Newsletter

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The Diet-induced Proinflammatory State: A Cause of Chronic Pain and Other Degenerative Diseases?

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Introduction:

John Hunter, a Scottish surgeon in the 1700's, proposed that inflammation is essentially a response to injury, rather than a disease entity itself. Many types of cell injury can cause inflammation, including hypoxia, physical agents such as trauma and burns, chemical agents and drugs, infectious agents, immunologic reactions, genetic derangements, and nutritional imbalances involving both deficiencies and excesses of various nutrients. Hunter also suggested that the purpose of inflammation is to restore normal tissue function.

Modern authors agree that inflammation should lead to tissue repair and remodelling, which allow for the restoration of function. However, when acute inflammation becomes chronic, tissue healing cannot occur. In this situation, the inflammatory process should be viewed as a disease process. Many diseases are, in fact, a manifestation of chronic inflammation. For example, rheumatoid arthritis, which is characterized by chronic inflammation of the synovial membrane, is classified as a disease and not as a transitional phase in the healing process. A recent review article states that acute respiratory distress syndrome, sarcoidosis, glomerularnephritis, psoriasis, inflammatory bowel diseases, rheumatoid arthritis, osteoarthritis, and atherosclerosis are all inflammatory diseases.

It is clearly inappropriate to view inflammation as merely a component of the healing process; rather, inflammation should be viewed as a key promoter of degenerative diseases, which kills millions of Americans each year. Indeed, 6 of the 10 leading causes of death in Americans are coronary heart disease, cancer, stroke, diabetes mellitus, atherosclerosis, and chronic liver disease and cirrhosis, all of which have been previously described as inflammatory in nature.

Discussion:

Today, we have overwhelming evidence that diets rich in vegetables and fruit but moderate in meat and fat are associated with a reduced risk of various forms of cancer, cardiovascular disease as well as other diseases such as arthritis, diabetes or cataract. Even the aging process appears to be favourably reduced by high fruit and vegetable intake.

If eating sufficient vegetables, fruits, and the proper fats can help to prevent inflammatory diseases, it is then reasonable to suggest that an inadequate intake of these foods would promote inflammation and disease and that such a diet should therefore be viewed as "proinflammatory." Regrettably, our consumption of fruit and vegetables and our intake of essential fatty acids is remote from recommended levels, which likely leads to a proinflammatory state and places us at risk for a host of diseases.

Fatty acid imbalances
Omega-6 versus omega-3 fatty acids

Fatty acid imbalances may actually form the foundation on which the proinflammatory state develops, as an excess of omega-6 fatty acids (linoleic acid and arachidonic acid) and a deficiency of omega-3 fatty acids may be involved the development of numerous diseases. For example, Eskimos eating their

traditional diet, which is high in omega-3 fatty acids and very low in omega-6 fatty acids, are almost free of the chronic degenerative diseases that plague those in Western societies who consume virtually no omega-3 fatty acids and excessive amounts of omega-6 fatty acids. Unfortunately, those of us who live in Western society consume a diet with an omega-6 to omega-3 fatty acid ratio of about 10:1 to 25:1, which is significantly greater than the 1:1 ratio on which humans evolved and on which our genetic patterns were established.

Omega-6 and omega-3 fatty acids are concentrated in cell membrane phospholipids. The human body contains trillions of cells, each of which is housed in a lipid bilayer membrane composed of phospholipid molecules. It is known that specific biochemical pathways produce phospholipids and that our diet directly influences their production. Dietary omega-6 fatty acids strongly predominate omega-3 fatty acids. Consequently, arachidonic acid, along with its proinflammatory potential, will be inserted into membrane phospholipids.

Linoleic acid is the vegetable oil precursor of arachidonic acid, both of which are omega-6 fatty acids. Although seeds and grains are rich in linoleic acid, they are devoid of arachidonic acid. However, animal cells readily convert linoleic acid into arachidonic acid. Thus, there are 2 ways in which humans increase tissue concentrations of arachidonic acid. First, we consume foods rich in linoleic acid, which is subsequently converted into arachidonic acid; second, we consume liberal amounts of arachidonic acid-containing animal products, such as beef, chicken, and eggs. In contrast, we consume minimal amounts of foods that are rich in linolenic acid, eicosapentanoic acid (EPA), and DHA, such as green leafy vegetables, fish, and fish oil. The outcome of this eating pattern is an excessive production of proinflammatory eicosanoids from arachidonic acid and a deficiency in the production of anti-inflammatory eicosanoids.

