

# NUTRI NEWS



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## Nutraceutical Interventions in Arthritis

Ronald Ritchie, D.C.

With the upsurge in desire to improve the quality of life and find alternatives to drugs in an aging society, there has been an explosion of research and knowledge in natural substances that address conditions common to aging. Arthritis is one such condition. It is estimated that some form of arthritis affects one in every eight Americans. Therefore treating arthritis through "natural" means is vital to any integrative physician.

There are several types of arthritis, each having both common and unique characteristics. Therefore determination of the specific arthritis present is necessary in order to construct a valuable health care program. Unique physiologic features of each patient such as metabolic type, allergies or sensitivities, digestive status, toxicity status, etc. must also be determined as these circumstances will influence the effectiveness of therapy or present conditions that must be first corrected before effective intervention can be introduced. Concurrent health conditions should be known such as diabetes, hypertension, renal disease, dysbiosis, circulatory problems, etc. for the same reasons. As I am sure you know some nutrients will not function optimally unless their metabolic avenues are clear of traffic. Detoxification, adequate hydration (40% of body weight in ounces daily without underlying cardiac, pulmonary or renal complications), reduction of allergic load, reduced sugar consumption, etc. will all "clear the road" for nutraceuticals to do their work in the best possible way.

Exercise is also a major factor for all patients with arthritis. But the same exercise for all arthritis sufferers will not work either. Generally speaking, aerobic level activity will provide a good constitutional basis. For most patients with arthritis aquatic exercise seems to work the best. The buoyancy of the water helps mitigate gravitational and impact load on the joints while providing moderate resistance. There are many fine books that will give guidance in this area. Focusing the patient on proper form and the purpose for the exercise as well as challenging specific muscle groups or joints should be a focus for all physicians. Care must be taken not to over stress arthritic joints but this usually is not a problem. More often than not keeping the patient motivated when they do not immediately improve is a greater problem.

Specific nutrients that are useful for those patients with arthritis are the following. This is certainly not an exhaustive list as the constellation of nutraceutical substances that address the various aspects of arthritis is vast. All of these nutrients are not necessary for every patient so let's try to specify which is most valuable for

specific patients.

### Glucosamine Sulfate

Glucosamine is an amino sugar component of chitin, heparan sulphate, chondroitin sulphate and many complex glycosaminoglycans (mucopolysaccharides). Proteoglycans are large carbohydrate-rich molecules present in virtually all cartilage and many connective tissues. Glucosamine sulfate provides the basic building block for cartilage matrix<sup>1</sup>. Proteoglycans are hydrophilic and provide resiliency, load distribution, shock absorption, and compressive resistance functions especially as it relates to joints. Loss of fluid content and degradation of type II collagen (the major collagen component of cartilage<sup>2</sup>) appears to be a key to the pathological process common in many forms of arthritis<sup>3,4</sup>. Early investigations of glucosamine sulfate appeared to demonstrate the ability of the substance to actually rebuild and restore thickness to joint cartilage. More recent studies regarding disease modification<sup>5</sup> demonstrate glucosamine sulfate's ability to prevent cartilage thickness loss<sup>6</sup>. There also appears to be an anti-inflammatory effect<sup>7</sup> of glucosamine but in clinical trials has not worked as well as NSAIDs. Individuals taking NSAIDs and glucosamine concurrently have found less benefit than with glucosamine alone. This is hypothesized to be a consequence of COX suppression and therefore decreased availability of all eicosanoids within cartilaginous tissues. Glucosamine sulfate appears to be absorbed intact with one study indicating greater than 88% absorption<sup>8</sup>. Glucosamine sulfate is the form which has been studied in many clinical and laboratory trials, and it is this form that has been repeatedly demonstrated as effective<sup>9</sup>; however, it is believed that glucosamine HCl

*Continued on page 2*

### INSIDE THIS ISSUE

<b>Nutraceutical Interventions in Arthritis</b> .....	page 1
by Ronald Ritchie, D.C.	
<b>NSAIDs</b> .....	page 3
by Ronald Ritchie, D.C.	
<b>Arthritis: An Overview</b> .....	page 6
by Ronald Ritchie, D.C.	
<b>The Potential Multi-Modal Benefits of Joint Support Nutrients for Anti-Aging</b> .....	page 7
by Dr. Ronald Klatz and Dr. Bob Goldman	

## **Nutraceutical Interventions – Continued from page 1**

should be equally as effective. There has been some recent debate regarding blood sugar problems when giving glucosamine sulfate to diabetics<sup>10</sup>. There is currently no definitive answer as to the effect of glucosamine on blood glucose, as it has not been a primary outcome variable of any of the glucosamine studies. It should be noted that studies have demonstrated that the sugar portion of glucosamine is not metabolized through “normal” pathways.

