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AS WE SEE IT

Eating Food Cooked At High Temperature Accelerates Aging

A new study published in the Proceedings of the National Academy of Sciences¹ reveals that eating foods cooked at high temperature may increase the rate at which we age. According to this study, the ingestion of high temperature cooked foods causes chronic inflammation and the formation of advanced glycation end products.

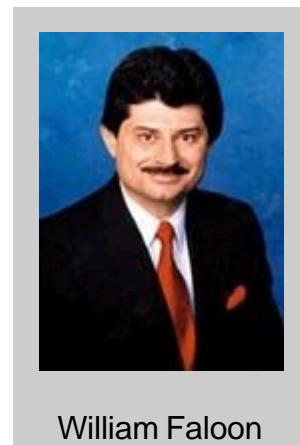
Life Extension members have been frequently warned about the dangers of chronic inflammation and glycation. For the benefit of new members, I will succinctly explain these two lethal processes.



As humans age, there is a systemic increase in inflammatory cytokines (destructive cell-signaling chemicals) that contribute to many degenerative diseases. Rheumatoid arthritis is a classic disorder where excess levels of cytokines cause or contribute to the destructive inflammatory syndrome. While inflammatory cytokines can cause agonizing pain, they also disrupt the linings of our arteries, mutate DNA and degrade brain cells. Chronic inflammation is directly involved in diseases as diverse as cancer, atherosclerosis, diabetes, aortic valve stenosis, congestive heart failure, Alzheimer's disease and kidney impairment.

In aging people with multiple degenerative diseases, we often find elevated blood levels of C-reactive protein, indicating the presence of an inflammatory disorder. When a cytokine blood profile is conducted in these individuals, we usually discover excess levels of one or more of the pro-inflammatory cytokines. The most common pro-inflammatory cytokines are tumor necrosis factor-alpha, interleukin-6, interleukin-1(b) and/or interleukin-8.

Chronic inflammation inflicts devastating effects, especially as humans grow older. The lethal consequences of inflammation are clearly established in the medical literature.²⁻¹⁴ The good news is that many of the nutrients, hormones and drugs being taken by Life Extension members suppress the production of these deadly inflammatory cytokines. As you will soon read, avoiding foods cooked at very high temperatures can also reduce production of inflammatory cytokines.



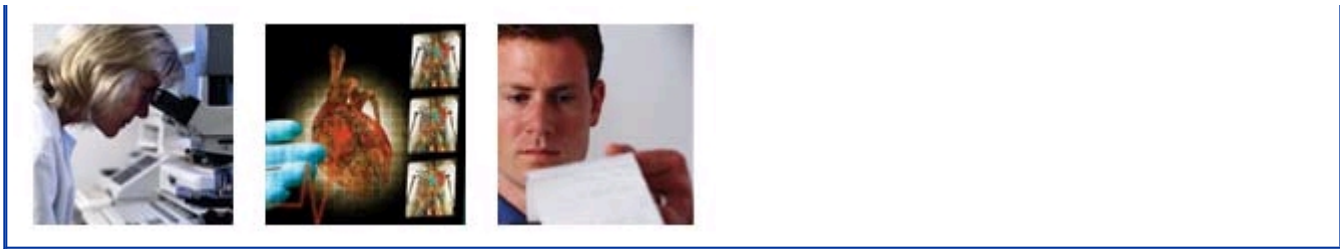
William Faloon

How glycation cooks us to death

The glycation process that turns a chicken brown in the oven is exactly what happens to the proteins in our body as we age. When body proteins react with sugars they turn brown and fluorescent, lose elasticity and cross-link to form insoluble masses that generate free radicals. The resulting advanced glycation end products (glycotoxins) accumulate in our collagen and skin, cornea, brain and nervous system, arteries and vital organs as we age. Unfortunately, glycotoxins are highly resistant to the normal processes of protein turnover and renewal that maintain the healthy tone of youthful body tissues and organs.



How does the body cope with these chronic assaults on proteins? Long-lived cells, such as neurons and muscle cells, contain high levels of a dipeptide called carnosine, made up of histidine and beta-alanine. Unlike ordinary antioxidants, carnosine blocks numerous pathways involved in the glycation process.



