The Oxygen Battlefield

by Gary Null, Ph.D.

American society, with its get-the-job-done attitude, expects a fast solution to every problem. This mentality has seeped into the medical model, which people expect to provide quick-and-easy solutions to their health problems. In some cases, the medical community can indeed supply that type of quick cure. Penicillin, for example, certainly does its job to kill some bacteria. But the success of Penicillin also has fueled the mentality that for every disease state there is a magic bullet to cure it.

This puts a burden on the physician to deliver better and faster magic bullets. At the same time, it downplays the importance of each person's natural resistance to ailments and disease. If more focus were put on this issue, we would learn to work with the body's wisdom and support its natural ability to resist a bacteria or virus through the defense system. Zinc, for example, plays a major role in the body's production of immune system cells such as T lymphocytes. Thus, providing the body with a physiologic mineral such as zinc would strengthen its natural defense apparatus.

The concept of building our natural resistance has become extremely vital in recent years, as we become more aware of the damage that can be caused by infectious agents other than bacteria, including viruses, yeast and parasites. All of these must be viewed as an interaction between the person and his or her environment.

However, we also need to address another type of invader - the "free radicals" that attack us at a biochemical level. Simply put, free radicals are molecules that have an unpaired electron, which makes them capable of damaging cells, tissues and organs. These dangerous molecules can weaken many vital aspects of body functioning, including our cardiovascular, neurological and immune systems.

For many people, the idea that biochemical invaders may be altering their health and immunity is difficult to grasp. After all, these invaders are not directly visible to us because they affect the molecules of our cells. By contrast, the impact of invaders such as bacteria may be easier to observe because we can see an overgrowth of bacteria on the skin or an exudate on the tonsils. Likewise, a virus may manifest as a herpes blister and a yeast overgrowth may be seen as a vaginal discharge or a thrush infection in the mouth.

Free radicals can stem from external pollutants or from our internal biochemical processes.

Free radicals, though less visible, can be every bit as harmful to our health. In fact, a growing body of research shows that free radicals contribute to the aging process and to a long list of disorders, including heart disease and cancer, which now rank as two of the leading killers in our society. To understand how this damage occurs, we must look at the molecular events that take place in the body. Here, a silent oxygen battle is waged between the "prooxidants" (free radicals) and the "antioxidants" (certain nutrients), whose job it is to neutralize free radicals.

This discussion takes us far beyond the organs and glands of the immune system - and even beyond the cellular aspects of immunity. By considering the functions of molecules, the building blocks of our cells, we can gain a deeper understanding of how to protect the body from oxidation damage and optimize its immune performance. To start, let's look at the origin of free radicals.

What are free radicals?

The atoms that make up our molecules consist of a nucleus surrounded by electrons, which are the negatively charged part of the molecule. Electrons contribute to a molecule's stability because they are in orbit around its nucleus. Therefore, a molecule's balance may be disturbed if it loses one of its electrons. Such a molecule is called a "free radical" because its electrons are unpaired and its altered energy state makes it highly reactive.

Once a free radical is formed, it will try to restore its balance by stealing an electron from another molecule. This electron theft can unleash a destructive cycle because the stolen electron may come from a normal cell. Every time a molecule loses an electron, then, it may damage a healthy molecule in the process. As a result, the body's normal function will be impaired. A single free radical can destroy an enzyme, a protein molecule or an entire cell.[1]

As Derrick Lonsdale, M.D., points out, a free radical will react rapidly with any nearby substance. "Its half-life is measured in fractions of a second, and such reactions often result in a cascade of free radical formation in a multiplying effect, rather like an atomic explosion. These highly reactive molecules thus produce new compounds rapidly," states Dr. Lonsdale in *Free Oxygen Radicals and Disease*.[2]

What causes free radicals?

Free radicals can stem from external pollutants or from our internal biochemical processes. The four primary sources are:

The environment. Unfortunately, the environment is full of toxins that either contain free radicals themselves or generate free radicals after we breathe or swallow the substances. These toxins include the nitrogen dioxide and nitrogen oxide in polluted air, cigarette smoke (which is loaded with nitrogen oxides), smog and soot in urban air and automobile exhaust.[3] In addition, ionizing radiation, toxic wastes, pesticides and herbicides can generate free radicals.