With all of these concepts in mind, treatment of most types of arthritis with glucosamine sulfate is appropriate although the most effective use is in patients with osteoarthritis. Therapeutic dosage of 1500 mg daily in divided doses is appropriate.

### **Chondroitin Sulfate**

Chondroitin sulfate is a glycosaminoglycan that is a major component of the extracellular matrix and connective tissue of animals, found on the outside of the cell membranes of some animal cells. They are repeating polymers of glucuronic acid and sulphated N-acetyl-glucosamine residues that are highly hydrophilic and anionic. It was initially thought that chondroitin sulfate (because of its molecular size) would not be absorbed intact and therefore accounted for some of the failure in treatment. Recent studies have demonstrated chondroitin’s absorption and availability in the disaccharide form<sup>11</sup>; however, it is not as well absorbed as glucosamine. Chondroitin sulfate has a similar anti-inflammatory effect to glucosamine<sup>9</sup> although other studies demonstrate that it may act via a different mecha-

nism<sup>12,13</sup>. Many of the benefits attributed to glucosamine can also be related to chondroitin sulfate. Chondroitin appears to protect existing cartilage by decreasing water loss from the matrix and inhibiting the breakdown of cartilage by enzymatic reactions. Many recent studies have demonstrated combined glucosamine/chondroitin therapy seems to be more effective for certain individuals or types of arthritis<sup>14,15</sup>. Although glucosamine is a precursor for chondroitin synthesis and logic would seem to indicate that administration of glucosamine would address all cartilage maintenance and repair issues, this process requires a significant amount of metabolic energy. In some individuals there are circumstances where this metabolic energy is limited or unavailable, therefore administration of chondroitin may spare this metabolic pathway and help protect cartilage better than glucosamine sulfate.

In my practice I have found that individuals with a significant number of concurrent health conditions such as asthma, diabetes, digestive disorders, etc. will respond more favorably using a combined glucosamine/chondroitin formulation. I have also found that patients with rheumatoid arthritis have better results using chondroitin sulfate with MSM than glucosamine sulfate alone. Chondroitin sulfate should be given at 1500 mg daily in divided doses.

### **MSM** (methylsulfonylmethane)

MSM is a source of organic sulfur found naturally in the human body and in many foods. It is the major metabolite of DMSO (dimethyl sulfoxide), is 34% elemental sulfur, and is the primary component that appears to be of the greatest benefit to the body<sup>16</sup>. While sulfur supports many functions, it is well known for maintaining connective tissue health and therefore supports those tissues with significant amounts of collagen and keratin such as ligaments, tendons, arteries and cartilage. Type II collagen degradation by enzymatic action is a major component in the pathogenesis of arthritis. MSM provides additional elemental sulfur to aid the body in the repair process of these tissues. MSM may support the body in regulating insulin production, improving skin smoothness and elasticity, regulating environmental and allergic sensitivities, enhancing bowel function and liver detoxification, and enhancing respiratory function<sup>16</sup>. Some studies have demonstrated immunosupportive effects of MSM<sup>17</sup>. Lastly sulfur is a key element necessary in the detoxification processes which is highly valuable in many patients with arthritis. Given this information, MSM is very useful in the treatment of most types of arthritis but RA patients seem to respond the best. Dosages vary from 850 to 3000 mg daily. Some authorities advocate even higher amounts.

### **Bromelain**

Bromelain is a proteolytic enzyme complex derived from the stalk of the pineapple plant which demonstrates anti-edematous, anti-inflammatory, anti-thrombotic and fibrinolytic activities. Bromelain is absorbed intact through the GI mucosa with up to 40% being detected in the blood after consumption<sup>18</sup>. Bromelain’s therapeutic actions are only partially due to its enzymatic activity. It has several biologic effects including directly affecting bradykinin production<sup>19</sup>; selectively removing certain cell surface molecules that affect lymphocyte migration and activation<sup>20,21</sup>; has immunomodulating properties<sup>22</sup>; enhances T-cell responsiveness<sup>23</sup>; stimulates increased phagocytosis, pathogen killing capacity and

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*Continued on page 4*

# NSAIDs (Nonsteroidal Anti-Inflammatory Drugs)

Ronald Ritchie, D.C.

