

# ARTHRITIS: DON'T LET JOINT PAIN SLOW YOUR JOURNEY

By John Clark M.D. NorthernLightsHealthEducation.com

## ARTHRITIS AND AMERICANS

According to the (Centers for Disease Control) CDC, arthritis is the leading cause of disability in the United States. Twenty-three million Americans (about 11 percent of the U.S. population) report symptoms of joint arthritis but have never sought medical care for relief. Another 42.7 million Americans (about 20 percent of the U.S. population) have been diagnosed with arthritis by a Physician. Thus, nearly one out of three Americans suffer disabling joint pain, much of which could be alleviated or entirely averted if they only knew how to better care for the health of their joints<sup>1</sup>.

So, you may ask, "What can I do to improve the health of my joints--to make sure they last as long as I do?" In this article we will explore the contribution of diet, exercise, obesity, and water-drinking to joint health and longevity.

Because the knee is a very vulnerable joint to arthritis, I will use it as a model in our discussion. I could have just as easily used the spinal discs, hip, shoulder, or ankle.

The junction of the femur, often called the thighbone, and the tibia, sometimes referred to as the shinbone, form the knee joint. The end of the femur and the top of the tibia are covered with a layer of cartilage about one eighth of an inch thick. This cartilage provides protection, shock absorption and smooth motion for the joint.

Lubrication fluid is held in the knee by the joint capsule, this capsule is like a bag that surrounds the entire knee joint. When a person complains of having "water on the knee" it usually means that they have extra joint fluid in their joint capsule.

Cartilage is a rubbery material that has no blood vessels running through it. It depends on

nutrients diffusing or soaking into it from the bone and joint capsule for health and repair<sup>2</sup>.

To maintain good cartilage nutrition, blood must be kept flowing by the joint. Blood vessels so small that only one red blood cell can pass through them at a time, line the joint capsule. These vessels are called capillaries. Nutrients have to pass from the blood cell in the capillary to the cartilage cell in the cartilage. This involves moving nutrients from the blood cell, across the capillary wall, through the joint capsule into the joint fluid. The joint fluid must then pass through the layers of cartilage to reach the cartilage cell. To remove the waste products from the cartilage cell the whole process must work in reverse. Good cartilage nutrition depends on the diffusion of fluid from the blood vessel, across the synovial membrane or joint capsule, into the joint space. Cartilage health also depends on the diffusion of waste products back across the synovial membrane and back into the blood vessel.

Anything that inhibits the free flow of fluid, to and from the cartilage, compromises cartilage health and longevity. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair produce arthritis.

## CARTILAGE AND WATER

Sixty-five to eighty percent of cartilage is made up of water. In cartilage, water functions like a "shock absorber." Water also lubricates and nourishes the cartilage. Water is the medium that carries nutrition to the cartilage from the blood cells and waste products away from the cartilage back to the blood stream. Dehydrated joints become acidic, and oxygen

starved. This can cause cartilage cells to become sick or die.<sup>3</sup>

If you do not drink enough water, you starve your cartilage cells for nutrition and drown them in their own waste products. Cartilage depends on water for health and repair. Poor hydration causes a failure in repair and produces arthritis.

## **CARTILAGE AND EXERCISE**

Cartilage has no blood vessels directly supplying it. It depends on cyclic weight bearing to squeeze or pump nutrients in and waste products out of its sponge-like matrix<sup>4</sup>.

If you do not exercise, nutrition will not be pumped to and waste products from the cartilage. Cartilage depends on exercise for health and repair. A sedentary lifestyle with failure of cartilage repair can produce arthritis.

## **OBESITY AND CARTILAGE**

Overweight people carry immense loads on their cartilage, thus increasing wear. Cartilage is like a sponge and when it is constantly compressed, as happens in obesity, fluid is not pumped to and from the cells.<sup>5,6</sup> Constant pressure on the cartilage presses out the water from its matrix, thus dehydrating it. The result is poor cartilage nutrition, increased accumulation of metabolic acid, and cartilage cell death. As the cartilage deteriorates, narrowing of the joint space between the femur and the tibia can often be seen on x-ray.

Obesity stops fluid flow to and from the cartilage, thus compromising cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair produce arthritis.

## **CARTILAGE AND DIET**

“You are what you eat” and your joints may be the first to protest your dietary choices. Few people understand the connection between

how their joints feel and what they eat and drink. Joint health and joint longevity are dependent on daily care of their nutritional needs and vulnerabilities.

Our goal is to explore the relationship between diet and cartilage health. We will be looking at risky foods by category including refined foods, inflammatory foods, vasoactive foods, slow transit foods, and plaque-forming foods.

---

The effect of eating refined foods on the blood cells is to cause them to stick together in stacks or chains.

---

## **REFINED FOODS**

Refined foods are foods that have been highly processed to break down complex nutrients into very basic nutrients. This process tends to destroy or remove nutrients such as vitamins, minerals, and fiber. Refined foods tend to be calorie dense making it easy to eat more calories than your body needs.

