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The metabolic syndrome as currently defined by the Adult Treatment Panel III includes multiple components. This article describes the background for these components' inclusion in the syndrome, measurement of these factors, and the appropriate interventions. The factors are highly interrelated and the true utility of this diagnostic entity is under critical evaluation as new and existing data are evaluated concerning the role of the syndrome in the development of vascular disease and other clinical outcomes.

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This article emphasizes the importance of weight reduction in obese individuals as the main nutritional focus relevant to the metabolic syndrome. Although other nutrients influence insulin sensitivity, these effects are modest in comparison with the benefit achievable with weight reduction. This article therefore initially discusses the dramatic rise in the prevalence of the metabolic syndrome, especially in the Asian-Pacific region where insulin resistance and the high conversion rate to type 2 diabetes are almost certainly related to weight gain.

**Focus on Lifestyle Change and the Metabolic Syndrome** 493  
Neil J. Stone

The National Cholesterol Education Program's Adult Treatment Panel III identifies persons with multiple metabolic risk factors or

"metabolic syndrome" as candidates for intensified therapeutic lifestyle changes. This article reviews the important role of weight reduction, diet, and exercise in improving the metabolic syndrome and its risk factors of abdominal obesity, impaired fasting glucose, dyslipidemia, and coagulation/inflammatory factors. The article also provides practical strategies.

### **Management of Metabolic Syndrome: Statins**

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Antonios M. Xydakis and Christie M. Ballantyne

Individuals who have the metabolic syndrome are at increased risk for cardiovascular disease. Combined dyslipidemia is an important component of metabolic syndrome, contributing to excess cardiovascular risk. Lifestyle and pharmacologic interventions are warranted for effective management of this syndrome. This article discusses the current evidence supporting the use of statins and their beneficial impact on lipid and nonlipid aspects of metabolic syndrome-related pathology.

### **Management of Atherogenic Dyslipidemia of the Metabolic Syndrome: Evolving Rationale for Combined Drug Therapy**

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Gloria Lena Vega

Atherogenic dyslipidemia is prevalent in various conditions associated with central obesity, hypertension, hyperurecemia, and impaired  $\beta$ -cell function (ie, the metabolic syndrome). Because of clinical trial evidence, most high-risk patients with atherogenic dyslipidemia require statin therapy. Coadministration of drugs targeted to reduction of low-density lipoprotein precursors, however, is likely to improve the metabolic profile of all non-high-density lipoproteins and produce a significant rise in high-density lipoprotein cholesterol. Large-scale clinical trials with combined drug therapy that show coronary heart disease (CHD) risk reduction or improvement in CHD are needed. It is also possible that new drugs are needed to target fatty acid metabolism and inflammation. As understanding of the metabolic origins of atherogenic dyslipidemia increases, it is possible that new targets of therapy will be identified and that new drug combinations will prove to be even more efficacious than those currently available for treatment of this condition.

### **Fibrates in the Metabolic Syndrome and in Diabetes**

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George Steiner

There is increasing evidence that fibrates can reduce coronary artery disease. This finding seems to be particularly the case in patients with the metabolic syndrome or with diabetes. Their beneficial effects can be explained partly by their effects on lipoproteins, but these effects may also result from some of their

nonlipid pleotropic effects. Clinical trials are still needed to determine the potential role played by such pleotropic actions.

## **Management of the Metabolic Syndrome—Nicotinic Acid**

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C. Daniel Meyers and Moti L. Kashyap

Nicotinic acid effectively treats each of the common lipid abnormalities found in the metabolic syndrome, and much progress has recently been made in understanding its mechanisms of action. Early concern that nicotinic acid can precipitate or worsen diabetes has been eased with recent trials, which demonstrated its safety and effectiveness in insulin-resistant states. Furthermore, nicotinic acid prevents cardiovascular disease and death in persons with a high prevalence of risk factors for the metabolic syndrome. When used by an experienced physician and taken by a motivated patient, nicotinic acid can be safe and effective in treating the dyslipidemia of the metabolic syndrome.

## **Management of Metabolic Syndrome: Aspirin**

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T. Matthew Shields and Charles H. Hennekens

Cardiovascular disease (CVD), which includes myocardial infarction (MI), stroke, and peripheral vascular disease, remains the leading cause of death in the United States and in most developed countries. In the United States today, 25% of patients have metabolic syndrome—including those who have had a prior occlusive vascular disease event, those who are having an acute MI or ischemic stroke, and finally, the largest segment of the population, namely those who have not yet experienced a clinical CVD, but whose risks are substantial (10-year risk  $\geq 10\%$ ). This article reviews the totality of evidence for aspirin in the treatment and prevention of CVD and emphasizes its importance as adjunctive therapy for patients with metabolic syndrome.

## **Glitazones and the Management of Insulin Resistance: What They Do and How Might They Be Used**

595

Daniel Einhorn, Vanita R. Aroda, and Robert R. Henry

Thiazolidinediones (glitazones) are the only compounds currently available that specifically target tissue insulin resistance. The two currently available drugs in this class, pioglitazone and rosiglitazone, are approved by the Food and Drug Administration for the treatment of type 2 diabetes mellitus only. The therapeutic potential of the glitazones for other consequences of insulin resistance has stirred considerable interest, especially with regard to their potential beneficial impact on atherosclerotic cardiovascular disease and diabetes prevention. They also have been considered in the management of polycystic ovarian syndrome, nonalcoholic fatty liver disease, and other consequences of insulin resistance. The nonglycemic potential of glitazones is a clinical area in rapid

evolution, wherein most data are on the impact of the glitazones on surrogate markers that are associated with diseases, not on disease outcomes. This article provides insight and guidance to clinicians on the diverse nonglycemic potential of glitazones until conclusive outcome data become available.