Since the purification of a white powder from willow bark, its laboratory stabilization and synthesis in the early 1800s, aspirin (being documented as a pain reliever as early as 5BC) has become a staple of medicine. In the 1970s its action was more clearly elucidated and consequently other nonsteroidal anti-inflammatory drugs (NSAIDs) were developed. NSAIDs, are a classification of substances that have analgesic, antipyretic and anti-inflammatory effects that are chemically and physiologically distinct from steroids. With the discovery of the existence of cyclooxygenase-II (COX-II) in 1991, additional chemical substances were introduced further expanding the class. In recent years many NSAIDs have become available over-the-counter leading to broad and long-term use by the general public. In 2001, NSAIDs accounted for 70 million prescriptions and 30 billion over-the-counter doses sold annually in the US<sup>1</sup>.

## Mechanisms of Action

Virtually all NSAIDs act as modifiers of inflammation by competitively inhibiting (either indifferently or selectively) cyclooxygenase from converting arachidonic acid into prostaglandins<sup>2</sup>. Three isoenzymes of cyclooxygenase have been identified; COX-I, COX-II and recently COX-III. COX-I is present in virtually all cells and is constitutively expressed at low levels. It has a significant and persistent presence in the gastric mucosa, microvasculature, platelets and renal glomeruli. Consequently COX-I activity is vital in the regulation of platelet aggregation, microvascular blood flow in the kidneys and stomach, and gastric mucosa maintenance and secretions<sup>3</sup>. COX-II is considered an "inducible" enzyme and is more exclusively related to the inflammatory process<sup>4,5</sup>. It was originally thought that selective inhibition of COX-II would not interfere with COX-I and eliminate much of the gastric consequences. COX-III was discovered in 2002 with continuing investigation as to its specific role<sup>6</sup>. Acetaminophen is the only currently known COX-III modifier. Additional mechanisms exerted by NSAIDs that contribute to their anti-inflammatory action are a reduction of superoxide radicals, induction of apoptosis, decreased nitrous oxide synthesis, decreased pro-inflammatory cytokines (TNF- $\alpha$  and IL-1), modified lymphocyte activity, and cellular membrane permeability changes<sup>7</sup>.

NSAIDs are thought to induce analgesia through interference of prostaglandin E1, F2 and F2  $\alpha$  mediated pain formation or with neurotransmitters or modulators in the nociceptive system. There is also the thought that there may be a central action of the drugs by opioid peptides, inhibition of serotonin release or inhibition of excitatory amino acid receptors<sup>8</sup>. None of the NSAIDs is known to have a direct effect on pain centers as do narcotic agents. Additional effects of NSAIDs include CNS stimulation, increased CO<sub>2</sub> stimulation, vasodilation and depression of vasomotor centers, and increased clotting times<sup>9</sup> as a consequence of altered prostaglandin synthesis. Generally speaking most NSAIDs available over-the-counter are non-selective inhibitors of both COX-I and COX-II whereas many available by prescription are more selective COX-II inhibitors. Many of these drugs affect both isoenzymes to varying degrees.

## Uses of NSAIDs

NSAIDs are mainly effective in treatment of pain in which prostaglandins sensitize nociceptors and instigate inflammation. At lower doses most NSAIDs have a good analgesic effect but anti-

inflammatory activity requires higher dosage administrations. There seems to be little clinical efficacy difference between NSAIDs at equivalent doses other than dosing regimens, route of administration and tolerability. They are routinely prescribed for the treatment of arthritis, headache, dysmenorrhea, bone pain, bursitis, muscle pain, inflammation from injuries, etc<sup>10</sup>. Over-the-counter doses are usually accurate for analgesia and anti-pyretic effects.

## Adverse Effects

Pharmaceutically, two primary areas of adverse reactions are recognized, gastrointestinal and renal. Most of these effects appear dose-dependent. An estimated 10 to 20% of patients taking NSAIDs experience some form of GI disturbance and gastrointestinal events are estimated to result in 103,000 hospitalizations and 16,500 deaths per year in the US representing 43% of drug-related emergency visits. It is also estimated that NSAIDs were over-prescribed in 42% of patients<sup>11</sup>. Common GI problems include nausea, dyspepsia, ulceration and bleeding, and diarrhea<sup>12</sup>. This is especially true of aspirin and the other non-specific COX inhibitors. These conditions occur as a result of the loss of the cytoprotective effects of prostaglandins from COX-I inhibition and the direct action of the acidic drug on the impaired stomach mucosa. When these GI symptoms present, the generally accepted medical treatment is to prescribe H2 or proton pump inhibitors.

The GI disturbance results in a cascade of downstream dysfunctions. The addition of chemical substances that further raise stomach pH or diminish proteolytic enzyme production exacerbates these effects. The protein mal-digestion, introduction of incompletely digested proteins into the lower GI tract and colon, altered gastric pH, and vitamin and mineral mal-absorption will have significant impact. Dysbiosis, bowel content putrefaction, regional gut wall irritation (possible "leaky gut" syndrome), absorption of toxins and/or immunoreactive proteins, biliary dysfunction, pancreatic enzymatic imbalances, and small bowel neuroendocrine dysfunctions are all potential sequelae.