Eating refined foods causes the red blood cells in our blood vessels to stick together in long chains or stacks. Scientists call these stacks or chains of blood cells rouleaux. Rouleaux do not flow freely through small capillaries, they tend to flow very sluggishly and slowly, if at all.<sup>7</sup>

Sugar, refined starches, oil, alcohol, and cream are a few examples of refined foods that create rouleaux.<sup>8,9</sup>

Rouleaux impede fluid flow to and from the cartilage; this interferes with cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair result in arthritis.

The unrefined vegetarian diet has been shown to improve blood flow.<sup>10,11</sup> This is because vegetables, seeds, and nuts are high in Omega-3 fatty acids,<sup>12</sup> which promote blood flow. It is also more difficult to overeat on an unrefined vegetarian diet.<sup>13,14</sup>

Dehydration thickens the blood which favors the formation of rouleaux. Drinking plenty of water is important in preventing thickening of the blood.<sup>15</sup>

Stress has also been correlated with increased blood thickness<sup>16</sup>. Reducing the stress in your life can be an important means of preserving vital blood flow to joint tissues.

### **INFLAMMATORY FOODS**

Inflammatory foods, when eaten, increase inflammation throughout the entire body. This increased inflammation tends to cause thickening of the blood vessel walls. Thickened capillary walls restrict the free flow of fluid to and from the cartilage cells.<sup>17</sup>

Examples of inflammatory foods include meat,<sup>18,19</sup> especially pork,<sup>20</sup> dairy, especially cheese,<sup>21</sup> and ice-cream.<sup>22</sup>

Foods that are produced through the process of fermentation or rotting contain aflatoxins which also increase inflammation. This includes foods like wine, vinegar, certain mushrooms, and peanut butter made from moldy peanuts. Any food on which mold has grown tends to accumulate aflatoxins, especially foods with *Aspergillus* mold.<sup>23</sup>

Inflammation thickens vessel walls impeding fluid flow to and from the cartilage, thus interfering with cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair can result in arthritis.

Believe it or not, some forms of fasting have been shown to decrease inflammation when followed by a vegetarian diet.<sup>24</sup> Studies show that it is the naturally occurring substances found in fruits, vegetables, grains, bark, roots, stems, and flowers called flavonoids that contain the anti-inflammatory properties.<sup>25</sup>

Soy products have also been discovered to possess anti-inflammatory properties.<sup>26</sup>

We have already discussed the benefits of omega-3 fatty acids for promoting blood flow. These fatty acids,<sup>27</sup> as found in flaxseed<sup>28</sup> and

olive oil,<sup>29,30</sup> have been discovered to have anti-inflammatory effects.

### **VASOACTIVE FOODS**

Blood vessels have muscles in their walls that change their size or diameter. When the muscles tighten, the vessel gets smaller and fewer blood cells can travel through it. Vasoactive foods are those foods that contain substances that cause blood vessels to constrict or get smaller in diameter. When a blood vessel that allows only one blood cell to pass through it at a time constricts, all blood flow stops, and no nutrients are delivered to the joint tissues.

Examples of vasoactive foods include foods containing caffeine<sup>31</sup> such as coffee,<sup>32</sup> tea, and colas. Nicotine is also a vasoactive substance.<sup>33,34</sup>

Vasoconstricted blood vessels impede blood flow. This affects fluid transfer to and from the cartilage thus compromising cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair produce arthritis.

Dietary changes known to improve vascular responsiveness include: a vegetarian diet,<sup>35</sup> tomatoes,<sup>36</sup> mono-unsaturated vegetable oils<sup>37</sup>—like olive oil,<sup>38</sup> and diets rich in antioxidants,<sup>39</sup> vitamin E,<sup>40</sup> zinc,<sup>41</sup> and copper.<sup>42</sup> Foods known to impair vascular responsiveness include diets high in cholesterol,<sup>43</sup> salt,<sup>44</sup> fat,<sup>45</sup> sugar,<sup>46</sup> and excess calories.<sup>47</sup>

### **SLOW-TRANSIT FOODS**

By slow-transit foods we mean foods that take a long time to travel through the body from the mouth to the anus. They spend a long time in the stomach and intestines. Slow-transit foods are usually slow because they are high in fat and low in fiber. Fiber is the bulk in stool that helps keep food moving down the digestive track.<sup>48</sup>

Because low fiber food is in the colon so much longer, bacteria tend to multiply.<sup>49</sup> This results in bacterial overgrowth. When bacteria over grow they produce many toxins.<sup>50</sup> These toxins can produce all the effects we have already talked about up to this point: (1) thicken or coagulate the blood;<sup>51,52</sup> a similar effect to that of rouleaux, (2) vasoconstriction,<sup>53</sup> and (3) inflammation.<sup>54,55,56</sup>

---

**Slow transit foods are usually high in fat and low in fiber, and include meat, fast foods, pastries, especially donuts, fried foods, and greasy foods.**

---

Foods eaten late at night tend to pass more sluggishly through the digestive system thus they have the same effect of fostering bacterial overgrowth and decreasing circulation to the joints.<sup>57</sup>

Slow-transit foods impede fluid flow to and from the cartilage, thus compromising cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair cause arthritis.