One example of a potent free-radical generator is ozone, which results from vehicle exhaust and becomes a highly reactive air pollutant. When we breathe in ozone, it forms free radicals in the lung tissue. These ozone-induced free

radicals may then affect blood cells of all types. Considering that the action is in the lung - the oxygen receiver of the body - the free radicals may diminish the amount of natural, energy-stable oxygen available to the body.

Free radical chain reactions. An initial free radical, with its unstabilized energy, may form a second unbalanced free radical, which produces a third, and so on. If this chain reaction is not stopped, cellular damage may occur. Consider this analogy: A car tire blows out suddenly, throwing the vehicle off balance. It swerves and hits another car, bringing them both to a stop. At this point, a third car hits them from behind, another car hits that vehicle, and so forth. This begins a chain reaction as more cars join the pile up. In the body, the instrument that damages the first tire is like a free radical that initiates damage to molecules and electrons.

Internal production of free radicals. The body continually forms free radicals because they are required for many normal biochemical processes to take place, says Jeffrey Bland, Ph.D., in *The Nutritional Effects of Free Radical Pathology*. The trick is to control these free radicals so that they do not become destructive.[4] In the process of providing the cells with energy, for example, stable atmospheric oxygen reacts with a variety of biochemical substances. Unfortunately, this energy-producing process also gives rise to harmful free radicals, including the superoxide and hydroxyl radicals. Even the phagocyte cells - important members of the body's immune defenses - generate free radicals in the process of killing off bacteria, viruses and other invaders.[5]

Stressors on the body systems. In this case, free radicals occur as normal by-products of the healthy body's response to stressors. Aging, trauma, certain medications and some diseases all can lead to an increase in the production of free radicals. One such stressor is an infection in the body. In one animal study, mice that were exposed to a flu virus had 8 times as many free radicals in their lungs as control animals.[6] Athletes should be aware that vigorous exercise also may increase the number of free radicals produced by the body's need for more oxygen.

What are the mechanisms of free radical formation?

As oxygen-dependent organisms, we are always at risk of free radical damage. When the body metabolizes oxygen, it naturally produces free radicals. The oxygen-containing radicals that stem from this process are among the most reactive types of free radicals around. Thus, the energy released through cellular respiration can carry a heavy price tag in terms of its harmful effects on the body.

Through the process of oxygen metabolism, however, we can also see how free radicals are produced at a biochemical level. In the *American Journal of Clinical Nutrition*, Anthony T. Diplock describes the step by step process by which free radicals are formed and their subsequent actions in the body. The primary types of free radicals include the following:[7]

➤

PAIN TREATMENT SEMINAR

Tired of treating musculoskeletal pain symptoms?

The American Osteopathic Academy of Sclerotherapy
Presents its 1995 Spring CME Seminar
April 6-9, 1995 • Fort Worth, Texas

Topics include special introductory courses, including: hands-on workshops of ligamentous sclerotherapy (also known as reconstructive therapy) of the lumbar, thoracic and cervical spine, non-surgical treatment of hernias, and varicose and spider veins. Also, orthomolecular adjuncts to a medical practice, and anatomy laboratory workshops at University of North Texas Health Sciences Center in Fort Worth.

Call now – space is limited

American Osteopathic Academy of Sclerotherapy, Inc.
107 Maple Ave.
Wilmington, DE 19809
1-302-792-9280 or fax 1-302-792-9283

➤

Superoxide anion radical. To release energy, the body must reduce the molecules of oxygen down to water. In the process, says Diplock, a superoxide anion radical is produced. This free radical has a single-minded goal: to restore its balance by gaining a new electron. The obvious sources of this much-needed electron are the electron transfer chain, which is located in the mitochondria of the cell, and nearby organic or inorganic substances. Once the superoxide anion radical has gained an electron from one of these sources, it becomes a peroxyl anion.

Hydrogen peroxide. Peroxyl anion reacts with two hydrogen atoms to form hydrogen peroxide, which can trigger the formation of free radicals. Therefore, the body must remove both superoxide anion and hydrogen peroxide from the system as soon as they are formed. Otherwise, minerals such as iron or potentially copper may interact with these molecules to create yet another free radical, the highly reactive hydroxyl radical.