Photosensitivity is a common adverse effect of many NSAIDs and appears to be a direct result of the metabolism of the drugs themselves<sup>13</sup>. Hepatotoxicity has recently been found to be a significant problem with elevated liver enzymes appearing during long-term administration. The VIGOR trial, which resulted in the withdrawal of Vioxx (rofecoxib) from the market, was to show that this drug had less GI upset than naproxen. Although Vioxx did cause less stomach irritation there was a significantly higher incidence of myocardial infarction<sup>14</sup>. Other studies have found the same potential relationship with the more conventional NSAIDs<sup>15</sup> such as ibuprofen. It is hypothesized that interference with nitric oxide production, platelet aggregation, cellular apoptosis in vascular endothelium, and membrane permeability alteration accounts for the increased MI events. There are additional adverse reactions involving NSAIDs<sup>16-19</sup> that many physicians believe are "acceptable risks in light of the benefit obtained" when alternative drugs or lack of treatment have much worse consequences. Whether these adverse reactions are acceptable risks is up to each practitioner and patient. Fully informing the patient of what could be in store for him or her as a result of the administration of a drug or pharmaceutical should be part of every physician's routine. There are some very valuable alternative substances for inflammatory conditions that much of the "main stream" medical world does not consider or value. Weaning patients from toxic chemical dependency to healthier sub-

Continued on page 5

## **Nutraceutical Interventions – Continued from page 2**

reactive oxygen species production<sup>24</sup>; produces post-traumatic and post-surgical edema reduction<sup>25</sup>; and was able to induce increased natural killer cell activity in immunocompromised individuals<sup>26</sup>. Studies comparing bromelain's anti-inflammatory effects against pharmaceuticals demonstrate greater levels of improvement and decreased dependency on analgesics<sup>27</sup> with bromelain. All of this recent elucidation of the mechanisms of action of bromelain only goes to strengthen the therapeutic value and necessity of use in inflammatory disorders such as arthritis but should also include digestive disorders<sup>28</sup>, pulmonary disease, vascular disease, etc.

The most effective dosage for bromelain is 5,000 m.c.u. (milk clotting units) - three times daily between meals. I have found that getting patients to take it twice daily is about the best they can do so I prescribe two twice daily. Bromelain must be taken on an empty stomach (two hours after or one hour before a meal) and be undenatured in order to have the desired effect for arthritis. Taken with meals bromelain is an excellent aid in protein digestion.

### **Omega-3 Fatty Acids**

Fish source omega-3 (n-3) fatty acids have long been known for their cytoprotective capacity. In the past 10 years over 4500 studies have been performed on these valuable fats. They are cardioprotective reducing mortality significantly, anti-arrhythmic, induce lower triglycerides, reduce joint tenderness in RA patients, are anti-inflammatory, anti-tumorigenic, and anti-thrombotic<sup>29</sup>. Virtually all cell membrane phospholipids are composed of n-3 or n-6 fatty acids from which are derived the various components of the arachidonic acid cascade. Deficiency in either n-3 or n-6 fatty acids will cause imbalance in eicosanoid production<sup>30</sup>. Studies have demonstrated the following functions of n-3 fatty acids. A decrease in arachidonic acid concentrations with decreased clotting times and increased fibrinolysis<sup>31</sup>; decrease in multiple inflammatory markers in many conditions<sup>32,33</sup>; decrease in TNF and IL1 in chronic inflammatory diseases<sup>34</sup>; down-regulation of inflammation by enhancing IL10 expression<sup>35</sup>; reduced IL1 and LTB4 in many tissues<sup>36</sup>; and is a potent inhibitor of leukocyte adhesion receptor expression and leukocyte-endothelium interactions<sup>37</sup>. Omega-3 fatty acids exert effects outside of the eicosanoid synthesis pathways. The net effect of n-3 fatty acids is to reduce heart attack and disease risks<sup>29</sup>, stabilize myocardial membranes<sup>38</sup>, decrease cancer cell growth rates<sup>39</sup>, have anti-depressant effects (several major medical trials under way presently), and improve chronic inflammatory disease<sup>40</sup>. As it relates to arthritis, n-3 fatty acids will reduce inflammation and edema in joints as well as aid in the repair process of many of the damaged tissues. High doses are valuable especially in RA but also in OA during inflamed episodes.

