Whole Wheat Heart Attack Part 2: The Role of Lectins

In last month’s newsletter we discussed the process of Atherosclerosis and pointed out the important factors involved in its development. The fatty streak is the early non-fatal atherosclerotic lesion. A state of chronic inflammation causes the fatty streak to progress to a mature atherosclerotic plaque, and the rupture of the fibrous cap surrounding the plaque is the often-fatal final step in the process. This month I will explain what dietary lectins are and how they affect all of these steps in the development of cardiovascular disease.

Although dietary lectins may not need introduction to some regular readers of this newsletter, let me clearly define them so everyone’s on the same page. The word “lectin” is derived from the Latin verb legere, meaning to “select,” and because of their high affinity to bind just about everything in biological systems, lectins indeed “select.” Lectins were originally defined by their ability to agglutinate (clump) erythrocytes (red blood cells) in tissue cultures, but more recently have been described by their ability to reversibly bind specific monosaccharide (simple) or oligosaccharide (complex) sugars. Lectins are omnipresent proteins found in the plant kingdom and likely evolved as toxic defensive mechanisms to ward off predators. Most dietary lectins are benign and non-toxic to humans, however the primary exceptions are those lectins capable of binding to gut tissue.

In order for dietary lectins to be promoters of atherosclerosis, the following physical and physiological processes must occur: 1) they must survive cooking and processing; 2) they must survive digestive enzymatic degradation; 3) they must bind gut tissue; 4) they must cross gut tissue barrier; 5) they must resist immunological and hepatic (liver) disposal; 6) they must arrive in peripheral circulation intact in physiological concentrations; 7) they must interact with one or more mechanisms known to influence atherosclerosis. The first six of these seven steps are known to transpire, as ingested lectins rapidly appear intact in the bloodstream of humans

THIS MONTH’S FOCUS:
Dietary Lectins: An Unrecognized Risk Factor for Cardiovascular Disease, Part 2

This Month’s Focus:
Dietary Lectins
animals and cross the intestinal barrier in human cultured tissues.

So, we know that dietary lectins can get into the bloodstream of humans and animals, and we know that chronic, low-level inflammation is essential for all facets of atherosclerosis. Is there any evidence that lectins are involved in the progression or acceleration of atherosclerosis? Further, is there any evidence that dietary lectins may promote chronic, low level inflammation in humans?

**Peanut Lectin and Atherosclerosis**

Despite being high in monounsaturated fats (36 – 59 % energy) and theoretically a heart-healthy oil, peanut oil has been unexpectedly shown to be highly atherogenic in rats, rabbits and primates. An atherogenic diet (40 % fat as peanut oil) resulted in heart attacks in 2 of 6 (30%) rhesus monkeys over a 16-month period. Despite serious atherosclerosis, the heart attack rate (2.3 %) was lower in animals fed lard in lieu of peanut oil. Upon autopsy, coronary arteries showed severe narrowing (>75 %), mineralization, and evidence of previously healed heart attacks. Reduction of the lectin (PNA) content in peanut oil reduces its atherogenicity. Unfortunately, in these early studies, the inflammatory response to a high peanut oil diet simply was not measured, as inflammation was not yet suspected to be an integral feature of atherosclerosis.

**Lectins, Inflammation and Atherosclerosis**

One of the intriguing factors that may implicate dietary lectins in atherosclerosis involves the specific location of plaque formation along the arteries. Plaques only form in turbulent flow areas along the artery, such as sites where arteries branch (Figure 1), but not where blood flow is smooth (laminar flow), such as in small arteries and at non-branching or non-curving sites. Until recently, the mechanisms underlying this phenomenon were poorly understood.

