



**Please provide an overview of the metabolic syndrome, including its definition, importance, recognition, management and relation to disease risk.**



The “metabolic syndrome” appellation embraces multiple clinical signs that, in association, define the syndrome itself. It has emerged over several decades to assume increasing importance as a contributor to cardiovascular disease (CVD), type 2 diabetes and other serious health problems. According to the International Diabetes Federation (IDF), the syndrome, possibly affecting up to 25% of the adult population, doubles CVD risk and, for non-diabetics, increases the risk of type 2 diabetes fivefold.

The disorder, defined by Gerald Reaven, MD, Stanford University, was initially named syndrome X. Lipid experts were among the first to recognize the significant contribution of this syndrome to CVD risk. Nutritionists and medical professionals at that time were paying attention primarily to hypercholesterolemia as a lipid risk factor, and LDL cholesterol, in particular, as the culprit in raising CVD risk. Hypertriglyceridemia, a cardinal feature of syndrome X/metabolic syndrome, was neither considered an important risk factor nor were treatment options (i.e., pharmaceutical management) considered worthy of commercial development and marketing. Statin drugs revolutionized treatment of high blood cholesterol, with enormous impact on CVD prevention and lessened morbidity and mortality from coronary heart disease. The importance of triglycerides (TG), newly termed triacylglycerol, became clear. The National Cholesterol Education Program’s Adult Treatment Panel III (ATP III) gives TGs appropriate recognition and recommends treatments.

Several groups, including the World Health Organization (WHO), the American Heart Association (AHA) and ATP III, have defined the metabolic syndrome. While these definitions differ somewhat in the details and indicators, there is agreement on the core components of obesity, dyslipidemia, elevated blood pressure and impaired fasting glucose. For example, using the ATP III definition, an individual would be identified as having metabolic syndrome if at least three of the following were present:

- ❖ **Abdominal Obesity** (measured as waist circumference)
  - Men: >102 cm (>40 inches)
  - Women: >88 cm (>35 inches)
- ❖ **Elevated Serum Triglycerides** (blood triglycerides  $\geq$ 150 mg/dl)
- ❖ **Low HDL Cholesterol**
  - Men: <40 mg/dl
  - Women: <50 mg/dl
- ❖ **Elevated Blood Pressure** (blood pressure  $\geq$ 130/ $\geq$ 85 mm Hg)
- ❖ **Impaired Fasting Glucose** (fasting blood glucose  $\geq$ 110 mg/dl)

In 2005, IDF proposed a new, worldwide definition of the metabolic syndrome. The criteria are: central obesity, measured as waist circumference  $\geq$ 94 cm for Europoid men and  $\geq$ 80 cm for Europoid women, *plus* two of the four following factors: raised TG  $\geq$ 150 mg/dl or specific treatment for this lipid abnormality; low HDL cholesterol of <40 mg/dl in males or <50 mg/dl in females; elevated blood pressure (systolic  $\geq$ 130, diastolic  $\geq$ 85 mm Hg) or treatment of previously diagnosed hypertension; or raised fasting plasma glucose  $\geq$ 100 mg/dl or previously diagnosed type 2 diabetes. Although the IDF criteria are more stringent, at present ATP III criteria will likely continue to be used in the US for clinical purposes.

While the cause of the metabolic syndrome is not entirely clear, most experts agree that it is likely an expression of multiple causes that need differentiation in each patient. Insulin resistance appears to be a common factor contributing to the metabolic abnormalities observed, although the degree of insulin resistance can vary widely among individuals. Probably a combination of genetics and lifestyle (e.g., excessive positive energy balance) exists. Sedentary lifestyle is another factor to consider. Lack of regular exercise contributes to obesity, which in turn is a risk factor for both CVD and type 2 diabetes.

The metabolic syndrome frequently surfaces in midlife. However, with the increasing incidence of obesity in children and adolescents, a growing concern is that metabolic syndrome is also becoming more prevalent in young people. Thus, identification of individuals at risk for the syndrome becomes more important among a broad age range.

A key goal in managing the metabolic syndrome is to treat the underlying insulin resistance. Encouraging patients to make aggressive lifestyle changes (ATP III refers to these as therapeutic lifestyle changes), including diet, weight management and increased physical activity, is a primary step. Tailoring eating and exercise plans to manage an individual's risk factors and account for personal preferences is critical for success. Even a moderate weight loss in insulin resistant people who are overweight or obese can improve insulin sensitivity. As diet and lifestyle changes are implemented, it is important that healthcare professionals monitor patients for changes in: body weight (especially measurement of waist circumference), blood glucose, blood lipids and blood pressure. Such monitoring will help determine if and when additional medical therapies are required to treat individual risk factors.

ATP III and the AHA have published guidelines for the metabolic syndrome, healthy levels for TGs and recommendations for lifestyle interventions and CVD risk calculations. The National Lipid Association also provides information for nutritionists, pharmacists, lipid experts and primary care physicians, including self-assessment programs and continuing education courses to update this rapidly changing entity. Scientists continue to investigate intermediary metabolism of lipids and lipoproteins and the interrelationship with carbohydrate metabolism. These pinpoint intracellular and circulatory factors (enzymes, hormones, cofactors, etc.) that may lead to a better understanding of how "metabolism" contributes to disease. Data should lead to newer, imaginative categories of drug interventions to prevent or ameliorate the metabolic syndrome, normalize its components, control symptoms and reduce risk of CVD, type 2 diabetes and other associated health conditions.

### Further Reading

American Heart Association: <http://www.americanheart.org>

International Diabetes Federation: <http://www.idf.org/home/>

National Institutes of Health: <http://www.nhlbi.nih.gov/about/ncep/>

The National Lipid Association: <http://www.lipid.org>

Reaven GM. *Syndrome X*. New York: Simon and Schuster, 2000.

Reaven GM. The insulin resistance syndrome: definition and dietary approaches to treatment. *Annu Rev Nutr*. 2005; 25:391-406.