Age-accelerating effects of glycation

The other pathological aging mechanism exacerbated by eating high temperature cooked food is the formation of advanced glycation end products (A.G.E.'s). Glycation can be described as the binding of a protein molecule to a glucose molecule resulting in the formation of damaged protein structures. Many age-related diseases such as arterial stiffening, cataract and neurological impairment are at least partially attributable to glycation. These destructive glycation reactions render proteins in the body crosslinked and barely functional. As these degraded proteins accumulate, they cause cells to emit signals that induce the production of inflammatory cytokines.

The glycation process is presently irreversible, though a recent study indicates a drug in clinical trials may be partially effective. Life Extension members take supplements to help protect against glycation. According to the Proceedings of the National Academy of Sciences study, consuming foods cooked at high temperature accelerates the glycation process, and the subsequent formation of A.G.E.'s.

A more succinct descriptive term for "advanced glycation end products" is "glycotoxin", since "advanced glycation end products" are toxic to the body. We will use the word "glycotoxin" from here on to describe the term "advanced glycation end products".

Cooking and aging have similar biological properties

Cooking foods at high temperatures results in a "browning" effect, where sugars and certain oxidized fats react with proteins to form glycotoxins in the food. Normal aging can also be regarded as a slow cooking process, since these same glycotoxins form in the skin, arteries, eye lenses, joints, cartilage, etc. of our body.

The Proceedings of the National Academy of Sciences study shows that consuming foods high in glycotoxins might be responsible for the induction of a low-grade, but chronic state of inflammation. In addition, the glycotoxins in food cooked at high temperatures also promote the formation of glycotoxins in our living tissues. The implication of these findings is profound.

Feeding foods rich in glycotoxins to diabetics

The presence of glycotoxins in the blood of individuals with diabetes has been known for quite some time.¹⁵ To ascertain reasons for this, a group of diabetics were studied to assess the difference between consuming a diet high in glycotoxins compared to diet low in glycotoxins. The high glycotoxin diet was induced by heating food for a longer period at higher temperatures compared to the lower glycotoxin diet. Using a variety of foods, the scientists were able to increase the glycotoxin content five-fold by cooking the food at high temperatures.

After only two weeks, diabetics on the high glycotoxin diet showed a 50% to 100% increase of glycotoxins in their blood and urine compared to the group consuming the low glycotoxin diet. The group eating the high glycotoxin food also showed increased levels of inflammatory blood markers such C-reactive protein and pro-inflammatory cytokines such as tumor necrosis factor alpha. In order to determine whether these significant changes were merely an acute response to an altered diet, the scientists carried out a second study that lasted for six weeks. Again, those consuming a diet high in glycotoxins had higher concentrations of glycotoxins in their bodies, along with increased inflammatory cytokines in their blood.

Medical establishment finally recognizes importance of C-reactive protein testing

The Life Extension Foundation long ago advised members to have an annual C-reactive protein blood test to detect systemic inflammation that could increase the risk of heart attack, stroke, cancer and a host of age-related diseases. In fact, the C-reactive protein blood test has long been included in the Male and Female Panels that are ordered annually by many Foundation members.

On January 28, 2003, the American Heart Association and Centers for Disease Control & Prevention (CDC) jointly endorsed the C-reactive protein test to screen for coronary-artery inflammation to identify those at risk for heart attack.

The value of the C-reactive protein test was evident to the Life Extension Foundation many years ago. Millions of Americans needlessly suffered crippling strokes, sudden death heart attacks and other diseases that could have been prevented if the medical establishment had utilized the C-reactive protein blood test sooner.

The researchers also found that eating diets low in glycotoxins reduced the level of other potentially harmful substances in the blood, including LDL cholesterol ("bad cholesterol"). During the two-week, low-glycotoxin diet, diabetics had lower LDL levels than those on a high-glycotoxin diet. A six-week, low-glycotoxin diet caused a 33% reduction of LDL, while a high-glycotoxin diet increased LDL by 32%.

