

# **James L. Holly, M.D.**

## **Effects of Exercise and Diet on Chronic Disease Part V**

### **Metabolic Syndrome**

**By James L. Holly, MD**

**Your Life Your Health**

*The Examiner*

**August 17, 2006**

We continue our summary of the review article in the November, 2005 issue of *Journal of Applied Physiology* entitled, "Effects of exercise and diet on chronic disease."

Previously, we have looked at the effect of diet and exercise on heart disease, hypertension and diabetes. Today, we review their effect on the Metabolic Syndrome.

One of the earliest references to the metabolic syndrome was in 1966; however, it was not until 1988 when the description of this syndrome began to receive more interest. At that time, it was called "syndrome X," and in 1989 it was called "the deadly quartet," referring to insulin resistance (hyperinsulinemia – elevated insulin levels in the blood), hypertension, hypertriglyceridemia, and obesity around the abdomen.

Insulin resistance -- the decreased responsiveness of the liver, muscles and other body systems to the effects of insulin – is the underlying condition of the metabolic syndrome and once that develops, those with a genetic predisposition will develop other aspects of the syndrome. However, diet, physical exercise, and body weight can modify insulin resistance, suggesting that the final manifestation of the genetic tendency involves both genetic and acquired influences. The syndrome was renamed the "insulin resistance syndrome" to highlight the fact that insulin resistance preceded other aspects of the syndrome.

Thus this fascinating and important condition has been called: Syndrome X, "the deadly quartet," the Metabolic Syndrome and "the insulin resistance syndrome." Recently, the American Diabetes Association (ADA) recommends that it be called the "Cardiometabolic Risk Syndrome."

What the ADA calls the "Cardiometabolic Risk Initiative" is described on their website. They state, "The term "cardiometabolic risk" (CMR) describes a set of risk factors that when viewed together, paint a picture of a person's overall risk of developing heart disease and type 2 diabetes. These risk factors include obesity, hypertension, high LDL ('bad') cholesterol, high blood fat (triglycerides), low HDL ('good') cholesterol, high blood pressure, smoking and physical inactivity. Each of these risk factors pose a danger to good health, and the more one has, the greater the risk of heart disease and type 2 diabetes.

“Using this model as a basis for overall health management, the Cardiometabolic Risk Initiative is a national effort focused on encouraging health care providers and the general public to focus on the prevention, recognition and treatment of all risk factors, helping patients achieve better health outcomes.

“Through a variety of educational and public awareness activities, the Initiative will empower Americans with information to help them fully engage in their personal health management and, with their physicians, to improve understanding of their risk for heart disease and diabetes. Major components of the initiative include:

- Educating health professionals on the cardiometabolic risk factors facing millions of Americans
- Promoting CMR by engaging a consortium of leaders from industry, cardiology, general medicine, endocrinology, and the obesity arenas
- Developing a ‘CMR Manager’ -- an interactive, easy-to-use tool to assess one's risk for diabetes and cardiovascular disease and help manage existing risk factors/
- Raising awareness about CMR and the CMR Calculator through a broad public education initiative emphasizing the advantages of regular health check-ups.”

SETMA applauds the ADA’s initiative. Several years ago, SETMA began its **LESS Initiative** which includes evaluating the patient’s risk of having insulin resistance and risk of developing hypertension and/or diabetes. Included in SETMA’s program is an exercise program and a weight assessment and encouragement to stop smoking and/or to eliminate exposure to second hand smoke.

Several additional characteristics have been suggested to be components of the metabolic – cardiometabolic risk -- syndrome, including:

- **Dyslipidemia** --including small, dense LDL particles and depressed HDL-C -- both of which increase the risk of heart disease
- **Enhanced clotting factor activity involving elevated levels of fibrinogen and tissue plasminogen activator inhibitor-1** – both of which increase the changes of blood clots being formed and therefore of heart attacks taking place. Both fibrinogen levels and plasminogen activator inhibitor-1 levels can be measured clinically. While insurance companies do not pay for these measurements at present, they are helpful in assessing the risk of heart disease and stroke.
- **Endothelial dysfunction** – endothelium is the lining of the arteries in the body. Originally thought to be inert (inactive) cells, we now know that they are very active. When endothelial dysfunction sets in, arteries do not relax and dilate as they should and increase the risk of blood clots, heart attacks and strokes.
- **Inflammation** – this really is the ultimate affect of the metabolic syndrome. Inflammation in the body and particular in the arteries increases the changes of developing heart disease and stroke. There are many “markers” which indicated the level of inflammation in the body which can be measured clinically including C-reactive protein, homocysteine, uric acid, white blood cell count

The clustering of these risk factors in the same individual results in a very high risk of developing heart disease and/or stroke.