A word about fatty acids. Many studies have demonstrated the need for balance in the consumption of n-3 and n-6 fatty acids. A recent NIH survey states that the average American consumes n-6/n-3 fatty acids in a 47:1 ratio whereas the proper ratio for good cellular health is 7:1. Also the source of n-3 fatty acids should be natural fish. There are many recent endeavors to prove that n-3 from vegetable or grain sources are comparable to fish oil. Most plant sources of omega-3 fatty acids do not provide EPA and DHA, the two major omega-3 fatty acids found in fish sources. While fatty acids such as alpha-linolenic acid (ALA) certainly have health

benefits, it is not clear that they are metabolized by the body in a fashion similar to EPA and DHA. We do not have data to show that the data on fish oil supplementation can be completely replicated by supplementing with plant sources of omega-3 fatty acids. Also be aware of the "trans" problem which are fats mutated into the trans configuration by high temperature processing and cooking. Be sure the n-3 you and your patients consume are from a reliable source. Therapeutically valuable dose range is 2000-6000 mg daily in divided doses for arthritis<sup>29</sup>.

### **Hyaluronic Acid**

A relatively new player in the arthritis treatment market is hyaluronic acid. Since HA is a component of the cartilage matrix, it may be valuable in the treatment for arthritis. It has been demonstrated that inflammation within joints will cause fragmentation of HA and degradation of the cartilage matrix<sup>41</sup>. The vast majority of HA administration has been by intra-articular injection, implantation of surgical films and gels, and the like. Intra-articular injections of HA have proven effective in long-term studies<sup>42</sup> and have been used for many years. Studies have demonstrated that HA administration in osteoarthritis will reduce inflammation and promote fibrinolysis<sup>43</sup>. Glucosamine and chondroitin sulfate have both been demonstrated to increase HA production within joints with long term administration<sup>44</sup>. Other therapeutic uses of HA have been performed for many years mainly directed towards ligament and tendon repair, and connective tissue support. The exact dosages orally to provide the best benefit is still unclear.

### **Type II Collagen**

Type II collagen is a major component of connective tissues and cartilage. Conditions that generate long term inflammatory processes such as RA seem to cause a biochemical change whereby these collagen fibers are replaced with less hydrophilic and flexible material. Studies have demonstrated that type II and V collagen are those most commonly affected in those with arthritis and may even be the focus of the auto-antigens of RA. Administration of purified type II undenatured collagen will act almost like an "allergy shot" to reduce inflammation in joints of RA patients by activating the GALT system<sup>45</sup>. This response appears to be dose dependent giving greater immuno-responsiveness at slightly higher doses<sup>46</sup>. There may be a double benefit by decreasing inflammation through immune modulation and providing raw materials for connective tissue repair and maintenance. The dose rate of 10 mg daily appears to have the greatest clinical evidence presently<sup>47</sup>.

### **Herbs/Minerals**

Arnica applied topically in a homeopathic remedy form to the site of inflammation has proven very beneficial<sup>48</sup>. The carotenoid astaxanthin demonstrates an anti-inflammatory effect possibly by COX modulation<sup>49</sup>. There are a number of additional plant products (Curcumin, Boswellia, Quercetin, Devil's claw, Lignum vitae, and feverfew to note a few) with anti-inflammatory and complementary effects that would augment any therapeutic regimen. Lastly let's not forget our minerals. Virtually all patients with arthritis will require calcium in a form most suited to their body, usually matched to urine pH. Magnesium is also a major consideration and I have found that equal portions of calcium to magnesium have the best results. With any type of bone demineralization

## Nutraceutical Interventions – Continued from page 4

boron is always needed. Usually 3 mg daily is adequate for most physiologic demands. Other minerals may be needed based upon the unique requirements of each patient.

As you can see there are many alternative nutraceutical therapies that are as valuable as medical therapies and in many ways superior since they work within the body's functions to produce improvements "naturally" instead of chemically. Many of these substances work so well that the medical community is beginning to catch on.

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## NSAIDs – Continued from page 3

stances while improving diet and lifestyle seems to be a better way to provide "health care" to a patient and not just manage a disease.

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# Arthritis: An Overview

Ronald Ritchie, D.C.

Arthritis is a general term for conditions in which joints of the body become inflamed by various mechanisms usually accompanied by pain, frequently involving changes in joint structure with progressive deterioration<sup>1</sup>. Remembering basic joint structure, virtually all joints are lined with tissues composed predominantly of proteins (collagen and elastin)<sup>2</sup> proteoglycans, and synovial fluid consisting of proteins, a few antibodies, enzymes and WBCs<sup>3</sup>. This intricate and complex structure operates flawlessly until some event or condition causes inflammation and begins the degenerative process called arthritis.

