Obesity and Inflammation: Creating the Perfect Storm

by Dr. P. K. Doyle-Baker

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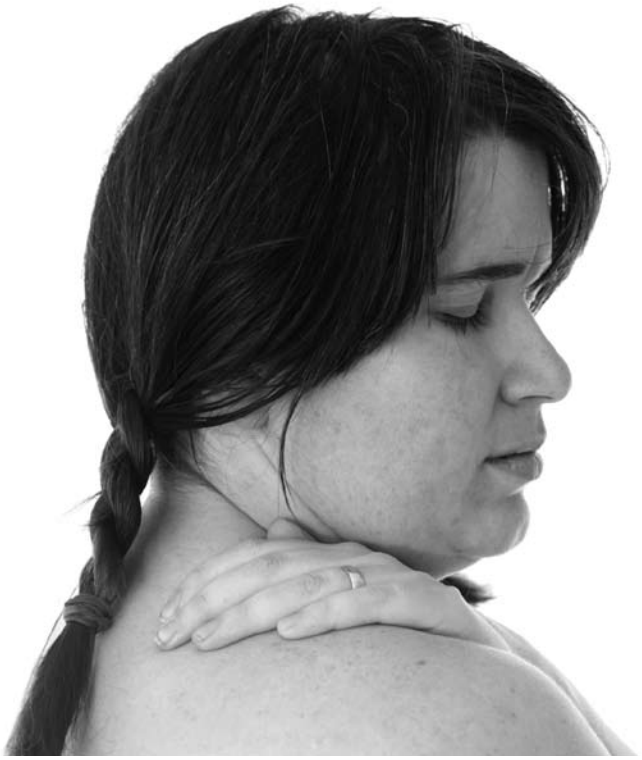

Obesity is known as a persistent health threat. Individuals who are overweight are at risk for developing many diseases and conditions including cardiovascular (CVD) and diabetes (DM). The prevalence of obesity and these associated morbidities (diseases), known as the metabolic syndrome, has reached epidemic proportions (Grundy et al., 2004).

Many of us are unlikely, however, to link obesity and inflammation with these diseases (Shoelson et al., 2007).

Inflammation

Typically, inflammation brings to mind the cardinal signs of:

- pain
- swelling
- redness
- heat, and
- loss of function.

We experience these signs when we develop an infection, such as with tonsillitis or an ear infection. This response is how the body fights agents of infection, particularly pathogens, i.e. those that cause disease which invade the tissues and are foreign to the body.

Acute Inflammatory Response

Inflammation is part of the body's natural defense system, not just against infection but also injury, toxins, and tissue irritation. A cascade of events follows in which the body's white blood cells and specific chemicals (cytokines) mobilize to protect us from these foreign invaders. This protective response occurs very quickly, is somewhat obvious, and in the case of tonsillitis or an ear infection is considered an acute reaction.

Chronic, Low-Grade Inflammatory Response

Excessive stimulation of the inflammatory process, however, can aggravate tissue damage. This process occurs much more quietly and insidiously than the acute response and is called a low-grade or chronic inflammation. Although the processes of acute and chronic responses are similar, chronic inflammation is not confined to a particular tissue and involves the endothelium (interior surface of blood vessels) and other organ systems. This type of inflammatory response has been identified in a number of chronic diseases and plays a key role in damage to the heart's blood vessels such as with atherosclerosis (Dandona et al., 2004).

White Blood Cells and Interleukins

The role of chronic inflammation as a cause and/or result of atherosclerosis was recognized a little over a decade ago with the discovery of interleukins (Dinarello, 1994). Interleukins (IL) are cytokines that are secreted proteins that act as signaling molecules and as mediators between white blood cells specifically, leucocytes which are part of the immune system. In other words, interleukins provide a means of cell-to-cell communication and many of them are produced by leukocytes and can also act on leukocytes.

Interleukins can be pro-inflammatory and others are anti-inflammatory (Bruunsgaard, 2005). A balance between the two is required to maintain control of the inflammatory process. A pro-inflammatory state can alter the function of the endothelium, for example, homeostasis can change and the endothelium will become predominately pro-coagulant (promotes blood clotting).

Obesity and Inflammation

Excess fat is an irritant and the body reacts to this

irritation by elevating the levels of several interleukins and other inflammatory markers (Bastard et al., 2000; Mohamed-Ali et al., 2001). These include: interleukin-6 (IL-6), interleukin-8 (IL-8), and tumour necrosis factor alpha (TNF alpha). TNF alpha is a pro-inflammatory marker produced also by white blood cells, specifically lymphocytes and macrophages that ingest foreign material. The expression or production of all of these cytokines is directly related to the degree of obesity of the individual (Mohamed-Ali, Pinkney et al., 1998; Hotamisligil et al., 1993; Mohamed-Ali et al., 1997). Recent studies have shown that macrophages are key cells in the development of obesity, wherein there is progressive infiltration of macrophages into the adipose tissue (Harford, 2009).