The NCEP's ATP III (NCEP – National Cholesterol Education Program Adult Treatment Panel III -- and the WHO (World Health Organization) have established criteria for diagnosis of metabolic syndrome. Southeast Texas Medical Associates, (SETMA) healthcare providers calculate the presence of the metabolic syndrome using both criteria in all patients who are at risk.

Commonly the ATP III criteria are used in the United States and the WHO criteria are used in Europe. The WHO criteria will include some individuals as having the Metabolic Syndrome which the ATP III criteria will exclude. The prevalence of the metabolic syndrome is extremely high in Westernized societies. "Westernized" refers to societies where people eat more than they need and have inactive or sedentary – couch potato – lifestyles.

As defined by the five elements of the ATP III diagnostic criteria (abdominal obesity, hypertriglyceridemia, low HDL, hypertension, and fasting hyperglycemia), a United States sample of 12,363 men and women 20 yr and older from the Third National Health and Nutrition Examination Survey found the metabolic syndrome present in 22.8% of men and 22.6% of US women. Metabolic syndrome was present in 4.6% of normal-weight, 22.4 of overweight, and 59.6% obese men. Physical inactivity was associated with an increased risk of developing the metabolic syndrome. Additionally, of those over 60 years of age, it has been estimated that 43% have the metabolic syndrome and 80% of those with diabetes have the metabolic syndrome. Given that the estimated prevalence is based on the Third National Health and Nutrition Examination Survey (1988–1994), it is likely that prevalence of the metabolic syndrome is currently higher.

Those with the metabolic syndrome have a significantly higher risk of coronary artery disease and all-cause mortality, even in the absence of cardiovascular disease and diabetes when first diagnoses with the metabolic syndrome. Middle-aged men with the metabolic syndrome have a 4.26-fold risk of death over an 11-year follow-up compared with healthy men. Men with four or five features of the syndrome have been estimated to have a 3.7-fold increase in risk for CAD and a 24.5-fold increased risk for diabetes compared with men with none.

Several studies have clearly demonstrated that the disease process of the metabolic syndrome is largely attributable to dietary factors and activity levels. Men who engage in moderate-intensity leisure time physical activity less than 1.0 hour per week were 60% more likely to have the metabolic syndrome than those engaging in greater than three hours per week. Men with poor aerobic condition were approximately seven times more likely to exhibit the metabolic syndrome than those with good to excellent aerobic conditioning. Across cardiorespiratory fitness (aerobic fitness) levels, as measured by maximal treadmill exercise test, prevalence of the metabolic syndrome in a population of 7,104 women was lower as cardiorespiratory fitness (aerobic fitness) increased. In the

least fit category, 19.0% had the metabolic syndrome, while in the most fit only 2.3% had it.

The odds of having risk factors for metabolic syndrome (elevated systolic blood pressure, serum triglycerides, fasting glucose, and central obesity) is much higher in men with lower fitness and much lower in men who are very fit. Low fitness predicts risk of metabolic syndrome as powerfully as conventional risk factors, such as elevated cholesterol, family history, tobacco use, etc.. Additionally, in a study of 5,159 men ages 40–59 yr, physical activity level was associated with metabolic syndrome factors, as well as risk of CAD and diabetes. **There is now compelling evidence for exercise providing a protective effect against mortality risk in men with the metabolic syndrome.**

Early studies suggested that physical activity and diet could mitigate risk associated with metabolic syndrome and both appear to be major factors in the progression of the metabolic syndrome. In diabetic and insulin-resistant patients, combined physical activity and diet intervention can result in decreases in glucose, insulin, blood pressure, and TG triglycerides.

One study investigated the benefit of exercise training in treating the metabolic syndrome in 621 black and white participants. The presence of the metabolic syndrome and component risk factors were determined before and after 20 wk of supervised aerobic exercise training. The prevalence of the metabolic syndrome was 16.9% in this sample (105/621) of healthy participants. Of the 105 participants with the metabolic syndrome at baseline, 30.5% were no longer classified as having the metabolic syndrome after the exercise training. Endothelial dysfunction, one critical factor of the metabolic syndrome, has been documented to be improved by exercise training, independent of changes in obesity or blood pressure. In addition, while the metabolic syndrome is associated with inflammation, physical activity has been shown to decrease levels of inflammatory markers in the blood.

The metabolic syndrome exhibits a prevalence at nearly 25% of the US adult population and shows the integrative nature of modern chronic disease, given its endocrine, metabolic, and cardiovascular foundations. Most notable is the relation between cardiovascular fitness and metabolic syndrome, given data that the mortality risk in unfit vs. fit men with the metabolic syndrome is similar to the same comparison in healthy men. Many studies show the effect of exercise and/or diet on the metabolic syndrome and have shown improvement of risk factors comprising the metabolic syndrome, including insulin resistance, blood pressure, lipid levels, inflammation, and endothelial dysfunction.

Often disease is not inevitable – choices can make a difference and the most important choices involve the food we eat and the way we spend our time. Remember, it is your life and it is your health.