Hydroxyl radical. This free radical can attack enzymes, proteins and the unsaturated fatty acids in cell membranes. In short, it has the ability to do considerable damage to the body. As Diplock states: "[The hydroxyl radical] can pluck an electron from almost any organic molecule in its vicinity, which will initiate further radical and nonradical processes that may lie at the heart of the etiogenesis of biochemical changes that will lead to disease."[8]

The only good news - if we could call it that - is the hydroxyl radical's short half-life in the body. The damage it wreaks may be quickly contained and eliminated, says Diplock, because the radical is so highly activated. Even so, the most important course of action is to prevent its formation in the first place. Two enzymes, superoxide dismutase (SOD) and glutathione peroxidase, accomplish this task by removing hydrogen peroxide and superoxide anion from the system.

In many cases, free radicals target the unsaturated fatty acids contained in cell membranes for their attack. When a free radical comes in contact with the membrane, it can steal an electron from the fatty acid. This theft leads to the formation of an unstable lipid peroxyl radical. Through a chain reaction of chemical events, the lipid peroxyl can cause even more damage to the lipids in the cell membrane.

Ironically, a vitamin E free radical is formed in the process of breaking this chain reaction because vitamin E donates an electron to the lipid peroxyl. But this free radical is not as reactive as the oxygen-containing free radicals. Also, it can be returned to normal vitamin E through a recycling process that involves both vitamin C and glutathione peroxidase. Thus, vitamin E and vitamin C help to control the membrane damage caused by free radicals. This damage may be related to many disease states.

Singlet oxygen. Another type of oxidation product that deserves attention is the so-called singlet oxygen. As Diplock explains, this metabolite is not a free radical in the strictest sense. But it also has an unbalanced electron in orbit around its nucleus, which leads it to bind with a free electron. The singlet oxygen may be formed during certain biochemical events, such as when polymorphonuclear white blood cells attack a microbe or bacteria. Much like a free radical, the reactive singlet oxygen may cause tissue damage.

How does the body defend itself against free radicals?

We must continually strive to balance the events taking place in the molecules of our bodies. Fortunately, nature has given us a way to achieve this balance: The body's built-in mechanisms for handling free radicals consist of antioxidant enzymes and nutrients that remove radicals before they can cause cellular damage.

The antioxidant enzymes include two forms of superoxide dismutase (SOD), two forms of glutathione and catalase. SOD, which neutralizes the superoxide anion radical, needs either manganese or a copper/zinc combination to do its work, depending on its location in the cell. Meanwhile, glutathione peroxidase and catalase share the job of metabolizing hydrogen peroxide. For the most part, glutathione works on low concentrations of hydrogen peroxide, while catalase removes high concentrations of the reactive substance.[9] Catalase requires iron as its cofactor nutrient and glutathione peroxidase depends on selenium. Glutathione peroxidase also can inactivate lipid peroxides.[10]

Likewise, antioxidant vitamins act as "scavengers" to remove various forms of free radicals from the body and prevent new ones from being formed. These potent nutrients include vitamin C, vitamin E and beta-carotene (a precursor to vitamin A). In addition to trapping free radicals, all three of these antioxidants can "quench" the highly reactive singlet oxygen.[11] In essence, they absorb the molecule's altered energy state, thereby returning it to normal without harming the system.[12]

How do free radicals cause trouble in the body?

In recent years, a variety of degenerative diseases have been linked to free radical activity. These diseases get their start in the biochemical processes of the body, during which free radicals can damage cells and tissues. In *The Antioxidants*, Richard A. Passwater, Ph.D., identifies five basic types of damage caused by free radicals that will lead to the chronic diseases so prevalent today, including arthritis, neurological disorders and cancer. The basic types of biochemical damage include:[13]

Lipid peroxidation. When free radicals attack the polyunsaturated fats of the body, the fatty acids become rancid and can produce even more free radicals.

Cross linking. Free radicals may alter the structure of DNA and protein molecules by causing them to fuse together. This cross linking inhibits the molecule's ability to function in the body.

Cell membrane damage. The cell membrane serves as a filter to the surrounding environment. Free radicals can cause direct damage to the structure of this filtering system, thereby impairing the cell's ability to absorb certain nutrients and eliminate waste products.

