The Surprising Cause Behind This Highly Destructive Process

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For a long time, scientists have known that free radical damage is an important component of insulin resistance, one of the most important factors leading to diabetes and other diseases. Up until now, scientists have thought that the excessive numbers of free radicals produced in prediabetic people with insulin resistance were a consequence of the insulin resistance rather than the cause. Recently, however, a study indicates that free radical damage might have an even more important role to play in insulin resistance than previously thought.

Free radicals are molecules known as reactive oxygen species (ROS). This group of molecules also includes oxygen ions and peroxides. ROS form as a natural byproduct of the normal metabolism of oxygen and have important roles in cell signaling. However, during times of environmental stress ROS levels can increase dramatically, which can significantly damage cell structures. This leads to a situation known as oxidative stress. ROS are also generated when the body is exposed to stress, pollution, chemicals, cigarette smoke, oxygen, radiation, alcohol, high-fat foods, ozone, food additives, and fuel emissions. ROS are also generated during physical exercise.

Under normal circumstances, cells can defend themselves against ROS damage through the use of enzymes such as superoxide dismutases and catalases. Antioxidants produced in the body also defend against ROS. However, when ROS levels rise dramatically, the levels of antioxidants produced in the body may not be enough to completely scavenge the destructive molecules. Consequently, ROS can damage DNA, RNA, and proteins, the process by which ROS and free radicals contribute to aging.

Instigators of Disease

The Free Radical Theory of Aging was proposed by Denham Harman in the 1950s. Harman and other researchers conducted studies that proved this theory is indeed viable. Gradually, free radical reactions were implicated in a growing number of diseases, including the two major causes of death—atherosclerosis and cancer.

The involvement of free radicals and reactive oxygen species in the development of inflammatory and degenerative disease has now been widely accepted. In the case of the development of atherosclerotic plaque that occurs during cardiovascular disease, LDL oxidation caused by free radicals appears to explain many of the detrimental events that occur during the life history of the plaque.1

A growing body of evidence indicates that free radicals are involved in the development of numerous other health conditions including Crohn's disease,2 ulcerative colitis,2 and Alzheimer's disease.3

The newest research is beginning to reveal that reactive oxygen species are a common thread strung between many other diseases. In fact, a recent study reveals that they could very likely be the cause behind one of the most damaging processes to occur in the body—insulin resistance. Before I discuss this study in more detail, however, I would like to touch briefly on the concept of insulin resistance.

Regulating Insulin

Insulin resistance occurs when cells lose their sensitivity to insulin. When this occurs, sugar is unable to enter the cells. The body essentially ignores the message that insulin is trying to send it, and to compensate, must produce higher and higher amounts of insulin. During insulin resistance, sugar builds up in the blood to a destructively high level.

According to the Neuroendocrine Theory of Aging, proposed by Vladimir Dilman and written about extensively by Ward Dean, MD, insulin resistance is a component of the metabolic pattern of aging. Vladimir Dilman originally proposed the metabolic pattern of aging in the 1960s, which preceded by decades the concept of the modern day metabolic syndrome, a symptom complex manifested by hyperinsulinemia (excess blood insulin), hypertension, and coronary artery disease. While mainstream medicine is finally beginning to recognize the role of insulin resistance in these conditions, Dilman's comprehensive hypothesis explained not only the link between hypertension and coronary artery disease, but also most other commonly occurring age-related diseases.

Current research continues to prove this link between insulin resistance and a variety of diseases. Insulin resistance has been linked to cognitive decline, various cancers, and even depression. High insulin levels have been associated with poor outcomes in breast cancer and it is thought that insulin resistance may be the reason why diabetic patients are more prone to the development of colon cancer. Insulin resistance is also thought to be the underlying factor as to why obesity is a risk factor for post-menopausal breast cancer, cancers of the endometrium, colon and kidney, and malignant adenomas of the esophagus.4-6

Now, a study has provided convincing evidence that free radicals are actually the cause of—rather than just a consequence of—insulin resistance.