Arthritis can be caused by injuries, infection, immune responses, mechanical abnormalities, genetic predispositions and other conditions<sup>4</sup>. We as clinicians regularly see patients with osteoarthritis, rheumatoid and post-traumatic arthritis; less commonly gout, AS, psoriatic arthritis, septic arthritis and rarely autoimmune (other than RA) or metabolic arthritides. Virtually all forms of arthritis demonstrate a sign of inflammation in and around the joint affected and is a major factor of treatment. Signs of inflammation include swelling, stiffness, tenderness, redness and warmth. Inflammation can begin suddenly (within minutes or hours) or gradually over months. Cartilage becomes eburnated from the inflammation, eroded or brittle and fragment. Synovial membranes can hypertrophy producing excess or viscous fluid with eventual intra-articular fibrin formation. Ligaments can become thin initially allowing joint instability then later hypertrophy adding to immobility. Juxta-articular and mechanically associated muscles will spasm then later atrophy. Articular bone can hypertrophy producing osteophytes or generalized joint enlargement or become osteoporotic further compromising joint integrity. Virtually all of these processes are the result of inflammation, either directly or indirectly, usually occurring in concert.

The three most common forms of arthritis are rheumatoid, osteoarthritis and post-traumatic arthritis. Post-traumatic arthritis is placed in the osteoarthritis category by many authorities but I do not consider them one and the same. In my experience osteoarthritis is more systemic with trauma events being an associated factor whereas post-traumatic arthritis has trauma as the exclusive cause and arthritic changes limited to the injured joint(s).

## Osteoarthritis

OA, also called degenerative joint disease or degenerative arthritis, is the most commonly encountered form<sup>5</sup>. OA affects one out of every ten persons in the United States, spanning all ages but most often affects persons over 45 years of age. Nearly 40% of individuals over 50 years of age present OA radiographically.

The symptoms of OA usually begin gradually over long periods of months or years and are diverse in presentation. One may experience progressive joint stiffness with mild pain starting more as an annoyance with progressive loss of joint motion. Joint crepitation is a common feature with infrequent tenderness<sup>6</sup>. Pain is usually worse after exercise accompanied by some inflammation. There is usually no severe joint inflammation as there is with RA but may occur as the condition progresses. This inflammation is without the defined redness and is less symmetrical than that of RA. Heberden's nodes<sup>7</sup> often appear at the DIP joints of both hands and feet. With progression the cartilage of the joint deteriorates exposing the subarticular

bone to direct contact. The pain of osteoarthritis comes from loss of articular cartilage, damage to connective tissues, muscle strain from abnormal biomechanics, inflammation and bone swelling.

A primary characteristic of OA is the osteophytes that form at the periphery of the affected joints. They occur as a consequence of proliferative chondrocyte reactions to the mechanical joint stresses and inflammation. Large osteophytes can obstruct movement severely and interfere with other body functions, especially in the spine. OA predominantly affects weight-bearing joints such as hips, knees, feet and spine but any joint can be affected. One common place is the carpometacarpal joint of the thumb and DIP of the fingers in individuals over 45 years of age. Also wrist involvement is rare with the exception of the variant known as erosive osteoarthritis<sup>8</sup>.

The specific cause of OA is unknown but genetic, metabolic, endocrine, biomechanical and hydrolytic enzyme factors have been suggested as potential etiologies<sup>9</sup>. It is hypothesized that increased loss of proteoglycans from the cartilage matrix or "aggregation" of these substances by enzymatic action through various mechanisms is key<sup>10</sup>. There appears to be a familial predisposition towards OA<sup>11</sup> or at least unusual joint stress from genetically determined body type that allows its development. Excess body weight provides a basis for stresses upon the large weight bearing joints that potentiate OA development. Weight loss with appropriate muscle conditioning, even when arthritis is present, will reduce the severity of symptoms or slow the progression of the disease. Traumatic events to individual or groups of joints is also a common factor and a point where some authorities believe OA should be divided into two subsets. Some authorities use the term osteoarthrosis to differentiate the more systemic condition from the regional or monoarticular trauma induced conditions<sup>12</sup>. I tend to agree differentiating osteoarthritis from post-traumatic arthritis, although the nutraceutical intervention for both is very similar.

Diagnosis is obtained by a careful history with observation as to onset, frequency, timing of painful episodes, joints involved and careful physical examination. Include in your history whether current or previous events of colitis, COPD, psoriasis and other systemic conditions have occurred as these may present migratory joint pain mimicking early OA. Laboratory tests can include an ESR that may be normal or only slightly elevated and a negative RF. X-rays reveal a decreased joint space, osteophytes, bone cysts and subarticular sclerosis<sup>13</sup>.

