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COVER STORY

The Metabolic Syndrome

Everyone is familiar with risk factors for cardiovascular disease such as obesity and increased cholesterol and blood pressure. The “risk factor” approach represents the first stage in our understanding of how cardiovascular disease develops and how to prevent it. But why do these risk factors tend to cluster together in the same individuals, and why does treatment of certain risk factors have less impact on cardiovascular health than scientists predicted?

Answers to these questions are beginning to take shape from research inspired by one of the grand theories of modern medicine. The Metabolic Syndrome hypothesis ties cardiovascular risk factors together with mechanisms of aging and, most importantly, with a basic metabolic disorder that at first glance has little to do with the heart and circulatory system.

It has long been observed that cardiovascular disease and diabetes tend to “spring from a common soil.” That soil is now thought to be a metabolic disturbance known as insulin resistance. Insulin is a hormone that regulates cellular nourishment. It is secreted when blood levels of glucose and amino acids rise, signalling the “fed” state. Cells with proper sensitivity to the insulin signal then absorb and metabolize nutrients from the blood. When cells become resistant to insulin, they do not respond adequately to the insulin signal and cellular metabolism goes awry. Insulin resistance is thought to result from an interaction of genetic factors with physical inactivity, abdominal obesity, diet, hormonal changes and aging processes.

In diabetes there is not enough insulin to properly regulate cellular nutrition. This can be because not enough insulin is produced by the beta cells of the pancreas (Type I), or because of insulin resistance (Type II). It is estimated that 25% of adults exhibit insulin resistance. Why don't most of these individuals develop diabetes? The body tries to compensate for insulin resistance by increasing insulin production. While this and other compensatory mechanisms succeed in most cases, there is nevertheless a price to be paid.

Insulin resistance is a complex cellular pathology that affects multiple organ systems and predisposes patients to a myriad of metabolic defects. It causes disturbances in biochemical responses at the cellular level that, combined with side effects of the body's attempts to cope with insulin resistance, are now thought likely to promote hypertension (high blood pressure), coronary artery disease and quite possibly aging (see the sidebar “Insulin Resistance and AGE's”).

Many studies have found that the disturbances of insulin/glucose regulation in insulin resistance cluster with other major cardiovascular risk factors. These include hypertension, obesity, a procoagulant state and an abnormal “lipid triad” (increased levels of triglycerides and small LDL particles, with decreased levels of HDL cholesterol). The complex of insulin resistance and the cardiovascular risk factors that cluster around it make up the metabolic syndrome, also aptly called “Syndrome X.” Given the complexity of this syndrome, a prodigious quantity of research will be needed to explain just how the pieces of the metabolic syndrome puzzle fit together.

In the future, treatment of the underlying metabolic syndrome could prove more effective than treating isolated risk factors for cardiovascular disease. A case in point is blood pressure-reducing drugs. They reduce coronary heart disease mortality and morbidity by only about 15%, as compared to a 40% reduction in strokes. Such drugs may not get to the root of the problem in cardiovascular disease. Insulin resistance predisposes patients to hypertension and reinforces other cardiovascular risk factors as well. When insulin sensitivity increases, blood pressure is reduced. The mechanisms linking insulin resistance to hypertension are not yet clear, but may include sodium retention in the kidneys, defective ion transport, and sympathetic nervous system stimulation.

Several studies have shown CoQ10 to reduce elevated blood pressure modestly, by roughly 10%. One interesting study tracked the number of antihypertensive drugs needed by patients taking supplemental CoQ10. Half of the 109 patients were able to discontinue

Insulin resistance and AGE's

Insulin resistance and the compensatory increase in insulin secretion bring about a state of chronically increased insulin and glucose levels in the blood (hyperinsulinemia and hyperglycemia). Excessive glucose tends to react with proteins to form, through a series of reactions, compounds called AGE's (advanced glycation end products). Some of these same reactions cause food to brown in the oven. AGE's are thought to hasten aging processes and promote degenerative diseases of aging such as Alzheimer's disease. AGE formation connects glucose to the free radical theory of

at least one such drug after an average of 4.4 months. However these studies were either very small or lacked a control group of patients taking placebo pills.

aging. Free radicals are often described as fixatives of glycation, and AGE's can generate oxidative stress. It has been suggested that the complications of diabetes may illustrate, at an accelerated pace, the consequences of insulin resistance and AGE formation. These include kidney impairment, neuropathy, cataracts and atherosclerosis. A calorie restricted diet, which lengthens lifespan in animal experiments, has been shown to reverse insulin resistance.

