June 2007

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DIET, NUTRITION, OBESITY AND THEIR ROLE IN ARTHRITIS

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Key Words: Obesity, nutrition, orthopaedic disease, dietary supplements.

Abstract

Obesity and poor nutrition, individually and together, have created costly musculoskeletal disease epidemic in the United States. Processed food, with abundant "empty" calories, has contributed greatly to our dietary woes. Much of the food consumed today is packed with calories but refined to the point that essential nutrients are lacking. Even worse, processed food may have ingredients added that are detrimental to good health. Abundant research has documented a close relationship between obesity, poor diet and orthopaedic problems. Dietary supplements have been proven to provide both disease prevention and therapeutic benefits. Unfortunately, many weight loss programs and methods are ineffective and possibly dangerous. Additionally, the FDA does not regulate the nutritional supplement industry and product quality is high variable. It is imperative that physicians treating patients with musculoskeletal complaints understand these disease producing relationships and have a network in place to refer patients to reputable weight loss entities and for high quality nutritional supplements.

Background

This article has been peer reviewed. It is the authors' final version prior to publication in Seminars in Arthroplasty 18(2):117-121, June 2007. The published version is available at http://dx.doi.org/10.1053/j.sart.2007.03.009,

Until a few generations ago, almost all of the food we consumed was harvested from the ground, picked from a tree or hunted, killed, and eaten after little processing. Processed food did not exist or was very scarce. Anyone who consumed enough food from diverse sources was adequately nourished both in terms of calories and essential nutrients. Today highly refined food packed with calories and taste is the primary staple for many Americans and for the first time in man's history, malnourished and overweight is a common problem. Delicious calorie rich "fast food" has led to an obesity epidemic in America. What's worse is that much of the processed food we eat lacks essential nutrients necessary for good health. Our dietary woes are common knowledge and were documented recently in the satirical film "Super Size Me". For those who have not viewed this movie, the significant weight gain demonstrated with a one month diet composed exclusively of fast food is appalling. However, more concerning is the tremendous negative health impact that this type of diet causes. In addition to vitamins, a processed diet may lack minerals, essential fatty acids, antioxidants and fiber, all of which we need for good health. The deleterious effects of obesity and poor diet extend well beyond the cardiovascular system. Recent research has shown that obesity and poor diet also causes musculoskeletal disease.[1, 2, 3,4,5,6] This article will review the relationship between these entities and evaluate ways that the physician can improve orthopaedic health or prevent disease through diet.

Obesity and Degenerative Joint Disease

The American obesity epidemic has led to a substantial increase in a plethora of diseases including diabetes, hypertension and cardiovascular pathology. Obesity related disease is estimated to account for an amazing 6.8% of all U.S. healthcare costs and with regards to the

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musculoskeletal system a close association between obesity and degenerative joint disease has been documented. [3,5,6] In one study of patients undergoing total hip or total knee arthroplasty, it was demonstrated that an increased body mass index (BMI) was closely associated with the need for joint replacement. Patients with a BMI between 37.5 and 40.0 have an odds ratio for needing a joint replacement of 9.4 compared with non-obese controls. [5] In the so-called "Nurses Health Study", women with a BMI $\geq$ 35 were twice as likely to develop hip or knee osteoarthritis compared with subjects having a normal body weight. [6] Women with an elevated BMI by 18 years of age were five times more likely to develop osteoarthritis. It has been estimated that obesity is directly or indirectly responsible for over 200,000 joint replacements in the United States annually. [7] How obesity causes arthritic disease is an obviously important question. The common and anecdotal explanation is that excessive joint loading leads to cartilage deterioration and eventually symptomatic arthritis. This joint overload theory simplifies the pathophysiology of degenerative joint disease. To exemplify this point, consider a 170 pound long distance runner. During a run, the force on the knee for this individual approximates 2.0 Newtons per millimeter^2. Conversely, at heel strike, a 250 pound individual, when walking, generates a knee joint force of approximately 2.0 Newtons per millimeter^2 . A long distance athlete may run upwards of 30 miles per week. Meanwhile an obese person is often sedentary. If excessive joint loading was the correct theory of osteoarthritis, there would be an epidemic of arthritic disease in runners and the obese would be sparred. In fact, clinical studies reflect just the opposite with evidence showing that running probably does not contribute and my even lower the risk of degenerative joint disease. [8] If it was just a mechanical issue, why are heavy patients prone to arthritis but less likely to have polyethylene wear after total joint replacement.[9] The most likely answer is that obesity related arthritis is caused by systemic inflammation.