![Figure 1. Atherosclerosis formation at laminar and turbulent flow sites along arteries.](image)

Let’s again examine the artery cross-section shown in Figure 2 and take a more detailed look at the true structure lining the inside of arteries, the glycocalyx. This wispy, hairy structure is composed of sugars and carbohydrate molecules that form a physical barrier between the red and white blood cells in circulation and the endothelial cell surface, thereby preventing white blood cells from attaching to adhesion molecules. In other words, one of the very first steps in atherosclerosis, the entry of monocytes into the intima, is blocked when the glycocalyx is fully intact. Only when the glycocalyx mass is reduced can monocytes and T-cells bind adhesion molecules and find their way into the intima. Turbulent flow areas are more susceptible to atherosclerosis because the glycocalyx mass is reduced in these areas. It is known that high-fat diets (which increase the rate of oxidized LDL formation) cause the glycocalyx size and mass to be reduced, as do inflammatory cytokines. From a physiological perspective, reductions in glycocalyx size and mass in response to injury or inflammation make sense. Shedding of the glycocalyx allows the white blood cells entry to the inflamed tissue from circulation and therefore begins the healing process by first destroying and then taking up the foreign substance.
Common dietary lectins are potent stimulators of inflammatory cytokines in white blood cell cultures. In Figure 3 you can see that lectins from lentils, kidney beans, peas and wheat potently increase the production of inflammatory cytokines (IL-12, IL-2, and INFγ). Wheat lectin (WGA) also stimulates production of two other inflammatory cytokines (TNFα and IL-1β) that promote the atherosclerotic process. Consequently, if dietary or environmental factors which facilitate synthesis of MMPs is not a good thing for cardiovascular disease patients. Well guess what? Lectins from wheat, WGA, and lectins from kidney beans, PHA23, cause tissue cultures of white blood cells to increase their production of MMPs.

Wheat lectin also influences the final and fatal step in atherosclerosis, the formation of a blood clot in an artery. Integral to the formation of clots are platelet cells, which circulate in the bloodstream. Platelets are normally activated when they contact collagen from a damaged blood vessel. WGA directly causes the activation of platelets and potently increases their aggregation (clumping). Hence, the consumption of whole wheat may be integral in the thinning and destruction of the fibrous cap as well as the formation of the fatal clot.

Now that we know how important dietary lectins are to the development of atherosclerosis and we know which foods they’re found in, dietary changes can be made to prevent the whole process. Following the Paleo Diet minimizes intake of beans, lentils and wheat and therefore minimizes exposure to dietary lectins and their accompanying inflammatory cytokines. This is a powerful and painless way to protect yourself from America’s number one killer, cardiovascular disease.
Grains and Milk may Increase the Risk for Kidney Cancer

In a recent case-control epidemiological study\textsuperscript{25}, including 767 patients (494 men and 273 women) younger than 79 years with renal cell carcinoma (the most common form of kidney cancer), and 1,534 controls (988 men and 546 women), researchers from Milan, Italy evaluated the relation between some foods and the risk of this type of cancer. They found that consumption of milk, yogurt, pasta, rice and bread were associated with an increased risk for renal cell carcinoma in this Italian population.

Although this was an epidemiological study that could only show relationships, not causality, there are other studies that give some biological plausibility to this hypothesis.

In 2004, researchers from Australia found\textsuperscript{26} that IGF-I stimulated growth in a cell line derived from metastatic renal cell carcinoma, and IGFBP-3 inhibited it.

As Dr. Cordain has pointed out\textsuperscript{27, 28}, hyperinsulinemia (an endocrine disorder caused by high glycemic load foods, milk and yogurt) elevates the IGF-1/IGFBP-3 ratio, thereby altering cellular proliferation and growth in a variety of tissues whose clinical course may promote epithelial cell carcinomas (such as breast and prostate cancer). Finally, recent papers\textsuperscript{29-31} confirm that milk and high glycemic load foods increase the IGF-1/IGFBP-3 ratio.

These studies provide a rationale to assume that the consumption of grains (in particular refined grains, such as bread), milk and yogurt may increase one’s risk of kidney cancer by increasing the IGF-1/IGFBP-3 ratio.

Berries May Reduce Cardiovascular Disease Risk

Epidemiological studies indicate that high fruit and vegetable intakes are associated with lower Cardiovascular Disease (CVD) incidence\textsuperscript{32-38}.