Lysosome damage. The lysosomes within our cells contain powerful digestive enzymes. But free radicals can destroy the lysosomes, allowing these enzymes to escape and "eat" important compounds within the cell.

Age pigment. Free radicals can cause a buildup of lipofuscin, an age pigment that may alter the chemistry of a cell.

What do these types of damage have in common? They occur in regions of the body that are rich in electrons, such as DNA, proteins and polyunsaturated fatty acids, says Dr. Bland. These biological molecules are so rich in electrons because they contain unsaturated bonds, or what a chemist would call "double bonds." The double bonds become the site of all biochemical activity of the free radicals.[14]

With lipid peroxidation, for example, the oxygen free radical attaches itself to the double bond of the unsaturated fat. It pulls off one of the electrons from the double bond to create a single bond, resulting in the creation of the free radical lipid hydroperoxide. This free radical contains only single bonds in its structure. Therefore, the transformation from a double bond to a single bond changes the structure of the unsaturated lipid and makes it functionally useless to the body.

What types of disorders are related to free radicals?

With an understanding of the biochemical mechanisms of free radicals, it is easier to see how the progression of this damage could lead to different diseases, depending on which cells and tissues are being attacked. Lipid peroxide activity, for example, may eventually lead to coronary artery disease. And as Diplock points out, in vitro studies also show that the body's free-radical generating systems may damage the structure of DNA. This damage could be a major contributor to cancer development.[15]

At this point, a variety of serious disorders have been linked to free radical pathology. According to Dr. Bland, these conditions include the following: cancer, coronary heart disease, diabetic cataract, alcohol-induced liver damage, adverse drug reactions, immune hypersensitivity, cardiac toxicity to adriamycin (a chemotherapeutic drug), arthritic tissue damage, inflammatory bowel disorders, neurological degeneration and traumatic inflammation.[16]

What's more, the aging process itself may be associated with free radical activity. Dr. Richard Passwater, a prominent researcher, explains the connection as follows: Free radicals impair or destroy healthy cells. Eventually, the cumulative loss of active cells can lead to a loss of the "reserve function" in various organs. In a nut shell, the loss of reserve function and the aging process are one and the same. "The stability of the aging living systems becomes progressively impaired by chemical reactions, not the passage of time," states Passwater. "If we can control the rate of these deleterious reactions, then we can control the advance of physiological aging."[17]

How do free radicals affect the immune system?

There are two sides to the story on the immune system and free radicals. On the one hand, a variety of immune system cells, including neutrophils, monocytes and macrophages, can generate free radicals in the body. According to Dr. Lonsdale, the neutrophils depend on these mechanisms in order to kill bacteria. This is one example of the body's legitimate need for free radicals.[18]

The flip side of this scenario, however, is the adverse effect free radicals can have on the immune response. When free radicals damage cell membranes, for example, the immune system cannot function properly. The reason: Its communication system depends on cell membranes, where the receptors for interleukins, hormones and immunoglobulins are placed. Also, two types of immunoglobulin help the phagocyte cells to "eat" foreign invaders by fixing an invader on the phagocyte's surface. A damaged cell membrane impairs this crucial immune response.[19]

How can we assist the body's defense mechanisms?

The foods we eat are our first line of defense against free radicals because they provide the body with nutritional support. We must obtain an adequate supply of the vitamins that contribute to the body's defenses against oxidant imbalance and the cofactor minerals that fuel our antioxidant enzyme systems. "The quality and quantity of nutrition emerge as the most important factors within human control," says Dr. Lonsdale.

For many people, however, the nutritional failings of the American diet and the onslaught of stressors may produce excess free radical activity and a deficiency in the antioxidants needed to remove them. This negative balance is called free radical pathology. To achieve the proper oxygen balance, which is an integral part of optimal health, the cellular metabolism must be able to neutralize the input of toxic free radicals with the antioxidant enzyme complex. This is no easy task in our modern industrial society, regardless of whether you live in an urban or rural area. We burn gasoline, oil and coal, operate garbage disposal plants and spray our foods with pesticides. All of these affect the quality of our oxygen.