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Obesity and poor nutrition activate the immune system and cause a low grade state of systemic inflammation. Intra-abdominal adipose tissue is metabolically active and generates inflammatory mediators. [10] Excess adipose tissue is associated with insulin resistance, hypertension, dyslipidemia, and prothrombosis. However, very importantly, it is also associated with a pro-inflammatory status. [10] Support for this theory of obesity associated arthritis is abundant. Anedotally, it has been observed that obesity is associated with not only a higher incidence of lower extremity arthritis, but also more degenerative disease of upper extremity joints. [11] Of course, these joints are non-weightbearing and a mechanical explanation for upper extremity arthritis is not rational. This finding suggests a systemic explanation for obesity related arthritis. A recent study demonstrated that obesity is associated with elevated levels of c-reactive protein and increased erythrocyte sedimentation rates, both markers for inflammation. [12] In addition, obese individuals have significantly higher levels of pro-inflammatory mediators including, interleukin-6 and tumor necrosis factor alpha. [12] The elevation of inflammatory markers and mediators is more profound in woman than men and this may explain the epidemic of arthritis amongst obese women. [13] In addition, individuals with an "apple shaped" (more intraabdominal adipose tissue) build have been shown to be much more likely to suffer from systemic inflammation than "pear shaped" morphotypes. [13] The basic science of the relationship between adipose tissue and inflammation has also been investigated. Adipocytes secrete adipocytokines which mediate inflammation. [10] Obese individuals have been found to have higher levels of adipocytokines in synovial fluid .[14] Adipocytes contain large quantities of arachidonic acid which is the building block for pro-inflammatory eicosanoids including prostaglandins, thromboxanes and leukotrienes. [14] Investigators have suggested that there is a "role of adipose tissue in arthritis". [10] The knee is a fat sequestering joint and large quantities

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of adipose tissue in the knee joint may explain the projected enormous rise in the number of total knee arthroplasties predicted for the next two decades.

The Role of Nutrition in Arthritis

Obesity alone does not completely explain the link between dietary habit and arthritis. While almost no one in the United States is starving for calories, the refined and artificial diet that many Americans consume, creates deficiencies of essential nutrients needed for optimal musculoskeletal health. Vitamins, trace minerals, essential fatty acids and antioxidants along with other substances can only be obtained in adequate quantities from a high quality diet or by consuming nutritional supplements. These agents are needed for good orthopaedic health and deficiencies lead to significant clinical sequelae. Unfortunately, high caloric, nutrient depleted, processed and flavored food is generally less expensive and tastes better than healthy fresh food. Healthy fresh food often requires expensive methods of preservation. Cost, taste, and lack of knowledge drives many Americans to eat low quality food which promotes less than optimal health. The problem is so ubiquitous and profound that in a country with abundant resources for producing food, nutritional deficiencies are common. All substances needed for good musculoskeletal health cannot be fully evaluated in this short manuscript but the role of key ingredients for a healthy orthopaedic diet can be described.

Dietary Supplements

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In a perfect world, we would all consume a diet providing everything needed for optimal health. Unfortunately, even educated, conscientious consumers frequently stray from ideal dietary habits. The difficulty of "eating right" all the time partially explains the exponential rise in sales for the dietary supplement industry. It seems ironic that many of us travel to our local supermarket to purchase nutrient depleted food and then on the way home, stop at a dietary supplement shop to purchase ingredients we believe are missing from our diet. The Foundation of Innovative Medicine has reported that 74% of surveyed consumers purchase dietary supplements. [15] However, 68% of supplement users are not confident that they are taking the correct products or using them properly. Many patients look to their physicians for advice on supplements, but may be uncomfortable asking about what they consider to be a deviation from mainstream medicine. The typical American diet today has deficiencies of vitamins, trace minerals, essential fatty acids, fiber, and antioxidants. The optimal diet should consist of the proper amounts of protein, carbohydrates, and fats. Studies have shown that ideally we should consume seven servings of fruits and vegetables daily. [16] To get enough omega-3 essential fatty acids, we need to eat four to five servings of fish per week. [17] Many of us lack the time, desire, energy, financial means, and knowledge to follow this sort of dietary regimen. Dietary supplements are meant to correct the "unbalanced", low nutritional value, high caloric diet. Use of dietary supplements is not the best option, eating correctly is. However, from a practical perspective, use of supplements is the second best method to ensure adequate intake of everything needed for optimal health. There is abundant evidence that dietary supplements can treat or prevent disease.