Specifically, berries have received attention for their potential to decrease CVD risk\textsuperscript{15,16}, but no intervention study had analysed specific risk factors until recently.

In a study published in the February edition of the American Journal of Clinical Nutrition, researchers from Finland investigated the effects of 2 months of berry consumption on blood pressure, serum lipids, and platelet function. The 72 subjects were middle-aged and un-medicated, with cardiovascular risk factors (hypertension, high blood glucose, elevated serum total cholesterol or triglycerides, and low HDL cholesterol\textsuperscript{41}.

Although total cholesterol and triglycerides were unaffected by the intervention, plasma HDL-cholesterol increased and systolic blood pressure decreased significantly more in the berry group than in the control group. The berry group also experienced an inhibition of platelet function\textsuperscript{41}, indicating that berry consumption may indeed decrease CVD risk.

These results may be due to the high antioxidant content of these foods, since plasma concentrations of polyphenols (a class of plant antioxidants) and vitamin C increased\textsuperscript{41}. Previous studies have revealed that berries contain the highest amount of total antioxidants compared to other plant.
Berries also contain folic acid, potassium, and soluble fiber, have a low glycemic load, and are net base yielding, making them a great addition to the Paleo Diet.

Higher Protein Intake To Prevent Sarcopenia

Pedro Bastos

The term Sarcopenia refers to the loss of muscle mass (3 - 8% per decade) and strength that begins in mid-life and accelerates after the age of 60. It is a fundamental cause of disability and falls, and may worsen the outcome of other illnesses. The estimated direct healthcare cost attributable to sarcopenia in the U.S. in 2000 was $18.5 billion ($10.8 billion in men, $7.7 billion in women), which represented about 1.5% of total healthcare expenditures for that year.

There are many underlying causes of age-related sarcopenia, such as hormonal changes and physical inactivity, but studies suggest that nutritional factors such as protein intake also play a major role.

In a recent epidemiological study published in the American Journal of Clinical Nutrition, researchers examined the association between protein intake and lean body mass (LM) in 2066 community-dwelling black and white men and women aged 70–79 over three years of follow-up. They found that participants in the highest quintile of protein intake (18.2% of energy - 1.1 g/kg/d) lost 40% less LM than did those in the lowest quintile (11.2% of energy - 0.7 g/kg/d). They also found that among those who lost weight over the three-year period, lower protein intake was associated with greater loss of LM.

These results show that the recommended diet...
tary allowance for protein (0.8 g/kg/d) may be insufficient to preserve LM. Nevertheless, a higher amount of protein may not be enough, if it doesn’t contain adequate amounts of specific essential amino acids, like leucine. Leucine is known to regulate protein synthesis (the formation of new muscle tissue), but there appears to be an age-related resistance of muscle proteins to the anabolic stimuli of leucine, particularly within the lower physiological range of intake, so a higher amount of this amino acid may be needed.

Palaeolithic diets were almost certainly higher in protein than western diets, containing 19% to 35% of total energy. Most of this protein came from animal sources which would have supplied a generous amount of leucine (as shown in the following table).

### Food sources of Leucine

<table>
<thead>
<tr>
<th>Food (100 Kcal)</th>
<th>Leucine (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg White</td>
<td>1774</td>
</tr>
<tr>
<td>Meat (average)</td>
<td>1474</td>
</tr>
<tr>
<td>Shellfish</td>
<td>1285</td>
</tr>
<tr>
<td>Milk</td>
<td>524</td>
</tr>
<tr>
<td>Cereal Grains (average)</td>
<td>303</td>
</tr>
<tr>
<td>Fruit (average)</td>
<td>31</td>
</tr>
</tbody>
</table>

This provides evidence that a high-protein Palaeolithic diet, accompanied by a well-designed exercise program, could prevent age-related sarcopenia. This is particularly likely if it is net base yielding (containing a high amount of fruits and vegetables), as a net acid yielding diet can lead to muscle loss.