The ability of your cells to produce sufficient quantities of the antioxidant enzymes depends upon your nutritional status, genetics and age. In a healthy young person who is not subjected to stressors, for example, the cells may produce sufficient amounts of enzymes to neutralize the free radicals that are normal byproducts of oxygen metabolism. But when stressors enter the picture - including chemicals, physical trauma, infections, emotional stress and even poor nutrition - free radicals will be produced beyond the normal levels. The body's ability to synthesize antioxidant enzymes also declines as we age. In the process, our natural scavenger activities decrease as well.[20]

In this case, the essential balance is off and the free radical activity overwhelms the body's antioxidant capabilities. To reestablish the proper balance, we must reduce the amount of stressors on the body and assist the natural defense mechanisms by supplying the antioxidants needed to defend the body against this pervasive damage.

Molecular Stress: A New View of Health and Disease

In today's environment, the molecular events in the body are generating much interest because the problems related to "oxygen stress" occur at that level. As a society, we have experienced an increase in allergies and chemical sensitivities of all kinds, in part because the level of oxygen stressors also has increased. The aging process also may be caused in part by oxygen stress. The key to understanding this oxygen battle is to study the molecular level of immune functioning. ➤

➤

Majid Ali, M.D., believes the answers to many questions about the disease process lie in the molecules of our cells. In "Intravenous Nutrient Protocols in Molecular Medicine," Dr. Ali defines human biology as "an ever-changing kaleidoscope of molecular mosaics." He divides these mosaics into two camps: The molecular events that preserve the integrity of cells, tissues and organs also preserve health; the molecular dynamics that injure cells and tissues also cause disease.[21]

Dr. Ali presents an interesting hypothesis: The interaction between oxygen and free radicals not only fuels disease but also plays a key physiological role in the aging process. Indeed, he believes the quality of our "redox reaction," the process by which we neutralize oxidative actions, determines the life span of a species. The redox reaction affects both metabolism and the extent to which tissues are poisoned by oxidants.

For each of us, the oxidant vs. antioxidant status moves along a continuum. Dr. Ali believes degenerative diseases and premature aging essentially result from accelerated "molecular burnout." In essence, that means the redox homeostasis is a battlefield for the war between oxidative stress (free radicals) and the antioxidant potential of the tissues. In this battle, the body is attempting to correct the oxidative poisoning.[22-26]

The ultimate issue is one of injury and repair. The body must defend itself from molecular injury and perform oxidative repair. All of this occurs at the molecular level, as a battle between energy forces. Dr. Ali uses the term "aging oxidative molecules" to describe the molecules that cause or facilitate physiologic changes in the aging and injury process, which is prompted by infectious or environmental agents. On the other side of the battlefield are the "life span molecules," which counter the aging molecules and protect us from molecular injury.

In short, the oxygen forces in the body are engaged in an ongoing struggle. The cells and tissues require oxygen to sustain themselves, but excessive oxygen will cause injury. Oxidation is part of the energy-giving process; the "reductive" actions that counterbalance such injury require the use of energy. If the body starts to lose this battle, disorders such as arthritis and arteriosclerosis may develop. Experimental and patient-related data illustrate this relationship, says Dr. Ali. The heart muscle, for example, has served as a laboratory to explore the concept of oxidative stress versus antioxidant protection.

What are the mechanisms of aging? According to one widely held theory, aging results from the free radical activity that is caused, in part, by the process of oxidation. Another theory maintains that aging is caused by the cross-linkage of proteins, says Dr. Ali. But this theory may not be so distinct from the first, since cross-linking also results from an oxidation injury. Both theories seem to imply that if the oxidative process is not properly controlled, the entire system deteriorates that much faster. Conversely, we can sustain health if the oxidative processes are regulated.

Accelerated oxidative molecular injury creates a chain reaction of negative events. In the earliest stages, these events include enzyme inactivation, cell membrane disturbances, plasma membrane peroxidation and protein cross-linking. Beyond that, at an intermediate level, molecular injury causes toxin-gene-enzyme immune phenomena, including a deficiency of vital minerals, toxicity to heavy metals and autoimmune injury. The late-stage events are the ones we currently understand best - structural injuries at the subcellular, cellular and tissue levels.[27]

To prevent this chain reaction, our first priority must be to preserve the structure and function of cells, which, in turn, helps to preserve the functioning of tissues and organs. But this will require a new approach to medicine, one that focuses on the molecular dynamics that lead to the injuries described here. As Dr. Ali points out, this is no small shift in perspective. Moving from a cellular level to a molecular level will require a breakthrough in medical thinking like the one that occurred in 1858, when a book called *Cellular Pathology* shifted the primary focus of medicine from organs and tissues to cells.