Aging control and weight loss

This study on human diabetics raises intriguing possibilities of preventing disease and slowing aging via proper food preparation. First of all, previous studies have shown that caloric restriction prolongs life span in rodents while simultaneously decreasing glycotoxin formation in body tissues.¹⁶ There is now considerable evidence that the same glycotoxin formation that occurs during cooking also occurs inside the body during normal aging¹⁷ and at an accelerated rate in diabetics.¹⁸ For example, glycotoxins accumulate faster in the skin collagen of diabetics compared to non-diabetics.¹⁹ We also know that glycotoxins engage cell receptors in such a way as to promote tumor growth and metastasis (via mechanisms that stimulate cell migration, tumor cell growth factors and enzymes that digest the extracellular matrix).²⁰

While this study on human diabetics is preliminary and needs confirmatory results in healthy populations, there were other benefits associated with consuming a low glycotoxin diet. Not only did the diabetics consuming the low glycotoxin diet lose weight, but their blood glucose levels also dropped. In the group eating the high glycotoxin diet, blood glucose levels increased. Elevated glucose levels can trigger production of deadly inflammatory cytokines.

It should be noted that the number of calories, carbohydrates, proteins and fat was the same in both the high and low glycotoxin diets. The diabetics consuming the low glycotoxin diet, however, lost weight. It is well known that reducing excess weight and glucose levels confers longer life.

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Small changes in cooking methods and diet can slow aging

Researchers at the Department of Geriatrics, Mount Sinai School of Medicine have determined that A.G.E.'s or glycotoxins are found in foods that are overheated or cooked at very high temperatures. This includes foods that have been fried, barbecued, broiled or cooked in the microwave. While the worst culprits are animal products, since they contain a higher amount of "bad" fats that speed up the formation of glycotoxins, any food that is exposed to extreme high heat can scorch the natural sugars in food and create glycotoxins. This is also true of many pre-packed foods that have been preserved, pasteurized, homogenized or refined, such as white flour, cake mixes, dried milk, dried eggs, dairy products including pasteurized milk, and canned or frozen pre-cooked meals.

While it may be impossible to totally avoid glycotoxins, it is possible to reduce exposure by changing the way food is prepared. Consider steaming, boiling, poaching, stewing, stir-frying or using a slow cooker. These methods not only cook foods with a lower amount of heat, they create more moisture during the cooking process. According to Dr. Helen Vlassara*, the study's lead researcher, water or moisture can help delay the reactions that lead to glycotoxins. Marinating foods in olive oil, cider vinegar, garlic, mustard, lemon juice and dry wines can also help. Finally, consider making small diet changes by adding more fresh fruits and raw and steamed vegetables to your diet.

* Vlassara H et al. Inflammatory mediators are induced by dietary glycotoxins, a major risk factor for diabetic angiopathy. Proc Natl Acad Sci U S A 2002 Nov 26;99(24):15596-601.

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Reversing glycation

In the August 2001 issue of this magazine, an article reported on a compound called ALT-711 that has been shown to partially reverse glycation. Regrettably, the company (Alteon, Inc.) trying to get ALT-711 through the FDA's approval process is woefully under funded, and clinical studies have progressed at a snail's pace.

On January 21, 2003, some encouraging results were announced from a preliminary analysis of a Phase II clinical trial evaluating the activity of ALT-711 in treating diastolic heart failure. The significance of these results is that diastolic heart failure (DHF) is one of the most common types of heart failure in the elderly. DHF is a poorly treated medical condition that is characterized by the inability of the heart to relax properly and fill with blood, due to stiffening (glycation) of the heart and subsequent impaired relaxation of the left ventricle. Diastolic dysfunction is estimated to account for 30% to 50% of all heart failure cases, which total nearly five million cases in the U.S. alone.

In this Phase II clinical trial, DHF patients who received ALT-711 for 16 weeks experienced a statistically significant reduction in left ventricular mass. The patients also had a marked improvement in left ventricular diastolic filling. Additionally, the drug had a positive effect on patients' quality of life, as measured by a well-established heart failure/quality of life questionnaire. This Phase II trial is ongoing, and additional analyses of the data are being conducted. Here is a quote about the significance of this study:

"ALT-711 offers promise as a novel therapy for diastolic heart failure because currently available therapies do not specifically target the stiffening heart and vessel walls caused by pathological glucose-protein matrixes called Advanced Glycosylation End-product (A.G.E.) Crosslinks. The formation of A.G.E. Crosslinks is a natural part of the aging process that can lead to stiffening and loss of function in tissues, organs and vessels including the heart and large arteries. In previous human clinical testing, ALT-711 has shown the ability to restore elasticity to blood vessel walls by cleaving A.G.E. Crosslinks.* Additionally,

in several preclinical studies ALT-711 has been shown to normalize the thickening of the left ventricle and remodel the heart."**

(Please note that these researchers use the term Advanced Glycosylation End-product (A.G.E.), which is another way of stating advanced glycation end products or "glycotoxins".)