As already mentioned, fiber plays a significant role in the time food stays in your system.<sup>58</sup> Increasing the amount of fiber you get in your diet is one way to improve joint health. Whole grains,<sup>59</sup> dried fruit,<sup>60</sup> and fresh vegetables are good sources of dietary fiber.

Mental health can also affect transit times, depression tends to slow transit and make it sluggish.<sup>61</sup>

## **PLAQUE-FORMING FOODS**

The next class of foods we want to discuss are those that favor the clogging of blood vessels with arteriosclerotic plaque. We call these plaque-forming foods. A plaque is a blockage in a vessel that restricts or stops the free flow of blood to and from the tissues, such as the knee joint, heart or brain.

Examples of plaque forming foods include foods high in cholesterol, like meat, butter, milk, and eggs.<sup>62,63</sup>

Foods especially prone to plaque formation are those containing cholesterol that has experienced oxidation. This oxidation of cholesterol makes it especially toxic to blood vessel walls and favors the formation of plaque.<sup>64</sup>

Cholesterol oxidizes in the presence of oxygen or air. Foods most likely to contain oxidized cholesterol are foods which have air and cholesterol mixed together in them; examples include pancake mixes containing dried egg, ice cream, because it is whipped full of air, and processed meats such as pork, beef, and chicken especially if they are grilled or roasted.<sup>65,66,67</sup>

---

**Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair can result in arthritis.**

---

High-fat foods contribute to plaque growth, especially foods like french fries and lard.<sup>68,69</sup>

The most dangerous fats are trans-fats. Trans-fats are produced in the process of hydrogenation. They can also be produced when frying or roasting because the oils are super-heated.<sup>70,71</sup> Foods high in trans-fat include hydrogenated margarines or cooking oils, and fried or roasted foods.<sup>72,73,74</sup>

Anything that causes deterioration in the blood circulation system can be detrimental to joint health. Hardening of the arteries compromises the circulatory system. Hardening of the arteries is facilitated by an elevated intake of salt.<sup>75</sup>

Plaque and hardening of the arteries impede blood flow to and from the joint, this compromises cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair result in arthritis.

To reiterate, anything that impedes fluid flow, to and from the cartilage, impedes

cartilage nutrition. Cartilage depends on its nutrition for health and repair. Poor nutrition and failure of repair produce arthritis.

What we have talked about so far is the contribution of water, exercise, and diet to joint health. Which might lead one to ask, "So! What should we eat, drink, and do?" This is a very fair question and one that we will do our best to start you on the road to answering.

Caldwell Esselstyn, Jr., MD, of the Cleveland Clinic has demonstrated on angiography that blockages in coronary arteries can be reversed by changes in diet. He makes these dietary recommendations for reversing heart disease: "The optimal diet consists of grains, legumes, vegetables, and fruit, with <10%-15% of its calories coming from fat." He goes on to say that this diet is beneficial for more than just coronary artery disease, "This diet minimizes the likelihood of stroke, obesity, hypertension, type 2 diabetes, and cancers of the breast, prostate, colon, rectum, uterus, and ovary. There are no known adverse effects of such a diet when mineral and vitamin contents are adequate."<sup>76</sup>

## **WATER**

The value of the sage old advice to drink at least eight glasses of water a day cannot be overestimated. Because cartilage is 65%-80% water it needs constant hydration. Starting the day with a large drink of water is one of the best things you can do for you joints. Drinking eight glasses of water a day ensures an abundant supply of fluid for cartilage hydration, nourishment, and lubrication. When cartilage is inflamed, it requires water to carry the products of inflammation away from it and healing nutrients back to it.

Another good use of water is in applying hot and cold treatments to painful arthritis joints. The usual regimen is to apply hot to the area for 3 minutes, followed by a cold application for one minute. Repeat this 5 times and end with cold. If it is an ankle you are treating, you can use two buckets of water, one hot and one cold. If it is a

shoulder or knee, you may want to use hot water bottles and an ice bag. You can alternate the hot and cold from these sources in the same pattern of 3 minutes hot and one minute cold.<sup>77</sup>

## **Charcoal**

The cause of pain and swelling, on the molecular level, in an injured or arthritic joint, is inflammation. Inflammation is facilitated by mediators called cytokines. A very good natural remedy for decreasing the impact of cytokines on joint tissues is activated charcoal.<sup>78,79,80,81</sup> The way to apply charcoal to a sore joint is as a poultice. The way we make a charcoal poultice is to cook one cup of water, with 3 tablespoons of activated charcoal, and 3 tablespoons of ground flax seeds. Bring it to a boil and let it cool. What you will have after cooking this mixture is a gel that is easy to work with. You can apply it directly to the skin or wrap it in one layer of damp paper towel and apply the damp paper towel to the skin over the painful joint. Then wrap the applied poultice and joint with plastic wrap and an elastic bandage, to hold it in place, and leave it on overnight. It should bring down the swelling and pain. People have avoided the need for a joint replacement using this simple home remedy.

