Obesity and Inflammation

A common theme that links many diseases and chronic illness is uncontrolled cellular inflammation. It is a factor in diseases including cardiovascular disease, diabetes, cancer, arthritis and many autoimmune-related conditions. Obesity has recently been added to this group of diseases as it is now known to present a low grade inflammatory response within many of the body’s tissues, which cause deleterious effects, often leading to the development of cardiovascular and metabolic disease. It is well known that being overweight is detrimental to one’s health, but until recently the known mechanisms were limited. Scientists over the last decade have started to unravel the mystery of why obesity leads to premature death. Although there is still much to learn, it is valuable to comprehend the known effects of chronic inflammation, as the prevalence of obesity continues to be a rising problem among the American population, particularly in children.

Inflammation is, by design, a protective response leading to the repair of tissue. When inflammation becomes chronic, as is the case with obesity, chemical mediators, derived from different cellular activities, change in dynamics causing a progressive state of decline. Fat cells are now considered an immune organ that secretes numerous immune modulating chemicals. Visceral fat, in particular, is associated with the low grade inflammation that seems to be a contributing pathologic feature for metabolic disease through insulin resistance and the promotion of atherosclerotic build-up in circulatory vessels. When high levels of visceral fat are combined with physical inactivity, overnutrition, and advancement in age, the effect becomes more pronounced. Visceral fat is highly metabolic and contributes to cytokine hyperactivity. Adipokines secreted from fat tissue influence the metabolic process and contribute to proper function. The consequent low grade inflammation associated with obesity causes disturbance in the secretion and function of adipokines. Research has identified changes in adiponectin, leptin, and resistin that exhibit harmful effects upon the body in obese individuals.

Adiponectin is an antatherogenic agent, meaning it helps prevent the development of atherosclerotic plaque in blood vessels and slows the progression of atherosclerosis in coronary vessels. It does this by acting directly upon the vessel wall, inhibiting adhesive molecules from contributing to plaque formation and acts as a blocking agent to the formation of foam cells. In the skeletal muscle and the liver, adiponectin serves to promote insulin sensitivity and a positive blood lipid profile. Visceral adiposity reduces adiponectin concentrations. Lowering the adiponectin concentrations lessens the cardioprotective effect, leading to increased cardiovascular risk.

Leptin regulates energy metabolism and balance in conjunction with the brain’s hypothalamus. Leptin is currently being touted as having cardioprotective benefits among its others roles in metabolism. Leptin concentrations adjust in response to obesity and contribute to insulin resistance. The changes in leptin concentration have also been recognized
as a risk factor for coronary heart disease. Likewise increased resistin concentrations correlate with obesity related inflammation and may be associated with the initiation and progression of atherosclerotic lesions. Resistin also promotes insulin resistance, although the actual mechanism is not known.

Insulin resistance due to adipokine dysfunction is further influenced by free fatty acids liberated directly into the liver from visceral fat tissue. Visceral fat releases chemicals and fatty acids into the portal system where they act on the connecting organs. The portal circulation system is a specialized network of blood vessels that connect the visceral organs to the liver. The excess fat in portal circulation has detrimental effects on insulin action, which is worsened by sympathetic hyperactivity in response to obesity. Sympathetic hyperactivity causes heightened lypolytic action resulting in excess free fatty acids in the blood. These actions combined with beta cell hypersecretion and reduced insulin clearance resulting in hyperinsulemia, lead to early stage diabetes.

Interleukin-6 (IL-6) is possibly another factor associated with inflammatory detriment within the portal system. High levels of IL-6 are a marker for inflammation and vascular pathology. Obese subjects demonstrated a 50% greater portal vein IL-6 concentration, demonstrating, again, the profound effect visceral fat has on pathogenic indicators. Portal vein IL-6 correlates with systemic C-reactive protein concentrations. C-reactive protein is associated with cardio- and peripheral vascular disease. C-reactive protein and oxidative stress are now presumed to interact in the early inflammatory processes of atherosclerosis. This is significant for young obese individuals. Although more research is necessary for conclusive association, C-reactive protein may be a new risk factor for CAD in individuals under 25 years of age.

The imbalance between increased inflammatory stimuli with a concurrent reduction in anti-inflammatory activity may be the foundation for the accelerated endothelial dysfunction and insulin resistance associated with obesity and the comorbid disorders of metabolic disease. More research is needed to clearly delineate the particular relationships, but it seems evident that the low grade inflammation caused by obesity and visceral adiposity lead to the premature development of disease. This, more so than ever before, identifies the importance of weight management during the developmental years and ongoing efforts to control weight throughout one’s lifespan. For individuals that are currently obese, there is still plenty of hope. Weight loss is related to reduction of oxidative stress and inflammation, and these beneficial effects likely translates into reduction of cardiovascular risk in obese individuals. Likewise, exercise and dietary management, along with pharmacologic intervention can lead to atherosclerotic reversal in the earlier stages of CAD. Individuals with central adiposity, poor blood lipid profiles, hypertension, and/or insulin resistance should seek immediate professional assistance to prevent further health detriment.