Although the term "diet-induced proinflammatory state" is new, it is still generally understood that our population suffers from the proinflammatory state. This understanding is demonstrated daily by the use of copious amounts of prescription and over-the-counter anti-inflammatory drugs to treat aches, pains, osteoarthritis, rheumatoid arthritis, heart disease, and cancer. NSAIDs function to inhibit the cyclooxygenase enzyme and thereby inhibit the production of a variety of proinflammatory eicosanoids. Although NSAIDs may offer a symptomatic relief from pain and inflammation and may delay the onset of heart disease, cancer, it should be obvious that NSAID therapy will never influence the proinflammatory state that is established by an unbalanced dietary intake of omega-6 and omega-3 fatty acids.

At present, the practice of omega-3 supplementation remains more art than science. Supplementation guidelines do not exist and, in reality, may never exist. Ultimately, the purpose of omega-3 supplementation is to shift the balance of omega-6: omega-3 ratios and the precise dose will be different for each person depending on individual dietary levels. It is quite conceivable that a patient who reduces the consumption of omega-6 rich grains and oils and ingests more omega-3 rich fish and green vegetables may need less omega-3 supplements compared with someone who subsists predominately on omega-6 rich foods.

On the basis of the available literature, it would be reasonable to suggest supplementing the diet with 1 to 3 g of omega-3 fatty acids per day as both a therapeutic and preventive measure.

The anti-inflammatory nature of fruits and vegetables

A diet rich in fruits and vegetables tends to be anti-inflammatory, while a diet deficient in these foods is proinflammatory. The nutritional quagmire in which researchers often find themselves revolves around the following question. What specific factors in fruits and vegetables account for their anti-inflammatory and disease-preventing effects? As of yet, no one can thoroughly answer this question. For example, in the case of cancer, we are told the following by the American Cancer Society: Vegetables and fruits are complex foods containing more than 100 beneficial vitamins, minerals, fiber, and other substances. Scientists do not yet know which of the nutrients or other substances in fruits and vegetables may be protective against cancer. The principle possibilities include specific vitamins and minerals, fiber, and phytochemicals—carotenoids, flavonoids, terpenes, sterols, indoles, and phenols—that are present in foods of plant origin. Until more is known about specific food components, the best advice is to eat 5 or more servings of fruits and vegetables each day.

Consider citrus fruits as an example, which contain more than 170 phytochemicals in addition to the known nutrients such as vitamin C. Citrus contains some 60 flavonoids, 40 limonoids, 20 carotenoids, as

well as terpinoids, and it is possible that no one may ever know the precise flavonoid, limonoid, or terpinoid that exerts the greatest anti-inflammatory effect in a given disease. Each fruit and vegetable is equal in its bewildering complexity, which also helps to shed light on the foolish notion that nutritional supplements can take the place of whole foods. In no way can an ascorbic acid supplement, for example, make up for the plethora of vitamins, minerals, and phytochemicals that are found in an orange or grapefruit.

In general, we now know that nuts, seeds, whole grains, herbs, spices, fruits, and vegetables, contain a host of health promoting and disease-fighting nutrients, such as vitamins, minerals, antioxidants, essential fatty acids, and numerous phytochemicals. Vegetables and fruits possess antioxidant activity, modulate detoxification enzymes, stimulate the immune system, decrease platelet aggregation, modify cholesterol metabolism, reduce blood pressure, and possess antibacterial and antiviral activity.

Several nutrients found in fish, vegetables, and fruits are known to offer anti-inflammatory benefits, especially the previously mentioned omega-3 fatty acids involved in eicosanoid synthesis and the broad family of anti-oxidants and phytochemicals.

Inadequate antioxidant intake
Free radical pathology

A free radical is a very reactive and unstable molecule because it has an unpaired electron in its outer orbital. When a free radical is formed it very readily gives up or accepts an electron to stabilize its unpaired electron. This exchange of electrons is very damaging to cellular structures. Free radicals are thought to damage lipids, proteins, membranes, and DNA.

Free radicals promote the release of arachidonic acid from cell membranes, which results in the production of proinflammatory PGE2 and LTB4. In addition, macrophages and neutrophils produce free radicals that can damage local tissues and promote inflammation.

Free radicals may also promote inflammatory damage by enhancing the production of various cytokines, such as tumour necrosis factor. “It is becoming increasingly apparent that in addition to promoting cytotoxicity, reactive oxygen metabolites may also initiate and/or amplify inflammation via the upregulation of several different genes involved in the inflammatory process, such as those that code for pro-inflammatory cytokines and adhesion molecules.” Clearly, free radicals are proinflammatory substances.

Free radical pathology and human diseases

Free radicals are involved in a general mechanism of tissue injury in most, if not all, human diseases. Indeed, free radicals have been implicated in more than 100 conditions, from arthritis and hemorrhagic shock to AIDS. For example, research suggests that free radicals participate in the pathogenesis of heart disease, aging, Parkinson's disease, amyotrophic lateral sclerosis, altered immunity, cataracts, and cancer. A recent review discusses most of these diseases and their relationship to free radicals and antioxidant therapy. Painful muscle dysfunction may also be promoted by free radicals. A recent article presented evidence indicating that fibromyalgia was mediated, in part, by free radical activity.

