Metabolic Syndrome, Inflammation, and the Aging Process
by Barry Sears, Ph.D.

Much of anti-aging medicine is currently focused on hormonal replacement, especially those hormones that decrease with aging. However, relatively little attention is placed on reducing the levels of hormones that increase with aging. In particular, the hormones associated with increased systemic inflammation are elevated levels of insulin and eicosanoids. The primary cause of the rise of these hormones is due to a condition known as metabolic syndrome that is ultimately caused by the diet. Thus, a more appropriate description of anti-aging medicine would be anti-inflammatory medicine and, therefore, frontline therapy for anti-aging becomes diet.

Description of Metabolic Syndrome
Metabolic syndrome is a cluster of chronic conditions associated with hyperinsulinemia. These include obesity, type 2 diabetes, heart disease, and hypertension. Since hyperinsulinemia is caused by insulin resistance, a better choice of terms to describe metabolic syndrome might be insulin resistance syndrome.

Description of Insulin Resistance
Insulin resistance occurs when insulin is unable to transmit its hormonal signal to the interior of the cell. This occurs when the insulin binds to its receptor on the cell surface; but the transmission of biochemical signals that normally result from insulin's binding to its receptor is now degraded. The result is that there is a decreased ability to remove excess blood glucose from the bloodstream.

The signal to release insulin from the pancreas is elevated blood glucose; the inability to reduce blood glucose levels due to insulin resistance forces the pancreas to secrete ever-higher levels of insulin creating hyperinsulinemia. Since insulin receptors are found in the liver, smooth muscle, and adipose tissues, the consequence of abnormal insulin signaling can have widespread negative metabolic consequences.

Although the exact cause of insulin resistance remains to be elucidated, the most likely candidate is cellular inflammation and the resulting intracellular production of inflammatory cytokines such as tumor necrosis factor (TNF). TNF primarily comes from immune cells such as macrophages that infiltrate into inflamed tissues. And here is the irony: Inflammation is not only the underlying cause of insulin resistance, but the resulting hyperinsulinemia causes further increases in inflammatory mediators known as eicosanoids, and the cycle is amplified.

Effect of Hyperinsulinemia on Silent Inflammation
The type of inflammation that causes insulin resistance is below the threshold of perceived pain; hence the term silent inflammation. Since there is no pain associated with silent inflammation, it can linger for years, if not decades, causing a continuing immunological assault on organs, until enough damage has been done to result in chronic disease. The primary diseases that are accelerated by silent inflammation include obesity, type 2 diabetes, heart disease, and hypertension.

These are exactly the same conditions that cluster together in metabolic syndrome, and accelerate the aging process.

Measuring Silent Inflammation
The first clinical marker discovered for silent inflammation was high sensitivity C-reactive protein (hs-CRP). However this particular marker is relatively crude and is easily increased by infection. A much more precise, and much earlier marker of the presence of silent inflammation is the ratio of two fatty acids in the bloodstream. One is arachidonic acid (AA) and the other is eicosapentaenoic acid (EPA). AA is an omega-6 fatty acid that is a building block for pro-inflammatory eicosanoids, whereas EPA is an omega-3 fatty acid that is the building block for anti-inflammatory eicosanoids. The ratio of AA/EPA in the blood is indicative of the inflammatory potential of each of the 100 trillion cells in the body. The higher the AA/EPA ratio, the more systemic silent inflammation is taking place through the body, and the faster you age.

System Consequences of Silent Inflammation
Now that silent inflammation can be measured, it becomes the best possible early warning signal that aging is accelerating in the body. Since silent inflammation is systemic, this means that every organ of the body is under potential inflammatory assault and this leads to recruitment of macrophages into such inflamed organs. One of the consequences of this macrophage infiltration is

Eicosanoids (eye.kah.sa.noids) were the first hormones developed by living organisms and are produced by every cell in your body. Although they might be considered to be primitive hormones, they control everything from your immune system to your brain to your heart. There are two kinds of eicosanoids, those that promote inflammation (pro-inflammatory) and tissue destruction and those that stop inflammation (anti-inflammatory) and promote healing. You need to have both kinds in the proper balance in order to be in a state of wellness.
the continuing release of inflammatory cytokines that include TNF and corresponding increase in insulin resistance at the cellular level.