Due to the fact that OA targets the cartilaginous elements of joints, therapy should be directed to these tissues to reduce inflammation, promote cartilage repair and rebuilding, and support subarticular bone integrity. Along with weight loss and nutritional therapies, specific exercise to strengthen the supportive musculature around the affected region is requisite.

## Rheumatoid Arthritis

RA is a chronic and fulminating immune mediated inflammation of joints and/or other internal organs<sup>14</sup>. This type and degree of inflammation separates RA from other forms. RA can affect people of all ages but most commonly appears between the ages of 25 and 50 affecting women ten times more often than men involving almost

*Continued on page 8*

# The Potential Multi-Modal Benefits of Joint Support Nutrients for Anti-Aging

Dr. Ronald Klatz and Dr. Bob Goldman

Inflammation is the body's normal response to assist in the removal of toxins, to ward off invading pathogens, and to remove damaged cells. Progressive destruction to tissue can occur when the inflammatory process becomes chronic. In the case of joints, a host of medical problems arise from chronic inflammation, causing osteoarthritis, rheumatoid arthritis, carpal tunnel syndrome, temporomandibular joint disorder, to name a few. Poor joint health is becoming increasingly commonplace, and millions of people worldwide have turned to prescription pain killers to relieve joint swelling and pain. Yet, the recent withdrawal and revised labeling on COX-2 inhibitors gives cause for concern. In this article we review the therapeutic value of various joint support nutrients, many of which have additional benefits for anti-aging purposes.

Glucosamine sulfate is a leading natural therapeutic employed in the treatment of joint inflammation. Glucosamine is a substance found naturally in the joints. However, as we age, and lacking proper nutrients, the body may produce less of it over time. Glucosamine is also a precursor to chondroitin, a key component in cartilage. As an oral supplement, glucosamine stimulates the production of glycosaminoglycans and proteoglycans, two key building blocks essential in the formation and repair of joint cartilage. Due to its cartilage rebuilding capacity, glucosamine has been shown to slow or halt the progression of osteoarthritis. In addition, glycosaminoglycans are polysaccharides that are major components of the extracellular matrix (ECM), necessary to maintain cellular hydration and cellular membrane elasticity throughout the body.

Scientists have observed that mitochondrial function declines and mtDNA mutation increases in an age-dependent manner. Age-related impairment of enzymes not only decreases ATP synthesis but also enhances production of reactive oxygen species (ROS) through increased electron leakage. When our mtDNA are subjected to high levels of ROS and free radicals, it becomes susceptible to oxidative damage and mutation. More than 100 human clinical conditions are now associated with elevated levels of ROS - not only arthritis, but atherosclerosis, heart disease, cerebrovascular incidents, diabetes, autoimmune diseases, cancers, and aging itself. New research published demonstrates that deletions within the mitochondrial DNA occur with increasing frequency in age and in disease. Now identified as the 4977 bp deletion or "common deletion" and suspected to result from ROS damage, these alterations are most pronounced in tissues of the brain, heart and skeletal muscle-tissues with the greatest demand for cellular energy. Antioxidants such as Vitamins A, C, E, selenium, and OPCs (oligomeric proanthocyanidins) are particularly valuable for their ability to reduce ROS damage to cells. As a result, antioxidants can reduce the body's inflammatory processes. In people with rheumatoid arthritis, serum levels of antioxidants typically are quite low, and thus oral supplementation is thought to be an important way in which to raise such stores.

Bromelain, a proteolytic enzyme derived from pineapple, has

been used successfully for a wide variety of inflammatory conditions of the joint, including rheumatoid and osteoarthritis. Studies demonstrate that bromelain inhibits the production of proinflammatory prostaglandins while simultaneously inducing favorable (non-inflammatory) prostaglandins. As a result, inflammation, swelling, and pain are reduced. For anti-aging purposes, bromelain functions as a natural anticoagulant that breaks down the blood-clotting protein, fibrin; clinical trials suggest that the enzyme can help to improve the symptoms of angina and thrombophlebitis. As well as thinning the blood, bromelain also thins mucus, and thus maybe of benefit to asthmatics and people suffering from chronic bronchitis. There is also evidence that bromelain can trigger beneficial changes in white blood cells, and thus may improve immune function.

The flavonoid quercetin, found naturally in apples, onions, beans, broccoli, and green tea also acts as a potent anti-inflammatory. Quercetin also helps to reduce two contributory factors in the onset of inflammation, namely body acidity (most arthritic individuals tend to be very acidic) and food sensitivities (ingestion of certain foods by those with arthritis causes symptoms such as increased joint pain and swelling, constipation, diarrhea, headache, and/or fatigue).