## **EXERCISE**

Because cartilage has no direct blood supply and depends on cyclic weight bearing to pump nutrition into it, walking is one of the best exercises for maintaining its health. Walks, especially after meals are of great benefit.

## **DIET**

"So! What should we eat?" The simplest and most direct answer that can be supplied is to eat an unrefined plant-based diet. There is a vegetarian advantage. Higher consumption of fruits and vegetables decreases the risk of

Osteoarthritis by 40%.<sup>82</sup> People who are low on vitamin C and vitamin D have a threefold risk of progression of osteoarthritis.<sup>83</sup>

## **BREAD, CEREAL, RICE & PASTA GROUP**

Bread, cereal, rice, and pasta group could make up the majority of your diet. Each of these foods should be kept unrefined so as to preserve their vitamins, minerals, and fiber. What we are talking about is eating an unrefined plant-based diet.

There are many breads on the market, but not all of them are 100% whole grain. One hundred percent whole grain breads contain more vitamins, minerals and fiber; thus they are more nutritious for the cartilage.

Oatmeal is a good example of a whole grain cereal. Refined or highly processed grains are deficient in vitamins, minerals, and fiber. Whole grain cereals are always better for joint health.

---

**“So! What should we eat?” The simplest and most direct answer that can be supplied is to eat an unrefined plant-based diet.**

---

Brown rice or wild rice is preferable to white rice because it has more naturally occurring vitamins, minerals, and fiber.

Whole grain pasta can also be purchased that does not contain refined or highly processed flours. Whole grain pasta, because it has all of the naturally occurring nutrients, is better than refined products when it comes to preserving joint health and promoting longevity.

## **FRUITS**

Fresh fruit is preferable to fruit that has been juiced or canned. During the juicing process much of the valuable fiber is lost. Juices often get pasteurized; this breaks down the more complex sugars into very simple sugars. Large

amounts of sugar are often added during the canning process, which when eaten cause the rouleaux effect that is so detrimental to joint health.

One very good fruit for avoiding or remedying arthritis is fresh pineapple. It is high in an antioxidant phytochemical, bromelain, which reduces arthritis pain.<sup>84</sup>

## **VEGETABLES**

Vegetables, prepared in a simple way, free from spice and grease make a healthful diet. Fresh or frozen vegetables are preferable to canned. Canned vegetables tend to have high amounts of added salt that contributes to elevated blood pressure and hardening of the arteries.

## **HERBS**

A couple of good herbs to be eaten or made into a medicinal tea are Turmeric and Gotu Kola. Gotu Kola herb reduces inflammation, balances antioxidants and reduces arthritis severity.<sup>85</sup> Turmeric is as anti-inflammatory as some commonly used arthritis treatment medications such as ibuprofen.<sup>86</sup>

## **NUTS AND BEANS**

Nuts, prepared free from added oil and salt, are a good source of protein. Beans are a good source of protein and fiber. Beans should be prepared in as healthful a way as possible, free from added oil and salt.

## **SOY AND TOFU**

The soybean is very nutritious and is a wonderful addition to the diet of someone battling with arthritis.<sup>87</sup> In the last few years soy products have become available almost anywhere in the world. In the town where I live, soymilk, tofu, soy burgers, and soy ice cream can all be purchased at regular grocery stores

making it easier to substitute for the more deleterious foods in the diet.

## DRIED FRUIT & DESSERTS

Many appetizing and healthful desserts can be made, which will be both tasty and good for the health of your joints. Dried fruit is an excellent source of minerals and fiber and makes a good dessert.

Anything that aids nutrient flow, to and from the cartilage, promotes cartilage health. Cartilage depends on its nutrition for health and repair. Good nutrition and vigorous repair promote cartilage longevity.

## LET'S PLAN TO AVOID ARTHRITIS!

- Can't do what you always have wanted to do.
- Pain, swelling, deformity, burden to others.
- Disability, inactivity, isolation, early death.

Instead:

- Drink adequate water.
- Exercise daily.
- Choose a wholesome diet.
- Try a few herbs.

Bon Appetite.

*For further ideas on how to incorporate what you have just learned into your daily life, see the article entitled, [Lifestyle Choices](#).*

<sup>1</sup> Targeting Arthritis: Reducing Disability for 43 Million Americans: At A Glance 2005. [http://www.cdc.gov/nccphp/aag/aag\\_arthritis.htm](http://www.cdc.gov/nccphp/aag/aag_arthritis.htm).

<sup>2</sup> Malinin T; Ouellette EA. Articular cartilage nutrition is mediated by subchondral bone: a long-term autograft study in baboons. *Osteoarthritis Cartilage* 2000 Nov;8(6):483-91.