Vitamin D and Calcium

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The role of vitamin D and calcium in phosphate absorption and bone formation is well known to orthopaedic surgeons. Deficiencies lead to rickets in childhood and adult osteomalacia. [18,19] The recommended daily dosage of vitamin D is 400 International Units (IU). However, because of the osteoporosis epidemic, the FDA has contemplated increasing this requirement to 1,000 IU. [20] Osteoporosis related fractures cause an enormous strain on our healthcare system both financially and measured by human suffering. Calcium deficiency coupled with inadequate vitamin D exponentially promotes the development of osteoporosis associated with aging. [21] The current recommendations for calcium and vitamin D intake are frequently not satisfied by many and osteoporosis is rampant. [19, 22, 23, 24]

In addition, vitamin D seems to have a beneficial effect on osteoarthritis minimallizing the symptoms associated with this disease. The Framingham Study which has carefully documented, over many decades, the relationship between lifestyle, diet and health revealed that individuals who consume large amounts of vitamin D are three times less likely to develop symptomatic arthritis. [25] While consumption of vitamin D did not effect the incidence of osteoarthritis, it did decrease the frequency of symptoms associated with this disease. Increases in bone stress associated with cartilage loss can cause pain and loss of cartilage resulting in deformity which significantly increases forces on the effected bone. This increase in stress leads to microfracture and painful inflammation. This phenomenon has been described by findings on MRI which are categorized as bone marrow lesions. [26] These bone marrow lesions equate to stress or insufficiency fractures of bone. Enhanced bone strength associated with vitamin D consumption may explain its positive role in this disease process. In the Framingham Study,

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individuals who consumed the most vitamin D ("highest tertile") were more than three times less likely to have symptomatic arthritis compared with those in the lowest consumption tertile. In addition, high levels of vitamin D are associated with a slower progression of radiographic deformity. This finding is likely explained by higher quality bone resisting deformity and erosion.

Glucosamine and Chondroitin Sulfate

Healthy chondrocytes manufacture glucosamine and in these same cells through a series of steps convert glucosamine to chondroitin sulfate, a glucosamineoglycan (GAG). GAG's are an essential component of the cartilage matrix and determine the durability and mechanical properties of the cartilage matrix.[27] Aging chondrocytes produce less glucosamine and deficiency of this substance is believed to lead to cartilage deterioration.[27] This relative deficiency of glucosamine may explain the relationship between arthritis and aging and the beneficial role of this agent for preventing age related degenerative joint disease. Commercially, chondroitin sulfate is frequently combined with glucosamine. Individually, chondroitin sulfate has been shown to stimulate GAG production and inhibit pro-inflammatory activity.[28] It is has

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been demonstrated that chondroitin sulfate and glucosamine have synergetic characteristics and anabolic effects are greater when these agents are combined. [29] Chondroitin sulfate and glucosamine have been shown to work as well or better than non-steroidal anti-inflammatory drugs for treatment of arthritic symptoms in several well controlled studies. [30,31,32,33,34,35,36] In a recent blinded, controlled NIH funded study of glucosamine and chondroitin sulfate this combination was found to be more effective than Celebrex for moderate to severe arthritic symptoms. [37]

Essential Fatty Acids

Fatty acids (examples are Omega 3 and Omega 6) are "essential" dietary constituents and cannot be endogenously produced. Their role in physiologic homeostasis is extensive, but pertinent to this article, they serve as important inflammation mediators. [16]

