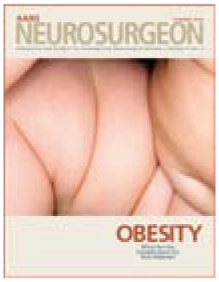
Bulletin: 2008 (Volume 17, Issue 2)

Feature

Metabolic Syndrome: What Neurosurgeons Should Know

By: Janet Lee, MD, and
William T. Couldwell, MD



(Click to view PDF)

The term metabolic syndrome, first introduced in 1988, has evolved in concept since that time. While the strict definition is subject to ongoing debate, the syndrome generally involves glucose intolerance, obesity, dyslipidemia and high blood pressure, which increase the risk of developing cardiovascular disease. The complex pathophysiology underlying this syndrome similarly has yet to be agreed upon but can be attributed largely, although not entirely, to insulin resistance and dysfunctional glucose and fat metabolism. This multifactorial syndrome highlights the complex association between noninsulin-dependent diabetes mellitus, coronary artery disease, and hypertension. An overview of factors contributing to the pathogenesis of metabolic syndrome may help neurosurgeons gain an understanding of this increasingly encountered disorder.

Insulin resistance and hyperinsulinemia are key pathophysiological components of metabolic syndrome. Glucose homeostasis requires that the feedback loop is maintained between insulin-producing pancreatic beta cells in response to a rise in serum glucose levels. In the setting of insulin resistance, the abnormally high levels of insulin produced in response to serum glucose elevations act not only to stimulate glucose uptake by muscles through a phosphatidylinositol 3-kinase pathway but also to induce mitogenic and proinflammatory effects via a MAP kinase pathway.

The phosphatidylinositol 3-kinase pathway increases nitric oxide, a potent inhibitor of vascular smooth muscle. In turn, vascular smooth muscle cell growth is stimulated by the MAP kinase pathway. In combination, glucose uptake is affected and atherogenesis may be enhanced.

Dysfunctional fat metabolism also contributes to insulin resistance and atherosclerosis. After food ingestion, the body first will store energy in triglycerides located in peripheral adipose tissue. When abnormal triglyceride levels exist and the peripheral adipocytes are saturated, free fatty acid concentrations become elevated, and triglycerides then are stored also in hepatocytes, skeletal muscle, and visceral adipose tissue, which can later lead to truncal obesity. Abnormally high triglyceride levels are associated with insulin resistance in myocytes and peripheral adipocytes. As fatty acids are released from adipocytes and taken up by the liver, the balance of lipoproteins in the blood shifts to high trigylericeds, low high-density lipoprotein cholesterol and high very-low-density lipoprotein, leading to increased risk of atherosclerosis.

Adipose tissue exhibits endocrine properties that also contribute to insulin resistance. An increase in adipose tissue mass has been associated with increased expression of hormones including adiponectin, angiotensinogen, tumor necrosis factor-alpha, resistin, and leptin. Adiponectin, a hormone secreted by adipocytes, modulates hepatic glucose production and fatty acid catabolism, resulting in a global increase in insulin sensitivity. There is an inverse correlation between circulating adiponectin levels and obesity, diabetes mellitus and insulin

resistance. Angiotensinogen is associated with development of hypertension in obesity. Increased adipose tissue mass causes increased production of angiotensinogen and angiotensin-converting enzyme, causing vasoconstriction that can lead to hypertension. Tumor necrosis factor-alpha is overexpressed in obesity and has been linked to insulin resistance. The link between resistin and insulin resistance continues to be debated. Many studies have found a positive correlation between resistin levels and obesity, although contradictory studies also exist. Leptin also is produced and functions to regulate appetite and metabolism. Since there is a positive correlation between leptin and obesity in humans, this suggests a leptin resistance similar to insulin resistance. Leptin receptors are located in the hypothalamus, which controls satiety.

Individuals who are diagnosed with metabolic syndrome or even with associated diagnoses such as atherosclerosis, hypertension, obesity and diabetes are likely to have a higher risk of surgical morbidity than individuals without these disorders. There is a multitude of targeted therapeutic interventions for modifiable components of metabolic syndrome. Lifestyle modification coupled with pharmacological intervention should be employed preoperatively when possible to reduce operative risk.

Janet Lee, MD, is a resident at the University of Utah School of Medicine. **William T. Couldwell, MD, PhD**, editor of the *AANS Neurosurgeon*, is professor and Joseph J. Yager Chair of the Department of Neurosurgery at the University of Utah School of Medicine. The authors reported no conflicts for disclosure.

Article ID: 52854