<sup>3</sup>BUCKWALTER, J. A., MANKIN, H. J. Articular Cartilage. Part I: Tissue Design and Chondrocyte-Matrix Interactions. *J Bone Joint Surg (Am)* 1997; 79-A; 600-11.

<sup>4</sup> O'Hara BP, Urban JP, Maroudas A. Influence of cyclic loading on the nutrition of articular cartilage. *Ann Rheum Dis* 1990 Jul;49(7):536-9.

<sup>5</sup> Milentijevic D, Torzilli PA. Influence of stress rate on water loss, matrix deformation and chondrocyte viability in impacted articular cartilage. *J Biomech*. 2005 Mar;38(3):493-502.

<sup>6</sup> Dawson J, Juszcak E, Thorogood M, Marks SA, Dodd C, Fitzpatrick R. An investigation of risk factors for symptomatic osteoarthritis of the knee in women using a life course approach. *J Epidemiol Community Health*. 2003 Oct;57(10):823-30.

<sup>7</sup> E Aegerter and JA Kirkpatrick, Jr.: "Orthopedic Diseases," 4th Ed., W.B. Sanders Co., 1975, p. 639.

<sup>8</sup> Cicha I; Suzuki Y; Tateishi N; Maeda N Effects of dietary triglycerides on rheological properties of human red blood cells (abstract). *Clin Hemorheol Microcirc* 2004;30(3-4):301-5.

<sup>9</sup> Mas JL; Boussier MG; Lacombe C; Agar N Hyperlipidemic dementia. *Neurology* 1985 Sep;35(9):1385-7.

<sup>10</sup> McCarty MF. Favorable impact of a vegan diet with exercise on hemorheology: implications for control of diabetic neuropathy. *Med Hypotheses*. 2002 Jun;58(6):476-86.

<sup>11</sup> Ernst E, Pietsch L, Matrai A; et. al. Blood rheology in vegetarians. *Br J Nutr*. 1986 Nov;56(3):555-60.

<sup>12</sup> Simopoulos AP. Essential fatty acids in health and chronic disease. *Am J Clin Nutr*. 2004 Mar;79(3):523-4.

<sup>13</sup> Poggi M, Palareti G, Biagi R; et. al. Prolonged very low calorie diet in highly obese subjects reduces plasma viscosity and red cell aggregation but not fibrinogen. *Int J Obes Relat Metab Disord*. 1994 Jul;18(7):490-6.

<sup>14</sup> Newby PK, Tucker KL, Wolk A. Risk of overweight and obesity among semivegetarian, lactovegetarian, and vegan women. *Am J Clin Nutr*. 2005 Jun;81(6):1267-74.

<sup>15</sup> Vlastos GA, Tangney CC, Rosenson RS. Effects of hydration on blood rheology. *Clin Hemorheol Microcirc*. 2003;28(1):41-9.

<sup>16</sup> Pignatelli C, Ricci R, Santini M. Psychological stress and sudden death. *Ital Heart J Suppl*. 2002 Oct;3(10):1011-21.

<sup>17</sup> Matsubara T; Velvart M; Odermatt BF The thickening of basement membrane in synovial capillaries in rheumatoid arthritis. *Rheumatol Int* 1983;3(2):57-64.

<sup>18</sup> Pattison DJ; Symmons DP; Lunt M; et. al. Dietary risk factors for the development of inflammatory polyarthritis: evidence for a role of high level of red meat consumption. *Arthritis Rheum* 2004 Dec;50(12):3804-12.

<sup>19</sup> Choi HK. Dietary risk factors for rheumatic diseases (In Process Citation ) *Curr Opin Rheumatol* 2005 Mar;17(2):141-6.

<sup>20</sup> Wilhelmi G. Potential effects of nutrition including additives on healthy and arthrotic joints. I. Basic dietary constituents *Z Rheumatol* 1993 May-Jun;52(3):174-9.

<sup>21</sup> Parke AL; Hughes GR. Rheumatoid arthritis and food: a case study. *Br Med J (Clin Res Ed)* 1981 Jun 20;282(6281):2027-9.

<sup>22</sup> Zhang X; Dong F; Ren J; et.al. High dietary fat induces NADPH oxidase-associated oxidative stress and inflammation in rat cerebral cortex. *Exp Neurol* 2005 Feb;191(2):318-25.

<sup>23</sup> Hinton DM; Myers MJ; Raybourne RA. et. al. Immunotoxicity of aflatoxin B1 in rats: effects on lymphocytes and the inflammatory response in a chronic intermittent dosing study. *Toxicol Sci* 2003 Jun;73(2):362-77.

<sup>24</sup> Danao-Camara TC, Shintani TT. The dietary treatment of inflammatory arthritis: case reports and review of the literature. *Hawaii Med J*. 1999 May;58(5):126-31.

<sup>25</sup> Middleton E Jr. Effect of plant flavonoids on immune and inflammatory cell function. *Adv Exp Med Biol*. 1998;439:175-82.