A new well-designed study advances this research in two ways. The study demonstrates rigorously that CoQ10 lowers blood pressure in heart patients, while dramatically improving measures of insulin/glucose regulation. The 59 patients in this study were admitted to the hospital for acute coronary artery disease including heart attacks. These patients had been taking blood pressure medication for at least one year. Half the patients were given 120 mg of CoQ10 per day, while the other half were given placebo pills; both groups continued to take prescribed medications.

After eight weeks the CoQ10 treated group showed significant reductions in heart rate, systolic and diastolic blood pressure, and triglyceride levels, along with a significant increase in HDL cholesterol levels, compared to the placebo group (see Table 1). What is intriguing is that the researchers also demonstrated major reductions in blood glucose and insulin levels, together with improvement in the insulin/glucose ratio. There was also a small yet statistically significant reduction in the waist to hip ratio, a measure of abdominal obesity, in both men and women. Thus CoQ10 treatment significantly improved four pillars of the metabolic syndrome—hypertension, blood lipoproteins, insulin resistance, and obesity—after eight weeks of treatment. It is to be hoped that similar research will be carried out on patients at earlier stages of cardiovascular disease.

While it is not yet clear whether CoQ10 has a role in diabetes prevention or therapy, preliminary studies in animal models show that CoQ10 levels are significantly depressed in the heart and liver mitochondria of diabetic rats, and that CoQ10 treatment prevents development of hyperglycemia in mice. In addition, studies suggest that insulin-producing cells may be especially susceptible to oxidative stress, low levels of mitochondrial DNA and bioenergetic deficit.

Immunity and cancer

Immunological senescence, the age-related decline of the immune system, parallels the decline of the thymus gland. The thymus produces T (“thymus-derived”) lymphocytes early in life, but as we age its ability to regenerate T lymphocytes rapidly diminishes. Two decades ago Emile Bliznakov demonstrated that a single dose of CoQ10 partially reverses the effects of immunological senescence in old mice (Bliznakov EG, 1979):

We have shown that senescent animals develop a marked deficiency of coenzyme Q[CoQ10]-enzyme activity in the thymus. This deficiency is paralleled by gross anatomical changes in this organ, described as age-involution, and a profound suppression of the immunological responsiveness. Administration of coenzyme Q (coenzyme Q10) partially restores this suppression.

In other animal studies he found that CoQ10 improved resistance to carcinogens and various bacterial and protozoal infections.

While Bliznakov's line of research has not been pursued by others, there has been a steady trickle of case reports and pilot studies on CoQ10 in cancer. CoQ10 deficiency appears to be relatively common in cancer, particularly in breast cancer. French researchers recently studied CoQ10 levels in 80 women with breast cancer. They found that negative prognostic indicators corresponded to deeper reductions in CoQ10 levels. In earlier research, CoQ10 pioneer Karl Folkers and colleagues presented five case reports of tumor regressions, including complete regressions, in “high risk” breast cancer patients treated with CoQ10.

Folkers, in collaboration with WV Judy and RA Willis, recently conducted a pilot study of CoQ10 therapy in 14 patients with recurrent prostate cancer. Ten of the patients (71%) responded to CoQ10 treatment, while the four non-responders were the oldest patients with the most severe cases, highest PSA levels, metastases and the largest prostate glands. After long-term CoQ10 therapy (600 mg daily for 360 days), the ten responders showed an average 73.6% reduction in PSA levels and 48.4% reduction in prostate mass, as well as restoration of lymphocyte counts to the high normal range.

Until large-scale clinical trials test the efficacy of coQ10 in specific cancers, this application area remains highly speculative. Such trials, which are very expensive, would perhaps already be underway if coQ10 were patentable. Conservative testing of coQ10 in combination with conventional cancer therapies could do more harm than good, since coQ10 might protect cancer cells from the cytotoxins used in chemotherapy as well as from the effects of radiation.

CoQ10 has long occupied a place at the Life Extensionist table as a cellular energizer, antioxidant and cardiovascular therapy. The research reviewed in this article brings CoQ10 to the head of the table as a bioenergetic/antioxidant therapy for aging.

Parameter	Placebo Group		CoQ10 Treated Group	
	Baseline	After 8 Weeks	Baseline	After 8 Weeks

Heart Rate	115	105	112	85
Systolic Blood Pressure	166	164	168	152
Diastolic Blood Pressure	105	103	106	97
Blood Insulin (Fasting)	64	59	65	36
Blood Glucose (Fasting)	140	129	142	95
Triglycerides (Fasting)	158	155	159	143
HDL Cholesterol	44	44	44	48

Table 1. Effect of CoQ10 treatment on metabolic syndrome parameters.

Notes: International units of measure have been converted to the units normally employed in blood test reports in the U.S. LDL cholesterol was not measured in this study. Adapted from Singh RB et al., 1999.

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