One Damaging Process Leads to Another

Because little is known about why insulin resistance occurs in so many contexts, researchers explored whether the various insults that trigger insulin resistance act through a common mechanism. Based on their results, scientists are beginning to believe that the common mechanism that triggers insulin resistance is free radical damage.

The researchers created two cell culture models of insulin resistance. The study authors induced insulin resistance in the cells by two different pathways then began to experiment with increasing and decreasing the amount of oxidative stress to which the cells were exposed. Following this experiment, the scientists also studied the effects of reactive oxygen species in obese, insulin-resistant mice.

Sampling of Conditions Linked to Insulin Resistance

- Cognitive Decline
- Diabetes
- Various cancers, including colon, breast and endometrial cancer
- Depression
- Heart Disease
- Hypertension
- Weight Gain
- Cross-linking

The results of both the cell culture and rodent studies, published in the journal Nature, demonstrated that higher levels of reactive oxygen species triggered insulin resistance,

whereas lower levels of reactive oxygen species reduced insulin resistance by approximately 50 percent.7

"ROS have previously been proposed to be involved in insulin resistance, although evidence for a causal role has been scant," the study authors wrote. "Together, our findings suggest that increased ROS levels are an important trigger for insulin resistance in numerous settings."

James Meigs at Massachusetts General Hospital, who was not one of the researchers conducting the above study, commented in an online edition of The Scientist that "This paper was the first convincing, comprehensive evidence that reactive oxygen species cause insulin resistance."

Meigs and colleagues decided to conduct their own study, in order to investigate whether the systemic oxidative stress that caused insulin resistance in rodents would have the same results in humans. The scientists measured insulin resistance in 2,002 nondiabetic subjects and tested the association between oxidative stress and insulin resistance in individuals without diabetes and among subgroups at elevated risk of diabetes.

The researchers found that insulin resistance increased in proportion to the level of oxidative stress that was occurring in the subjects. There was an 18 percent increase in insulin resistance in the subjects who had the least oxidative stress compared to a 29.4 percent increase in insulin resistance in subjects with the most oxidative stress. When the researchers broke down the results by subjects who were obese, subjects with metabolic syndrome, and subjects with impaired fasting glucose, there was still a strong association between high levels of reactive oxygen species and the development of insulin resistance.8

"Systemic oxidative stress is associated with insulin resistance in individuals at average or elevated risk of diabetes even after accounting for BMI," the study authors concluded.

Stopping the Damage

The newly established link between oxidative stress and the development of insulin resistance indicates that a two-step approach using both antioxidants and blood-sugar-maintaining nutrients is required. Because the body tends to become less sensitive to the effects of insulin as we age, this approach would be prudent for anyone undertaking an anti-aging supplement regimen, especially considering the large number of diseases to which insulin resistance and oxidant stress have been linked. With only 11 percent of Americans consuming the minimal standard of 5 to 7 servings of fresh fruits and vegetables per day, individuals usually aren't receiving beneficial quantities of antioxidants from their diet. The antioxidant-deficient food sources consumed in a typical American's diet along with the overabundance of blood-sugar raising carbohydrates in a typical meal, indicates that everyone can benefit from combining the following antioxidants with nutrients that restore insulin sensitivity.

If there is a causal link between oxidative stress and insulin resistance, it may explain why some of the most powerful antioxidants are also known to improve insulin sensitivity. N-acetyl cysteine has been shown to prevent fructose-induced insulin resistance in rats.9 The turmeric component curcumin also is beginning to emerge as an agent to improve insulin sensitivity, with a new study showing it normalizes antioxidant enzyme activities and lowers insulin resistance in diabetic mice.10

Green tea, which contains a number of well-researched antioxidant components, has improved insulin sensitivity in a number of animal studies. In obese insulin-resistant dogs, green tea improved insulin resistance by 60 percent.11 In a randomized, controlled, human trial of subjects with borderline diabetes or diabetes, although green tea had no effect on blood glucose levels, insulin levels declined based on the dosage of green tea polyphenols given.12