<sup>26</sup> Huang Y, Cao S, Nagamani M; et.al. Decreased circulating levels of tumor necrosis factor-alpha in postmenopausal women during consumption of soy-containing isoflavones. *J Clin Endocrinol Metab*. 2005 Jul;90(7):3956-62. Epub 2005 Apr 19.

<sup>27</sup> Pischon T, Hankinson SE, Hotamisligil GS; et.al. Habitual dietary intake of n-3 and n-6 fatty acids in relation to inflammatory markers among US men and women. *Circulation*. 2003 Jul 15;108(2):155-60. Epub 2003 Jun 23.

<sup>28</sup> James MJ, Gibson RA, Cleland LG. Dietary polyunsaturated fatty acids and inflammatory mediator production. *Am J Clin Nutr*. 2000 Jan;71(1 Suppl):343S-85.

<sup>29</sup> Alarcon de la Lastra C, Barranco MD, Motilva V, et. al. Mediterranean diet and health: biological importance of olive oil. *Curr Pharm Des*. 2001 Jul;7(10):933-50.

<sup>30</sup> Visioli F, Bellosa S, Galli C. Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages. *Life Sci*. 1998;62(6):541-6.

<sup>31</sup> Brodmann M; Lischinig U; Lueger A; et.al. The effect of caffeine on peripheral vascular resistance in isolated perfused guinea pig hind limbs. *J Cardiovasc Pharmacol* 2003 Oct;42(4):506-10.

<sup>32</sup> Hasenfratz M; Battig K Action profiles of smoking and caffeine: Stroop effect, EEG, and peripheral physiology. *Pharmacol Biochem Behav* 1992 May;42(1):155-61.

<sup>33</sup> Uematsu Y, Matuzaki H, Iwahashi M. Effects of nicotine on the intervertebral disc: an experimental study in rabbits. *J Orthop Sci*. 2001;6(2):177-82.

<sup>34</sup> Miao FJ; Helms C; Benowitz NL; et al. Chronically administered nicotine attenuates bradykinin-induced plasma extravasation and aggravates arthritis-induced joint injury in the rat. *Neuroscience* 1992 Dec;51(3):649-55.