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### Pollo Picadillo

1 pound skinless, boneless chicken breast
2 teaspoons olive oil
1 cup chopped onion
1 ½ teaspoons ground cumin
¼ teaspoon ground cinnamon
3 garlic cloves, minced
1 cup prepared salsa
1/3 cup golden raisins
¼ cup slivered almonds, toasted
¼ cup chopped fresh cilantro
Fresh cilantro sprigs (optional)

Place chicken in a food processor; pulse until ground.

Heat oil in a large nonstick skillet over medium-high heat. Add onion, and cook for 3 minutes, stirring occasionally. Add chicken, cumin, cinnamon, and garlic, and cook for 3 minutes or until chicken is done, stirring frequently. Stir in salsa and raisins. Cover; reduce heat, and simmer for 5 minutes or until thoroughly heated. Stir in almonds and cilantro. Garnish with cilantro sprigs, if desired.

Yield: 4 one-cup servings
NEWS/EVENTS

Back Issues of The Paleo Diet Newsletter –
Back issues of The Paleo Diet Newsletter are available on our website at www.ThePaleoDiet.com/newsletter/back_issues.shtml for $12.95 each. The entire back catalog is available for $99.95.

King Corn – This entertaining documentary looks at corn, a food that almost all Americans consume in some way, every single day. Corn is highly subsidized, uses massive amounts of fertilizer and herbicides; and ends up in our food supply as high-fructose corn syrup, feedlot raised cattle, corn oil, processed snack foods, and more. College friends Ian Cheney and Curt Ellis travel to Iowa to grow an acre of corn, stopping along the way to visit Loren Cordain in Colorado. This is a fascinating look at how the American food system works, and some of what has led to our current health crisis. The DVD is available at our new Paleo Webstore.

Cordain Interview – A brief interview with Dr. Cordain has been posted on http://www.asizableapple.com/2008/02/ask-pro-paleo-diet.html.

Paleo Nutritional Consultant – We are receiving an increasing number of inquiries from people looking for nutritional assistance. If you are an experienced nutritional consultant or physician who has a good understanding of the Paleo Diet, we would like to add you to our referral list. We are also currently looking for a sports nutritionist with an understanding of The Paleo Diet for Athletes. Please send details about your experience and services to nutritionist@ThePaleoDiet.com.

QUESTIONS & FEEDBACK

Duathlon Masters Athlete Soaring Performance

Editors note: This email was originally sent to Joe Friel, coauthor of The Paleo Diet for Athletes.

Dear Joe,

I have a love-hate relationship with you. I love the fact that you took the time, energy (and probably a lot of ridicule) for promoting the Paleolithic diet for use by athletes. I hate the fact that it works, and works so well that a majority of the foods I love and have been trained to cook over the last 20 years - I won't eat now. (okay, 95/5% rule) Fortunately, it is an easy choice.

I know you are busy, and this is a bit lengthy...but I need you to know that your actions have had a profound impact on someone else's life. You are an athlete, you work with athletes, and therefore you know that much of an athlete's soul is directly related to how he/she feels when pushing to go just a little harder and faster. In a nutshell, your actions have helped heal an old athlete's soul; I will forever be in debt to you.

I had to write you a note and thank you. According to your book, my reaction to the diet was probably very similar to that of many others, although probably a bit more profound. In five years I spent over $15K (insurance doesn't cover "athletic performance issues") in six different doctor's offices trying to find out why my performance had decreased so substantially over the course of one year when I turned 36.

I was told by M.D.s, N.D.'s, and nutritionists that I had everything from activity induced asthma, adrenal fatigue, Addison's disease, hyper/hypo thyroid, anxiety disorder, undefined cardiac discrepancies, and a list of many other maladies. During that period no one suggested it was what or when I was eating. For each thing a doctor suggested and prescribed that I saw no symptom change, I became more disheartened. I stumbled on your book only after I noticed that three of the doctors had mentioned that my blood/urine tests suggested I was carbohydrate loading all the time and that my blood pH was out of balance. Google is a beautiful thing; it took me right to your book.