Even a health-promoting activity such as exercise can promote free radical production. This occurs as a result of a 10- to 15-fold increase in oxygen uptake during exercise. Sen indicates that “regular physical activity in association with dietary habits to ensure adequate supply of a combination of appropriate antioxidants may be expected to be a prudent course.”

It should be clear that we cannot escape free radicals and their proinflammatory nature, because they are a normal component of human life. The only way to combat free radical damage is to ensure a continuous and adequate supply of antioxidants through diet and perhaps supplementation.

Antioxidant nutrient deficiencies in America

A deficiency of antioxidant nutrients permits free radical proliferation, a situation that could reach a catastrophic threshold. Indeed, “without continuous and abundant antioxidant and radical scavenging capability, survival would be impossible.”

Bioflavonoids also exert an inhibitory effect on eicosanoid synthesis. In fact, anti-inflammatory activity was the first known biologic effect of flavonoids. In both human and animal studies, flavonoids have demonstrated an anti-inflammatory effect. Athletes who consumed flavonoids recovered significantly faster after injury compared with those who did not take flavonoids. At the present time, some 500 different flavonoids have been identified. In addition to inhibiting eicosanoid synthesis, flavonoids function as accessory anti-oxidants and help to protect collagen. Flavonoids also affect inflammation by reducing capillary permeability and fragility.

Mechanical pain may be a biochemical condition

A new study commissioned by the Merck Corporation revealed that 9 in 10 Americans suffer with pain. Despite the high prevalence of pain, there is still no consensus about the genesis and etiology of most pain syndromes, which is probably a result of the fact that frank pathology and obvious tissue changes are not associated with most kinds of pain. Terms such as simple backache, somatic pain, nonspecific pain, muscular pain, nociceptive pain, and mechanical pain are used to describe such pain. The most common medical treatment approach involves the use of NSAIDs, which are known to provide both peripheral anti-inflammatory and central analgesic effects. Concerning this treatment approach, it is important to consider the mechanism by which NSAIDs inhibit pain. Pain results from the stimulation of peripheral nociceptors that are activated by numerous chemical mediators, including lactic acid, potassium ions, PGE2, LTB4, histamine, 5-hydroxytryptamine, bradykinin, IL-1, and TNF. NSAIDs are known to directly or indirectly antagonize some of these mediators, particularly prostaglandins.

Research within the last 10 years suggests that the treatment of musculoskeletal, or so-called mechanical pain, requires a safe and effective biochemical method. Phospholipase A2 (PLA2) is the enzyme that cleaves the unsaturated fatty acid from the C-2 position of cell membrane phospholipids. PLA2 can act on DGLA or EPA, resulting in the production of noninflammatory eicosanoids, or PLA2 may act on arachidonic acid and result in the generation of proinflammatory eicosanoids, such as PGE2. Consider the fact that both herniated disks and synovial fluid from degenerative joints contain PLA2, and that human lumbar disk PLA2 is 20- to 100,000-fold more active than any other phospholipase yet to be described. Perhaps this is why simple or mechanical back pain can often be debilitating and lead both doctors and patients to believe that a much more serious pathologic condition is responsible for the pain.

Sierkerka suggests that nutritional therapy should accompany any chosen treatment regimen to accelerate the healing of a damaged disk, the most integral aspect of acute therapy being the dietary addition of foods containing n-3 and the avoidance of those that contain arachidonic acid. Except for the work of Sierkerka, biomechanically oriented professionals, such as chiropractors and orthopaedic surgeons, have placed little emphasis on the importance of restoring fatty acid balance for the purpose of reducing pain and inflammation.

The main biochemical intervention for back pain, osteoarthritis, and rheumatoid arthritis continues to be NSAIDs, an approach that needs to change. Consider that NSAIDs are taken to reduce inflammation and that these medications merely act to inhibit a biochemical process acting on fatty acids that ultimately come from our diet. We literally eat ourselves into an inflamed and painful state and then seek out passive care from doctors to intervene on our behalf. Medications and chiropractic manipulation may reduce pain and inflammation, but they cannot influence the underlying diet-induced proinflammatory state. Dietary modification and nutritional supplementation appear to be the only interventions that can address the underlying cause.

Conclusion:

We can no longer view different diseases as distinct biochemical entities. Nearly all degenerative diseases have the same underlying biochemical etiology, that is, a diet-induced proinflammatory state. Although specific diseases may require specific treatments, such as adjustments for hypomobile joints, Beta-blockers for hypertension, and chemotherapy for cancer, the treatment program must also include nutritional protocols to reduce the proinflammatory state.