- <sup>35</sup> Lin CL, Fang TC, Gueng MK. Vascular dilatatory functions of ovo-lactovegetarians compared with omnivores. *Atherosclerosis*. 2001 Sep;158(1):247-51.
- <sup>36</sup> Sugauma H, Inakuma T. Protective effect of dietary tomato against endothelial dysfunction in hypercholesterolemic mice. *Biosci Biotechnol Biochem*. 1999 Jan;63(1):78-82.
- <sup>37</sup> Ryan M, McInerney D, Owens D, et al. Diabetes and the Mediterranean diet: a beneficial effect of oleic acid on insulin sensitivity, adipocyte glucose transport and endothelium-dependent vasoreactivity. *QJM*. 2000 Feb;93(2):85-91.
- <sup>38</sup> Vogel RA, Corretti MC, Plotnick GD. The postprandial effect of components of the Mediterranean diet on endothelial function. *J Am Coll Cardiol*. 2000 Nov 1;36(5):1455-60.
- <sup>39</sup> Sato J, O'Brien T, Katusic ZS, et al. Dietary antioxidants preserve endothelium dependent vasorelaxation in overfed rats. *Atherosclerosis*. 2002 Apr;161(2):327-33.
- <sup>40</sup> Ribeiro Jorge PA, Neyra LC, Ozaki RM, et al. Improvement in the endothelium-dependent relaxation in hypercholesterolemic rabbits treated with vitamin E. *Atherosclerosis*. 1998 Oct;140(2):333-9.
- <sup>41</sup> Browning JD, Reeves PG, O'Dell BL. Zinc deficiency in rats reduces the vasodilation response to bradykinin and prostacyclin. *J Nutr*. 1987 Mar;117(3):490-5.
- <sup>42</sup> Schuschke DA, Saari JT, Miller FN. A role for dietary copper in nitric oxide-mediated vasodilation. *Microcirculation*. 1995 Dec;2(4):371-6.
- <sup>43</sup> Lind L. Lipids and endothelium-dependent vasodilation—a review. *Lipids*. 2002 Jan;37(1):1-15.
- <sup>44</sup> Sofola O, Knill A, Myers D, et al. High-salt diet and responses of the pressurized mesenteric artery of the dog to noradrenaline and acetylcholine. *Clin Exp Pharmacol Physiol*. 2004 Oct;31(10):696-9.
- <sup>45</sup> Naderali EK, Williams G. Effects of short-term feeding of a highly palatable diet on vascular reactivity in rats. *Eur J Clin Invest*. 2001 Dec;31(12):1024-8.
- <sup>46</sup> Akbari CM, Saouaf R, Barnhill DF, et al. Endothelium-dependent vasodilatation is impaired in both microcirculation and macrocirculation during acute hyperglycemia. *J Vasc Surg*. 1998 Oct;28(4):687-94.
- <sup>47</sup> Sasaki S, Higashi Y, Nakagawa K, et al. A low-calorie diet improves endothelium-dependent vasodilation in obese patients with essential hypertension. *Am J Hypertens*. 2002 Apr;15(4 Pt 1):302-9.
- <sup>48</sup> Kelsay JL, Behall KM; Prather ES Effect of fiber from fruits and vegetables on metabolic responses of human subjects I. Bowel transit time, number of defecations, fecal weight, urinary excretions of energy and nitrogen and apparent digestibilities of energy, nitrogen, and fat. *Am J Clin Nutr* 1978 Jul;31(7):1149-53.
- <sup>49</sup> Erbil Y, Berber E, Seven R, et al. The effect of intestinal transit time on bacterial translocation. *Acta Chir Belg*. 1998 Dec;98(6):245-9.
- <sup>50</sup> Wigg AJ; Roberts-Thomson IC; Dymock RB, et al. The role of small intestinal bacterial overgrowth, intestinal permeability, endotoxaemia, and tumour necrosis factor alpha in the pathogenesis of non-alcoholic steatohepatitis. *Gut* 2001 Feb;48(2):206-11.
- <sup>51</sup> Yoshikawa T, Furukawa Y, Murakami M, et al. Experimental model of disseminated intravascular coagulation induced by sustained infusion of endotoxin. *Res Exp Med (Berl)*. 1981;179(3):223-8.
- <sup>52</sup> Levi M; van der Poll T. Coagulation in sepsis: all bugs bite equally (In Process Citation ) *Crit Care* 2004 Apr;8(2):99-100.
- <sup>53</sup> Grandel U, Grimminger F. Endothelial responses to bacterial toxins in sepsis. *Crit Rev Immunol*. 2003;23(4):267-99.
- <sup>54</sup> Bauer TM; Schwacha H; Steinbrückner B; et al. Small intestinal bacterial overgrowth in human cirrhosis is associated with systemic endotoxemia. *Am J Gastroenterol* 2002 Sep;97(9):2364-70.
- <sup>55</sup> Lichtman SN; Wang J; Sartor RB, et al. Reactivation of arthritis induced by small bowel bacterial overgrowth in rats: role of cytokines, bacteria, and bacterial polymers. *Infect Immun* 1995 Jun;63(6):2295-301.
- <sup>56</sup> Henriksson AE; Blomquist L; Nord CE, et al. Small intestinal bacterial overgrowth in patients with rheumatoid arthritis. *Ann Rheum Dis* 1993 Jul;52(7):503-10.
- <sup>57</sup> Roen PB. The evening meal and atherosclerosis. *J Am Geriatr Soc* 1978 Jun;26(6):284-5.
- <sup>58</sup> Gogler H. Intestinal transit time in Togo (Western Africa) and Germany. *Z Gastroenterol*. 1976 Apr;14(2):280-4.
- <sup>59</sup> Spiller GA, Story JA, Wong LG, et al. Effect of increasing levels of hard wheat fiber on fecal weight, minerals and steroids and gastrointestinal transit time in healthy young women. *J Nutr*. 1986 May;116(5):778-85.
- <sup>60</sup> Spiller GA, Story JA, Lodics TA, et al. Effect of sun-dried raisins on bile acid excretion, intestinal transit time, and fecal weight: a dose-response study. *J Med Food*. 2003 Summer;6(2):87-91.
- <sup>61</sup> Chaudhary HR. Study of intestinal transit time in patient with anxiety and depression. *J Assoc Physicians India*. 1989 Feb;37(2):156-7.
