METABOLIC SYNDROME: AN OVERVIEW

An example of the interrelation of nutrient intake and metabolism is what has been termed metabolic syndrome.

Metabolic syndrome refers to a clustering of a group of risk factors for cardiovascular disease (CVD), chronic kidney disease, and type 2 diabetes. The definition of metabolic syndrome has evolved over the past few years. The multiple definitions have included insulin resistance or glucose intolerance, hypertension, dyslipidemia, and central obesity.

Additionally, hyperleptinemia (elevated levels of leptin in the blood) and hyperuricemia (elevated levels of uric acid in the blood) have often been included as part of the syndrome. Note that this condition is called metabolic syndrome. Calling it a syndrome means that the condition is not a defined disease entity but is a set of symptoms that occur together. Not all of these symptoms must present in each person to classify that person as having metabolic syndrome.

A scientific statement from the American Heart Association and the National Heart, Lung, and Blood Institute of the National Institutes of Health has been published (Grundy et al., 2005) describing the diagnosis and management of metabolic syndrome. The American Diabetes Association and European Association for the Study of Diabetes made a similar statement, with a different conclusion (Kahn et al, 2005). They stated that although no doubt exists' that certain cardiovascular disease risk factors tend to cluster, metabolic syndrome is imprecisely defined, and a lack of certainty persists regarding its pathogenesis. They also noted considerable doubt as to the value of using the diagnosis of metabolic syndrome, rather than individual risk factors, to evaluate the risk of developing CVD. They feel that more research must be completed before patient treatment is based on a diagnosis of metabolic syndrome. Still other reviews are available for the interested reader (McKeown et al., 2004; McMillen et al., 2005; Reaven, 2005).

The cardiovascular physicians have adopted the term metabolic syndrome to provide the criteria for diagnosis. At this time, whether the diagnosis is clinically important in predicting or treating CVD is unclear. Other terms that have been used to describe this syndrome include syndrome X and insulin resistance syndrome. Syndrome X was first used to identify the clustering of these symptoms and has largely been replaced. Insulin resistance syndrome considers that the underlying defect that ties all of these symptoms together is insulin resistance.

Research in this area is very active, and the reader should monitor current findings. Because insulin resistance is considered by some to be the underlying factor in these syndromes, its mechanisms of action are considered briefly in the next section to provide a basis for understanding future research.

Insulin Resistance

Much controversy persists in this field but, based on current evidence, the following process appears to occur. Insulin resistance results in hyperinsulinemia (increased blood insulin levels). The pancreas apparently releases more insulin in an effort to maintain normal blood glucose levels. The insulin insensitivity, combined with the elevated insulin levels, results in either elevated fasting blood glucose levels, glucose intolerance, or both. The insensitivity to insulin is primarily seen in muscle and adipose tissue. Insulin resistant muscle loses its ability to stimulate glucose uptake. In adipose tissue, insulin no longer inhibits free fatty acid release.

These observations can explain the elevated blood glucose and free fatty acid levels. The liver and kidney retain their sensitivity to insulin. The elevated insulin levels stimulate the liver triacylglycerol synthesis (TAG). As a consequence of the elevated TAG synthesis and the VLDL-TAG synthesis and secretion, fasting serum triacylglycerol and VLDL-TAG levels are increased. TAG levels in the liver also increase, resulting in nonalcoholic fatty liver disease. The kidney responds to the elevated insulin levels by increasing renal sodium retention and decreasing uric acid clearance. This response results in an increased prevalence of essential hypertension and higher plasma uric acid concentration.

Weight Loss and Insulin Insensitivity

Not all overweight or obese people have insulin resistance. Therefore, weight loss will not reduce the risk for CVD in all obese people equally. No simple test exists to determine who is insulin resistant and who is not. Fasting insulin levels, fasting plasma glucose levels, and triacylglycerol-HDL-C ratios have all been used as indicators for insulin resistance, with varying degrees of success.

Considerable evidence demonstrates that if a person loses weight, insulin sensitivity improves. The hyperinsulinemia does not prevent weight from being lost. Energy balance and a discussion of different proportions of macronutrients in weight loss diets are covered in other overview papers.

However, variations in the macronutrient content of isocaloric diets have little effect on the improving insulin sensitivity. One common diet for weight loss is to lower the lipid content of the diet and replace it with carbohydrate. The problem with a low-fat, high-carbohydrate diet for a person with insulin resistance is that the additional carbohydrate requires more insulin to be secreted from the pancreas to maintain glucose homeostasis. If the person is insulin resistant, and the pancreas has the capacity, insulin levels will be elevated further.

The increasing prevalence of overweight and obese people makes the study of metabolic syndrome, insulin resistance, and obesity an important consideration for those studying nutrition. The study of the effectiveness of changing diet, lifestyle, and exercise patterns in decreasing the mortality and morbidity in people with metabolic syndrome as they age will be an active area of research and practice for the future.

References

Grundy, S.M., Cleeman, J.I., Daniels, S.R., Donato, K.A., Eckel, R.H., Franklin, B.A., Gordon, D.J., Krauss, R.M., Savage, P.J., Smith, S.C., Spertus, J.A. & Costa, F. (2005) Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 112, pp.2735-2752.

Kahn, R., Buse, J., Ferrannini, E. & Stern, M. (2005) The Metabolic Syndrome: Time for a Critical Appraisal. Joint Statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia*. 48(9), pp.1684-1699.

McKeown, N.M., Meigs, J.B., Liu, S.L., Saltzman, E., Wilson, P.W.F. & Jacques, P.F. (2004) Carbohydrate Nutrition, Insulin Resistance, and the Prevalence of the Metabolic Syndrome in the Framingham off Spring Cohort. *Diabetes Care*. 27, pp.538-546.

McMillen, I.C. & Robinson, J.S. (2005) Developmental Origins of the Metabolic Syndrome: Prediction, Plasticity, and Programming. *Physiology Review*. 86, pp.571-633.

Reaven, G.M. (2005) The Insulin Resistance Syndrome: Definition and dietary Approaches to Treatment. *Annual Review of Nutrition*. 25, pp.391-406.