One of the first organs to be affected by macrophage infiltration is the adipose tissue. As the inflammation in the adipose increases, so does the resulting insulin resistance. Although a primary goal of insulin is to drive down excess blood glucose levels, it has another important role to play: to inhibit the release of excess free fatty acids from the adipose tissue. As insulin resistance develops in the adipose tissue, there is a release of free fatty acids that can cause lipotoxicity in other organs. Lipotoxicity results when lipid droplets begin to form in cells where excess fat should be absent. If the formation of these lipid droplets is in the liver, the result is fatty liver. If it’s in the smooth muscle, there is more insulin resistance with less ability to remove glucose from the circulation. If there is lipotoxicity in heart muscle cells, it results in lipid accumulation that gives rise to atherosclerotic lesions. And, finally, if lipotoxicity takes place in the pancreas, it leads to the reduction of insulin secretion, itself, with the rapid development of type 2 diabetes.

Treatment

There is no drug that can reduce the earliest stages of silent inflammation. However, anti-inflammatory diets can. There are several components to such a diet. The first is reduction of the glycemic load of the diet by a decreased intake of grains and starches and increased intake of fruits and non-starchy vegetables. The result is a significant reduction of the glycemic load of the diet and corresponding reduction in the amount of insulin that is secreted to reduce the post-prandial blood glucose levels. The second component is adequate protein intake to stimulate the hormone glucagon. Glucagon helps maintain stable blood glucose levels, so that satiety is effectively maintained. The third factor is calorie restriction. This is the only proven dietary factor that can reverse the aging process. However, to be successful, you have to have the appropriate balance of the glycemic load from carbohydrates and protein to maintain satiety in the face of reduced calorie intake. The last factor is a reduced intake of inflammatory omega-6 fatty acids such as vegetable oils; replace them with monounsaturated fats such as olive oil. By reducing omega-6 fatty acids, you effectively reduce the body’s ability to make excess AA, thus decreasing inflammation. These are the hallmarks of the anti-inflammatory Zone Diet that was designed to keep insulin within a zone, thus decreasing the likelihood of developing insulin resistance.

To maximize the benefits of such an anti-inflammatory diet, there are two final components for an anti-inflammatory lifestyle. The first is to supplement the diet with adequate levels of fish oils rich in EPA.
The EPA supplies the necessary building blocks for the production of anti-inflammatory eicosanoids that effectively quell the flames of silent inflammation. Finally, there is consistent, moderate exercise to reduce any accumulated lipid droplets in the smooth muscles, thus reducing insulin resistance.

**Summary**

Aging can be viewed as a continuous inflammatory attack on the body that is hormonally driven. By treating food as if it were a drug and following an anti-inflammatory lifestyle, you have the ideal strategy to reverse insulin resistance and its associated inflammation. But, the door swings both ways. If you ignore the hormonal consequences of the diet, then other anti-aging strategies, such as hormonal replacement, will be highly attenuated, if not severely compromised. Bottom line: Reduce the hormones that increase with age, before you increase the ones that decrease with age, if you truly want to practice anti-aging medicine.

Dr. Barry Sears is a leading authority on the dietary control of hormonal response, and the author of the #1 best seller on the New York Times book list, The Zone. A former research scientist at the Boston University School of Medicine and the Massachusetts Institute of Technology, Dr. Sears has dedicated his research efforts over the past 30 years to the study of lipids. He holds 13 U.S. Patents in the areas of intravenous drug delivery systems and hormonal regulation for the treatment of cardiovascular disease.

To Learn more about The Zone Anti-Inflammatory Lifestyle Management program call 1-800-404-8171 or visit www.drsearszonefast.com. To find out more about the AA/EPA blood test, visit www.omega3testing.conv.physician.html.
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