- <sup>62</sup> RW Wissler: In, "Heart Disease: A Textbook of Cardiovascular Medicine," 2nd Ed., Editor E Braunwald, W.B. Saunders Co., 1984, pp. 1183-1204.
- <sup>63</sup> Armstrong ML, Megan MB. Arterial fibrous proteins in cynomolgus monkeys after atherogenic and regression diets. *Circ Res*. 1975 Feb;36(2):256-61.
- <sup>64</sup> Leonarduzzi G, Sottero B, Poli G. Oxidized products of cholesterol: dietary and metabolic origin, and proatherosclerotic effects (review). *J Nutr Biochem*. 2002 Dec;13(12):700-710.
- <sup>65</sup> Raith K, Brenner C, Farwanah H, et al. A new LC/APCI-MS method for the determination of cholesterol oxidation products in food. *J Chromatogr A*. 2005 Mar 4;1067(1-2):207-11.
- <sup>66</sup> Valenzuela A, Sanhuesa J, Nieto S. Cholesterol oxidation: health hazard and the role of antioxidants in prevention. *Biol Res*. 2003;36(3-4):291-302.
- <sup>67</sup> Conchillo A, Ansorena D, Astiasaran I. Combined effect of cooking (grilling and roasting) and chilling storage (with and without air) on lipid and cholesterol oxidation in chicken breast. *J Food Prot*. 2003 May;66(5):840-6.
- <sup>68</sup> Aguila MB, Mandarim-de-Lacerda CA. Aorta wall quantitative alterations due to different long-term high-fat diet in rats. *Food Chem Toxicol*. 2003 Oct;41(10):1391-7.
- <sup>69</sup> Davenport WD Jr, Ball CR. Diet-induced atrial endothelial damage—a scanning electron-microscopic study. *Atherosclerosis*. 1981 Oct;40(2):145-52.
- <sup>70</sup> Gomez-Alonso S, Fregapane G, Salvador MD, et al. Changes in phenolic composition and antioxidant activity of virgin olive oil during frying. *J Agric Food Chem*. 2003 Jan 29;51(3):667-72.
- <sup>71</sup> Lopez-Garcia E, Schulze MB, Meigs JB, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr*. 2005 Mar;135(3):562-6.
- <sup>72</sup> Mozaffarian D; Pischon T; Hankinson SE; et al. Dietary intake of trans fatty acids and systemic inflammation in women *Am J Clin Nutr* 2004 Apr;79(4):606-12.
- <sup>73</sup> Lopez-Garcia E, Hu FB. Nutrition and the endothelium. *Curr Diab Rep*. 2004 Aug;4(4):253-9.
- <sup>74</sup> Zock PL, Urgert R, Hulshof PJ, et al. Dietary trans-fatty acids: a risk factor for coronary disease. *Ned Tijdschr Geneesk*. 1998 Jul 25;142(30):1701-4.
- <sup>75</sup> Simon G, Jaeckel M, Illyes G. Altered structure and distensibility of arteries in salt-fed rats. *J Hypertens*. 2003 Jan;21(1):137-43.
- <sup>76</sup> Esselstyn CB Jr. Resolving the Coronary Artery Disease Epidemic Through Plant-Based Nutrition. *Prev Cardiol*. 2001 Autumn;4(4):171-177.
- <sup>77</sup> Fokmare P, Phansopkar P. The Effect of Contrast Bath Therapy and Knee Pad Device on Pain, Range of Motion, and Functional Disability in Patients With Osteoarthritis Knee: A Randomized Control Trial. *Cureus*. 2023 Oct 24;15(10):e47586.
- <sup>78</sup> Howell CA, Sandeman SR, Phillips GJ, Mikhailovsky SV, Tennison SR, Rawlinson AP, Kozynchenko OP. Nanoporous activated carbon beads and monolithic columns as effective hemoadsorbents for inflammatory cytokines. *Int J Artif Organs*. 2013 Oct 3;36(9):624-32.
- <sup>79</sup> Inoue S, Kiriyama K, Hatanaka Y, Kanoh H. Adsorption properties of an activated carbon for 18 cytokines and HMGB1 from inflammatory model plasma. *Colloids Surf B Biointerfaces*. 2015 Feb 1;126:58-62.
- <sup>80</sup> Tripisciano C, Kozynchenko OP, Linsberger I, Phillips GJ, Howell CA, Sandeman SR, Tennison SR, Mikhailovsky SV, Weber V, Falkenhagen D. Activation-dependent adsorption of cytokines and toxins related to liver failure to carbon beads. *Biomacromolecules*. 2011 Oct 10;12(10):3733-40.
- <sup>81</sup> Sandeman SR, Howell CA, Mikhailovsky SV, Phillips GJ, Lloyd AW, Davies JG, Tennison SR, Rawlinson AP, Kozynchenko OP. Inflammatory cytokine removal by an activated carbon device in a flowing system. *Biomaterials*. 2008 Apr;29(11):1638-44.
- <sup>82</sup> Han HS, Chang CB, Lee DC, Lee JY. Relationship between Total Fruit and Vegetable Intake and Self-Reported Knee Pain in Older Adults. *J Nutr Health Aging*. 2017;21(7):750-758.
- <sup>83</sup> McAlindon T, Felson DT. Nutrition: risk factors for osteoarthritis. *Ann Rheum Dis*. 1997 Jul;56(7):397-400.
- <sup>84</sup> Walker AF, Bundy R, Hicks SM, Middleton RW. Bromelain reduces mild acute knee pain and improves well-being in a dose-dependent fashion in an open study of otherwise healthy adults. *Phytomedicine*. 2002 Dec;9(8):681-6.
- <sup>85</sup> Sharma S, Gupta R, Thakur SC. Attenuation of collagen induced arthritis by Centella asiatica methanol fraction via modulation of cytokines and oxidative stress. *Biomed Environ Sci*. 2014 Dec;27(12):926-38.
- <sup>86</sup> Kuptniratsaikul V, Dajpratham P, Taechaarpornkul W, Buntragulpoontawe M, Lukkanapichonchut P, Chootip C, Saengsuwan J, Tantayakom K, Laongpech S. Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. *Clin Interv Aging*. 2014 Mar 20;9:451-8.
- <sup>87</sup> Arjmandi BH, Khalil DA, Lucas EA, et al. Soy protein may alleviate osteoarthritis symptoms. *Phytomedicine*. 2004 Nov;11(7-8):567-75.