Life Extension has long argued that the high cost of gaining FDA-approval denies Americans access to life-saving compounds such as ALT-711.*** It can take so long for a new compound to become an approved "drug", that many companies run out of capital before they are able to comply with the FDA's Byzantine regulatory procedures. The result is that Americans die even though potentially effective therapies sit in the FDA's waiting room.

Since we cannot yet reverse the pathological effects of glycation, it becomes critical for those seeking to prevent premature aging to at least slow this lethal process. Avoiding foods cooked at high temperature and supplementing with 1000 mg a day of carnosine are the best ways of mitigating the glycation process.

*Wolffenbuttel BH, et al. Breakers of advanced glycation end products restore large artery properties in experimental diabetes. Proc Natl Acad Sci USA, 1998 Apr 14;95:4630-4.

**Veronesi M et al. ALT-711, A collagen cross-link breaker, decreases myocardial fibrosis and improves endothelial dysfunction in hypertensive Dahl salt rats. American Heart Association 55th Annual Fall Conference and Scientific Sessions of the Council for High Blood Pressure Research, September 2001.

***Kanda T. C-reactive protein (CRP) in the cardiovascular system. Rinsho Byori 2001 Apr;49(4):395-401.

What you should do

Most Life Extension members follow a healthy lifestyle that helps prevent glycation and chronic inflammation.

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Inflammatory cytokine production can be suppressed with the proper supplementation of fish oil, DHEA, vitamin K and nettle leaf extract. If blood tests reveal persistently high levels of inflammatory cytokines, then 400 mg twice a day of a low-cost drug called pentoxiphylline may bring inflammatory cytokine levels down to safe ranges.

What one eats plays a major role in chronic inflammatory processes. Consuming low glycemic foods reduces the insulin surge that contributes to chronic inflammatory processes. It is also important to avoid over consumption of foods high in arachidonic acid (beef, egg yolk, dairy, etc.).

We now know that eating too much over cooked food causes an increase in inflammatory cytokines. Since most "junk" foods are cooked at extremely high temperatures, it makes sense to avoid french fries, hamburgers, potato chips, fried food and other snacks. These foods not only contain lots of glycotoxins, but they also create other metabolic disorders that can induce degenerative disease.

Consuming at least 1000 mg a day of carnosine, and/or 300 mg of the European drug aminoguanidine can inhibit pathological glycation reactions in the body. Avoiding foods cooked at high temperature not only

reduces pathological glycation processes, but also prevents the formation of numerous gene-mutating toxins that are known carcinogens.

When food is cooked at high temperatures, deadly gene-mutating toxins are created that increase human cancer risk. This warning has been communicated to readers of this publication for many years. Now that overheated food is associated with accelerated aging, health conscious individuals have an even greater incentive to pay attention to their diet. As a member of the Life Extension Foundation, you learn about documented methods of reducing disease risk years before the general public.

Those concerned that they are already suffering from the effects of a chronic inflammatory disorder should turn to the next page to learn how they can measure and suppress lethal pro-inflammatory cytokines.

For longer life,

William Faloon

Further Reading: Protecting against the lethal effects of chronic inflammation

Caution: Food is cooked to destroy bacteria and other pathogens that could cause a serious illness. It is important not to eat undercooked food, but avoiding food unnecessarily cooked at higher temperatures is desirable. Certain foods (like fried foods) have to cook at high temperatures. Health conscious people are increasingly avoiding fried foods because they are associated with many health risks.

Note: For more information about eating healthier, log on to www.lef.org and access the Obesity and Inflammation (Chronic) protocols listed under Health Concerns. Also refer to the January 2001 issue of Life Extension on this website and click the article Drugs That Inhibit Cox-2 May Cause Tissue Damage.



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