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After reading your book, I promised to give the diet one month. Then I could toss it on the pile of the worthless books and tests I had collected over the years in my attempt to find out what was going on. The first two weeks were absolute,
pure, unadulterated HELL. I thought I was going through drug withdrawal. But after three weeks I noticed I was not only feeling better, I was also sleeping better and many of my symptoms were lessened or gone. Unexpectedly, I was losing weight and getting lean really fast. Needless to say, I stayed on the diet. That was 6 months ago.

My wife and I, like you, are duathletes and love the sport. We have both been on the US World team for a number of years, and Heather won a gold medal in Gyor, Hungary this past May. I, however, received such an embarrassing ass-kicking that I swore I wouldn't race again until I found out what was going on.

When I turned 36, my run times dropped dramatically and my cycling power went down the drain. I couldn't train more than 8 hours a week without experiencing serious overtraining symptoms. And with that decreased activity level, I began putting on additional weight. Over the next year, along with rapidly decreasing athletic performance, I was experiencing night sweats, extreme hypotension, depression (more the more I trained,) mood swings, and a list of other strange symptoms.

Those and many other symptoms became much worse in each of the subsequent five years. Why these symptoms showed up so acutely when I turned 36, I have no idea. Now, after six months on the modified Paleolithic diet, nearly all of those symptoms are gone. The most amazing thing is what it has done for my athletic performance. I do not use the word miraculous often, and never to describe "fixes" for athletic performance, but what has happened in less than half a year is just this side of miraculous.

I did not start the diet with any expectations of losing weight because I believed I had a healthy "athletes diet". You have probably received many letters that tout great changes, but I am not only an athlete, I am a trained scientist and educator and I do not take numbers or statistics lightly. These are my conservative numbers...I have always fought weight gain, but I am down 22 pounds from March, and that includes an estimated 2-3 pounds of added muscle mass. I am down from 11% body fat to less than 6%. My 75% HR running pace (on treadmill) last year versus this year is down 1:18/mile. I have yet to find out what my race pace 5K/10K times are because I am still trying to figure out how to drive this new body and don't want to break it. However, the best part is my cycling power/watts (Computrainer test) have gone up over 12% over an hour TT session. I cycled as a Cat 1/2 for 2 years when I was younger and stupid, and would have given my (choices are many) to have gained 12% power over a 40K. The icing on the cake is that I can do an intense workout and WANT TO and CAN DO another in 8-12 hours day after day after day.

This, although many have suggested, is not just a matter of losing 22 pounds, because I had lost 15 pounds (slowly) two other times in the past 5 years hoping it would help. It didn't. It made almost all the symptoms worse.

Here's some anecdotal proof that your eating guidelines work. After 3 months on the diet I was starting to feel so good I decided I wanted a real test. I decided to do something really stupid and signed up for American Zofingen in New Paltz, NY, which was six weeks away. I had not run over 13 miles at one time in the last 3 years. I had not ridden over 70K at race pace in over three years. But what the hell, I wanted to see if I felt as good as I thought I did. I embarked on a five-week training schedule that was stupid and I knew I would toe the line without enough taper. My hope was to finish, not blow up, and hopefully go 10 hours.

I went 8 hours and 50 minutes, was 10th overall, and won the Master’s division. If someone in March had said I would be doing AmZof, I would have told them they were nuts. The diet works. I can't wait for next year's race season to start...and toe the line in Rimini, Italy for next year's Du Worlds. =-)

So, once again, thank you.
Cheers,
Mark Hofer, Ed.D
Legacy High School
Seattle, WA

Addendum - I am now on my 10th month of the Paleo Diet (for athletes) and would never have believed how I feel had I not tried it. The more people, especially athletes, who are willing to try it the better. It is not always an easy way to fuel given the social environment surrounding food and "healthy diet" trends, but if someone is willing to make the change...

Be well,
Mark
REFERENCES


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55. Cordain L; Friel J. The Paleo Diet for Athletes. Rodale, 2005