The essential mineral sulfur, in the form of MSM (methylsulfonylmethane), can act as an anti-inflammatory and pain reliever. Sulfur is the fourth most common element in the human body, and has many functions, all of which result from cellular-based detoxification. Over time, MSM deficiencies occur as a part of the aging process. Several animal studies have found that MSM appears to protect against cancer, however these findings have not been replicated in human studies. At moderate levels, MSM helps to maintain healthy skin, nails, and hair.

Anti-aging physicians and health practitioners employ vitamin supplementation in their treatment of patients who seek to prolong their healthy, vital, fit lifespans.

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**Dr. Ronald Klatz and Dr. Bob Goldman are physicians and co-founders of the anti-aging medical movement and of the American Academy of Anti-Aging Medicine (A4M; Chicago, IL USA; [www.worldhealth.net](http://www.worldhealth.net)), a non-profit medical organization dedicated to the advancement of technology to detect, prevent, and treat aging related disease and to promote research into methods to retard and optimize the human aging process. A4M is also dedicated to educating physicians, scientists, and members of the public on anti-aging issues.**

## Arthritis: An Overview – Continued from page 6

2% of the US population<sup>15</sup>.

RA may start gradually or with a sudden, severe attack including fever and fatigue. Common signs and symptoms are listed in the adjoining table and vary from person to person. They may be mild with asymptomatic intervals to exacerbations with severe pain and immobility. Some individuals will experience continuous pain with only gradual symptom change, progressive joint damage and disability<sup>16</sup>.

The process by which RA produces the pain and damage to joints is thought to be through a malfunction or inappropriate activity of the immune system. Why this occurs is still not understood but is thought to be triggered by an infection, possibly viral<sup>17</sup>. There is no present proof that a virus is the agent of tissue damage but it may be that the immune system challenge and subsequent antibodies generated activates and upregulates immune sensitivity to proteins of synovial membranes and connective tissues. It has also been postulated that RA develops because of genetic predispositions toward either immune system errors or DNA synthesis failures<sup>18</sup>. It seems most likely a combination; immune system upregulation and genetic predisposition.


Some distinguishing features of RA are that it affects the wrist, MCP and PIP but not the DIP. The inflammation tends to be symmetrical and fusiform. There is "soft swelling" around the joints initially with osseous hypertrophy appearing late in the disease presenting the classic "radial deformity." Tenderness is usual in and around affected joints with Haygarth's nodes at the PIP. Commonly other tissues are involved producing subcutaneous nodules, phlebitis, dry eyes and mouth, and other rheumatoid symptoms. RA tends to occur in families hence the belief that there is a genetic pre-disposition.

Diagnosis using the examination criteria noted is augmented as follows. RA panels reveal positive latex fixation (70% correlation) and positive antibody tests. ESR is elevated 90% of the time and a positive CRP is usually present. ANA may be positive. Normocytic hypochromic anemia is present in 80% of RA patients even in the early disease<sup>19</sup>. Radiographic findings include periarticular soft tissue swelling, bilateral

symmetry, uniform loss of joint space, marginal erosions, pseudocysts, juxtaarticular periostitis and joint deformity<sup>20</sup>.

Rheumatoid arthritis must be differentiated from erosive osteoarthritis via a negative RF, lack of rheumatoid nodulation and asymmetrical joint involvement. Both conditions involve the MCP, PIP and wrist, and present nodules on the PIP. But due to the fact that they are pathologically different, treatment for each condition will differ.

Given the complex nature of rheumatoid arthritis, the nutritional intervention takes more specific design. Detoxification is of paramount importance in RA treatment in contrast to OA. Allergy testing identifying offending substances and then eliminating these with detoxification will reduce the overall allergic load freeing immune and detoxification pathways. Glucosamine and chondroitin sulfates seem to be of less value than MSM due to the fact that RA affects connective tissues more so than cartilage.

With the aging of the American society, treatment of chronic disease is needed. Thorough understanding of the physiological processes of arthritis and proper diagnosis will provide a greater outcome for our patients' health. 

### Diagnostic Criteria for Rheumatoid Arthritis

1. Morning Stiffness
2. Joint tenderness or pain on motion
3. Soft tissue swelling
4. Swelling of at least one other joint
5. Symmetrical simultaneous joint swelling
6. Subcutaneous nodules over bony areas
7. X-ray changes typical of RA
8. Synovial fluid analysis of poor mucin precipitate
9. Positive agglutination tests
10. Characteristic histological changes in synovial membranes
11. Characteristic histological changes in nodules showing granulomatous foci.

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