewed (Roche 2005). The relationship between the amount of fat intake (high vs. low) and insulin sensitivity is still unclear (Foster et al. 2003; Samaha et al. 2003). More consistently, there appears to be evidence that saturated fatty acids are associated with insulin resistance and that replacing saturated fats with monounsaturated fats may improve insulin sensitivity (Perez-Jimenez et al. 2001; Vessby et al. 2001). However, another study did not find an effect of differering dietary fatty acids on insulin sensitivity, especially in lean individuals (Lovejoy et al. 2002).

After 12 years, men from the Health Professionals Follow-up Study in the highest quintile of dairy intake showed a relative risk for type 2 diabetes of 0.77 (0.62–0.95; p = 0.003) compared with men in the lowest quintile; an increase of 1 serving of dairy per day was associated with a 9% lower risk for type 2 diabetes (multivariate RR, 0.91; (0.85–0.97)) (Choi et al. 2005). Cross sectional data from NHANES III indicate an inverse association between quintiles of vitamin D concentrations and hyperglycemia, abdominal obesity, and hypertriglyceridemia, which may be due to an effect of vitamin D on insulin resistance (Ford et al. 2005).

**Atherogenic dyslipidemia**

Guidelines from the NCEP ATP III involve first lowering LDL cholesterol for those with abnormal levels through diet and drug therapy (Wilson and Grundy 2003). In the case of MetS, abnormalities in HDL cholesterol and plasma triglycerides also become important targets for prevention and treatment (Wilson and Grundy 2003). As discussed previously, dietary interventions for prevention of the syndrome have typically focused on blood lipid management, with a diet low in saturated and trans fat and cholesterol (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001, 2002). However, low-fat, high-carbohydrate diets can decrease HDL cholesterol and increase triglyceride concentrations and, therefore, are not ideal for MetS (Garg et al. 1992; Mensink and Katan 1992). Rather, low-carbohydrate diets have resulted in lower triglycerides and higher HDL cholesterol levels than have conventional diets (Foster et al. 2003; Stern et al. 2004; Nordmann et al. 2006). However, the quality of fat (Riccardi et al. 2004) and carbohydrate (McKeown et al. 2004; Aston 2006) has been a recent focus in addition to either very low fat or low-carbohydrate diets.

Healthy dietary patterns low in saturated fat and high in fruits, vegetables, and whole grains are among the most common recommendations for dyslipidemia. The DASH diet, which meets these criteria, significantly lowered total and LDL cholesterol and did not increase triglycerides (Obarzanek et al. 2001). Recently, a randomized controlled trial of the DASH diet resulted in higher HDL cholesterol and lower triglycerides, which remained significant after adjusting for weight loss. This would suggest potential benefit for the treatment of MetS (Azadbakht et al. 2005c).

High GI and glycemic load diets have been inversely associated with HDL concentrations (Frost et al. 1999; Ford and Liu 2001) and positively associated with fasting triglycerides, which appears stronger for overweight and obese women (Liu et al. 2001). Contrary to these findings, however, a 10 y follow-up study of elderly men examining dietary GI and unfavorable metabolic risk factors such as decreased HDL cholesterol, increased triglyceride, or increased fasting insulin or glucose concentrations found no association between GI and coronary heart disease (van Dam et al. 2000). Intervention studies have also reported conflicting results on the effect of GI on dyslipidemia (Aston 2006). A cross-sectional Swedish study of men with varying insulin sensitivities found that fatty acids typically in milk products were associated with a less atherogenic LDL profile (Sjorgen et al. 2004). Further, calcium supplements and calcium fortification of foods have been reported to decrease concentrations of LDL cholesterol and triglycerides and increase HDL concentrations (Tholstrup 2006).

**Inflammation**

A pro-inflammatory state has been associated with MetS (Esposito et al. 2003; Ridker et al. 2003; Tamakoshi et al. 2003) and has been indicated as a potentially important feature to examine in addition to the other components of the syndrome (Grundy et al. 2005; Alberti et al. 2006). Evidence from two recent reviews indicates that weight loss (Dietrich and Jialal 2005) and modification in dietary fat can influence inflammation (Esposito and Giugliano 2006). For example, acute effects of a high-fat meal include in-
creased levels of some adhesion molecules (i.e., ICAM-1 and VCAM-1) and two inflammatory cytokines, plasma interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), in healthy subjects (Nappo et al. 2002). Several studies have shown an association between higher consumption of saturated and trans fat and inflammatory responses such as increased C reactive protein (CRP), fibrinogen, and IL-6 (Baer et al. 2004). In a cross-sectional study of 730 women from the Nurses’ Health Study cohort, trans fat intake was positively associated with biomarkers of inflammation and endothelial function including CRP, sTNFR-2, E-selectin, sICAM-1 and sVCAM-1 (Lopez-Garcia et al. 2005). Others, however, have reported only weak to no association between CRP and dietary factors (Fredrikson et al. 2004).

A review by Esposito and Giugliano (2006) emphasizes the importance of healthy dietary patterns as a potential strategy to reduce inflammation and related metabolic risks. A Mediterranean style diet significantly reduced serum high-sensitivity CRP, IL-6, IL-7, and IL-8 compared with a control diet (Esposito et al. 2004). Additionally, a very low-carbohydrate and an energy-restricted, low-fat diet significantly decreased some biomarkers of inflammation, although this is thought to be a result of weight loss associated with the diets (Sharman and Volek 2004). This relatively new area of research requires more attention.

Gene–diet interaction

Roche et al. (2005) note that there are multiple genes involved in the development and progression of MetS. Although the prevalence of MetS has increased dramatically and continues to rise, the human genome has not changed much over this period of time. For this reason, environmental influences like diet have been identified as central factors contributing to incidence of the syndrome. Recently, researchers have identified a number of gene–diet interactions. For example, an interaction between the APOA1 G→A polymorphism and dietary intake of polyunsaturated fat led to differences in HDL cholesterol concentrations in women from the Framingham Offspring Study (Ordovas et al. 2002). Higher intake of polyunsaturated fats was associated with increased HDL cholesterol concentrations for women who were carriers of the A allele and, for women in the G/G group, the effect was reversed. Additionally, two studies discussed in the review by Roche et al. (2005) found that a polymorphism in the PPARγ gene (Pro12Ala) modifies the relationship between dietary fat intake and MetS components (Robitatte et al. 2003; Luan et al. 2001). Clearly, given the complexity of both the MetS and dietary intake, many such interactions will become apparent in this active research area, further clarifying whether individual differences can be identified in the future that would result in tailored dietary recommendations.

Conclusions

MetS has many components that are modifiable by diet, thereby providing important opportunities for prevention and treatment. Although a consensus has not been reached regarding the most appropriate dietary recommendations, the summary of research suggests that low saturated and trans fat (rather than low total fat) intakes, a balanced carbohydrate intake rich in dietary fiber, high fruit and vegetable intake (rather than a focus on low total carbohydrate), and the inclusion of low-fat dairy intake may be most beneficial for improving each of the individual components and thus reduce the risk of MetS. These recommendations closely resemble those for an overall healthy dietary pattern. Accelerating research on gene–diet interactions is likely to contribute interesting information that may lead to further individualized dietary guidance in the future.

Acknowledgements

This work was supported in part by the US Department of Agriculture Agricultural Research Service under USDA contract No. 53-3K06-5-10.

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