Fatty acids are the precursors of prostaglandins, thromboxanes and leukotrienes. Omega 6 fatty acids function as the building blocks for proinflammatory agents while omega 3 fatty acids generate inflammation suppressing mediators. Evidence exists that for optimal, healthy regulation of the immune system, omega 3 and omega 6 fatty acids should be consumed in approximately a 1:1 ratio. [16] Excessive intake of omega 6 fatty acids creates a proinflammatory state which leads to inflammatory related disease. [37] Unfortunately, omega 6 fatty acids are ubiquitous in the modern American diet. Omega 6 fatty acids are found in vegetable oils and these agents are frequently added to processed foods to enhance their appearance and taste. Supplemental use of omega 3 fatty acids has been shown to have therapeutic effects for many chronic inflammatory conditions including asthma, eczema, psoriasis, lupus and ulcerative colitis. [38]

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There are numerous studies demonstrating that omega 3 supplements produce beneficial effects on the symptoms of rheumatoid arthritis. [39,40,41,42,43,44,45,46,47,48,49] In one double blind, placebo controlled study patients with rheumatoid arthritis who consumed 1.8 grams of EPA (a type of omega 3 fatty acid) per day had less morning stiffness and joint tenderness. [41] Continuous use of this supplement provides extended relief of inflammatory arthritic symptoms. In a recent study, patients with rheumatoid arthritis taking 2.6 grams of omega 3 fatty acids per day continuously for one year reported significant clinical benefits and reductions in the need for drug therapy. [49] The efficacy of omega 3 fatty acids for the treatment of osteoarthritic symptoms has not been evaluated but the inflammatory component of this disease suggests potential benefit could be obtained using Omega 3 supplements.

Antioxidants

Reactive oxygen and nitrogen species (free radicals) have been shown to play a significant role in the parthenogenesis of inflammatory arthritis. [50] These highly reactive molecules can bind to substances in the cartilage collagen matrix disrupting the normal homeostasis of this network. Eventually deterioration of collagen occurs and osteoarthritis follows. Nitric oxide synthase is a key enzyme evolved in the formation of free radicals. Aspirin, tetracycline, steroids, and methotrexate have been shown to suppress nitric oxide synthesis and this may partially explain their anti-inflammatory properties. [50]

Dietary antioxidants can neutralize free radicals before they inflict tissue damage. Numerous studies have shown a beneficial effect when patients with arthritis consume adequate doses of antioxidants. [51,52,53] Vitamins A, C, E , and selenium have significant capacity to

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consume free radicals. Several studies have shown that vitamin E supplements are effective for the treatment of arthritis symptoms. [51,52,53] Combining vitamins C and E has revealed a synergistic effect between these agents for treating arthritis. The Framingham Arthritis Study demonstrated antioxidant supplements had a preventive effect on arthritis progression. [25] Based on radiographic parameters, there was a 3 fold reduction in arthritis disease progression for patients consuming the highest amount of vitamin C. Those same patients were much less likely to develop symptomatic osteoarthritis.

What Can Orthopaedic Surgeons Do?

Obviously the practice of good medicine is more than surgically replacing worn out joints. All orthopaedic surgeons should practice mindful of disease prevention and non-operative options. Overweight patients should be educated about the close relationship between orthopaedic disease and obesity. The physician should be knowledgeable about treatment options for obesity and be aware of the best sources for referral. Bariatric surgery has evolved as quickly as the obesity epidemic has grown and is safer and more effective than in the past. Morbidly obese patients should be appropriately referred to centers with the lowest complication rates and least invasive methods. For patients who are moderately overweight, weight loss centers are available and often effective. As we all know, entities promoting assistance with weight loss are not all reputable and safe. It is imperative that the physician be aware of the best weight loss resources and programs available in the area where they practice. A medically supervised weight loss program is in the patient's best interest. Larger groups practicing high volume joint replacement should consider employing a registered dietician developing an "in-

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house" medically supervised weight loss program that provides patients with enhanced care. In addition, this program can serve as a source of ancillary income. Patients often ask their doctors advice about dietary supplements. This is a rapidly growing industry with a plethora of available products. The evidence of clinical efficacy for each individual product is highly variable. Additionally, because the FDA does not closely regulate this industry, the quality of a specific product is very dependent on the manufacturer. It is important for physicians to be aware of the pertinent scientific evidence supporting a particular product. In addition, a well educated doctor knows about supplement quality and can assist his or her patient in making appropriate choices for selecting these products. Appropriate, high quality, nutritional supplements may be used to treat or prevent musculoskeletal disease in many patients. Considering that approximately 17,000 fatal complications related to non-steroidal anti-inflammatory medications occur annually, it seems prudent to consider alternative treatment options.

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