Visceral Adipose Tissue

Clearly, our traditional view of adipose tissue as a passive reservoir for energy storage is no longer valid (Kershaw and Flier, 2004; Berggren et al., 2005). We must forever remind ourselves that although fat is essential, it is also an endocrine organ that is highly active from a metabolic perspective (Berggren et al., 2005). A complete discussion of the complex physiology and mechanisms of adipose-related inflammation is beyond the scope of this article. However, it is increasingly evident that fat surrounding the trunk, that is, visceral adipose tissue (VAT), is responsible for secreting many pro-inflammatory cytokines. Visceral adipose tissue is now considered the common underlying condition linking insulin resistance/Type 2 DM, and the metabolic syndrome, thereby creating the "perfect storm". When visceral adipose tissue is accompanied by the risk factors of lower levels of high-density lipids (good cholesterol), elevated triglycerides (circulating fat), and high blood pressure, cardiovascular morbidity and mortality (death) are increased significantly (Lakka et al., 2002; Weisse, 2004).

Intervening

It is difficult to intervene successfully once this vicious cycle of cardiovascular risk factors and atherogenesis (plaque deposition on arterial walls) is established. Intervening at an earlier stage, for example, to reduce directly the development of intra-abdominal adiposity, may provide a more successful prospect for reducing the risk of a cardiovascular event.

Anti-Inflammatory Effect of Exercise

Exercise is known to lower blood pressure and decrease the overall risk for CVD and DM by lowering triglycerides, raising high-density lipids, and decreasing low-density lipoprotein (bad cholesterol). Several research studies identify the anti-inflammatory effects of exercise and allude to the possibility of a dose response such that greater levels of fitness are associated with an anti-inflammatory profile than are lower degrees of physical fitness (Bastard et al., 2002). As well, the anti-inflammatory effect of exercise may be mediated by a reduction in adiposity (Woods et al., 2006).

Summary

In summary, persistent, low-grade inflammation that occurs with obesity is an independent predictor of several chronic diseases and all-cause mortality. We know also that there are several potential mechanisms for the anti-inflammatory effects of exercise, including loss of body fat and reductions in macrophage accumulation in adipose tissue. Granted, further research is still needed to solidify our understanding of the endocrine function of adipose tissue and this will likely lead to more successful therapies for chronic metabolic disorders. Without a doubt, the most rational therapy we have today is adding a modest amount of exercise to our life by which we can reduce the likelihood of developing obesity-related inflammatory diseases, such as Type 2 DM and atherosclerosis. (PDC exam on page 20).

References available upon request.

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In the autumn 2009 issue of the *Fitness Informer* we published an article, "Where has all the Vitamin D Gone?" by Dr. Tish Doyle-Baker and graduate student Angie Karlos with the references removed. We normally do this as we are a non-peer reviewed periodical, but in this case, references should have been included for clarity and for accuracy. We apologize to the authors and our readers for this error. A copy of the article, with references, will be available in the *Fitness Informer* office.

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PDC EXAM: Obesity and Inflammation

1. Inflammation is now recognized as:
   a. A treatment for obesity
   b. A type of nonspecific immune response
   c. The act of inflaming or the state of being inflamed
2. A common theme that links many diseases and chronic illness is uncontrolled cellular inflammation.
   a. True
   b. False
3. The sequence of cellular and chemical events associated with an inflammatory response...
   a. Can vary
   b. Never varies
4. The discovery of interleukins over a decade ago helped in understanding how chronic inflammation plays a role in the cause of atherosclerosis.
   a. True
   b. False
5. A small protein released by cells that has a specific effect on the interactions between cells, such as on communications between cells or on the behaviour of cells is called:
   a. Vitamin D
   b. Cytokines
   c. Lymphokines
   d. Hormones
   e. RBC
6. Key cells have been identified in the development of obesity. These cells have progressive infiltration into adipose tissue. They are:
   a. Microphages
   b. Colony stimulating factor (CSF)
   c. Macrophages
   d. Interferon
7. It is increasingly evident that a specific type of fat is responsible for secreting many pro-inflammatory cytokines. What type of fat is it?
   a. Intramuscular
   b. Subcutaneous
   c. Visceral
   d. Brown adipose tissue
8. Fat cells are now considered an immune organ that secretes numerous immune modulating chemicals.
   a. True
   b. False
9. High levels of IL-6 are a marker for inflammation and vascular pathology.
   a. True
   b. False
10. Adipose tissue can be considered to have what type of function?
    a. Endogenous
    b. Endocrine
    c. Panocrine
    d. Exocrine
11. Exercise and dietary management, along with pharmacologic intervention can lead to atherosclerosis reversal. However, the more successful prospect for reducing the risk of a cardiovascular event is to avoid the development of intra-abdominal adiposity altogether.
    a. True
    b. False

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