Anthocyanins, antioxidant plant pigments found in bilberries, have been found to improve the function of fat cells (adipocytes), the dysfunction of which is strongly associated with the development of insulin resistance.13

Other antioxidants that have been shown to reduce insulin resistance, increase insulin sensitivity or reduce blood sugar levels include grape seed extract and rosemary.14-15

Two-Step Approach to Healthy Insulin Metabolism

Combining a supplement that contains the antioxidants mentioned above with one that maintains healthy blood sugar levels can be an effective two-part approach in a healthy aging supplement regimen. Goat's Rue, cinnamon (CinSulin®), bitter melon, quercetin and vanadyl sulfate have all been studied for their ability to lower blood sugar, increase insulin sensitivity and protect against the damaging effects of high blood sugar.

Galega officinalis (Goat's rue) has been used with success as an insulin-controlling agent. Goat's rue is rich in guanidine, its hypoglycemic component. The guanidine in goat's rue improves insulin sensitivity and is used to support the health of type 1 and 2 diabetics. Goat's rue causes a long-lasting reduction of blood sugar content in rats and an increase in carbohydrate tolerance. This herb lowers blood sugar in both normal and diabetic humans.16

Cinnamon is another blood-sugar supporting nutrient that improves insulin sensitivity during in vitro, animal and human studies. Cinnamon reduces mean fasting serum glucose by 18-29 percent in subjects with type 2 diabetes after 40 days of daily consumption of 1-6 grams of cinnamon. Furthermore, subjects with the metabolic syndrome who consume cinnamon have been shown to have improved fasting blood glucose, systolic blood pressure, percentage body fat and increased lean body mass compared with the placebo group.17 In women with insulin resistance associated with polycystic ovary syndrome, cinnamon supplementation has resulted in improvements in fasting glucose, glucose tolerance and insulin sensitivity.18

Cinnamon works especially well when combined with chromium, a mineral that has been found to improve insulin sensitivity.17 Chromium also is helpful in reducing carbohydrate cravings.

Bitter melon is another botanical that has reduced insulin resistance in animals, partly through its ability to improve the function of insulin receptors in the liver. It also has been widely researched in animal studies for its ability to improve glucose and insulin tolerance.19

Quercetin, another important component of any blood-sugar supporting formula, is a flavonoid known for its ability to enhance eye health in patients with diabetic cataracts.20 Recent research is unveiling additional properties of quercetin, including its ability to protect against oxidative stress in rodents with experimental diabetes and to prevent damage to the insulin-producing beta cells of the pancreas.21-22

Vanadyl Sulfate can work with goat's rue, bitter melon, and quercetin to help support healthy blood sugar levels. In one of the newest studies on this mineral, it protected against damaging changes that occurred in the aortas of rats with experimental diabetes.23 In obese humans with diabetes, vanadyl sulfate may improve a defect in insulin signaling specific to type 2 diabetes.24

Conclusion

Research is shedding new light on the damaging process known as insulin resistance. Reactive oxygen species and free radicals are now thought to be a possible cause of insulin resistance rather than just a consequence. Therefore, combining a good antioxidant supplement that contains N-acetyl cysteine, turmeric, green tea, bilberry, grape seed and rosemary with a blood-sugar supporting formula containing goat's rue, cinnamon extract, bitter melon and vanadyl sulfate, along with extra chromium, can help protect against free radical damage while supporting healthy insulin levels.

The fact that ROS are generated in so many ways—even during exercise—indicates that antioxidants are an important part of any supplement regimen, even for individuals leading a healthy lifestyle. Furthermore, as we age, nearly everyone becomes insulin resistant. Consequently, the two-part approach of combining a good antioxidant supplement with one that supports blood sugar control fits nicely into any anti-aging supplement program.

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