Today, medicine still emphasizes the functioning of cells and tissues, rather than the concept of molecular pathology. With a focus on "molecular medicine," says Dr. Ali, we could develop a better understanding of genetics, the body's molecular defense pathways, the effects of environmental toxins on molecular events, the functioning of enzymes and immune impairment.

When the body is attacked by environmental toxins, for example, it can call on four separate lines of defense to prevent injury, says Dr. Ali. These defenses include:[28]

The first line: the molecular duality of oxygen. In this early stage, the body directly responds to the initial effects of oxidative stress. Remember, oxidation causes molecular injury; reduction causes molecular recovery. Both are a part of the same oxygen system, which must be balanced by the antioxidant mechanisms to prevent damage.

The second line: enzymatic detoxification pathways. These detoxification pathways include sulf-oxidation, carbon oxidation, phosphorylation, conjugation and glucornidation. Dr. Ali offers this example of how they protect the systems: Cysteine oxygenase facilitates the oxidation of cysteine into organic sulfate. When this process of sulphur oxidation is impaired, autoimmune disorders such as cirrhosis, rheumatoid arthritis and systemic lupus may get their start.[29-31]

The third line: TGEI dynamics. Environmental disorders involve complex interrelationships between toxins, genes, enzymes and immunity (TGEI). The important point is that toxins can directly affect DNA molecules. The DNA in our cells is usually tightly packed and difficult to reach. But if it becomes more accessible, the likelihood of injury increases.

The fourth line: our classical immunologic mechanisms. Dr. Ali stresses that the fourth line of defense only comes into play at the "tail end" of a disease. To practice preventive health and medicine, we must focus on the "front end" of the disease process, where the energy and oxidation events take place.

One essential aspect of preventive health is to supply the body with the antioxidants it needs for free radical protection. Dr. Ali says that we must create "a high gradient of nutrients

between the intra- and extra-cellular compartments to deliver 'nutrient boluses' to meet the increased demands of tissues for those nutrients in various disease states (accelerated oxidative molecular damage). The critical issues here are the flushing of tissues with a high gradient of various critical nutrients and the concurrent availability of nutrients in optimal proportions."[32]

The enzymes SOD, catalase and glutathione peroxidase defend against oxidant damage at an intracellular level, while plasma protein and vitamin C provide extracellular protection. The hydrophobic cell membrane compartment also needs fat-soluble nutrients, primarily vitamin E and carotene, for antioxidant defense. In addition, our molecular defenses and cellular health depend upon the integrity of the plasma membrane and the oxidative enzyme systems in the mitochondria of the cell, which protect the electron transfer events. Diseases get their start when the electron transfer defenses do not function properly.

Indeed, Dr. Ali believes the greatest threat to our survival today comes from toxic chemicals, heavy metals and daily oxidative stress on the body systems. These stressors now outrank the infectious agents that plagued us in the late 1800s and focused our attention on the "microbial threat." The health problems of our times – allergies, chronic fatigue, chronic headaches, environmentally induced illnesses, chronic viral infections, hypoglycemia and immune disorders – all share the common denominator of oxidative molecular injury.[33]

Cataracts:
A Model of the Aging Process

There's no denying that aging is a major issue in our society. Who wouldn't want to declare war on the aging process and prevent it from affecting their lives in destructive ways? For that reason, theories about how aging takes place always prove interesting. But much of this scientific work – including the theories on aging discussed here -is as yet unproven. In the coming years, further research may bolster the underlying premises of these and similar theories.

In the meantime, the practical aspects of aging continue to plague us, lowering the quality of life for many people in their later years. Rather than leave this discussion at a general and philosophical level, we want to look at how certain nutrients relate to one specific aspect of aging-the formation of cataracts. This type of vision impairment is an excellent model of the aging process; not only is it an extremely important issue among the aged population, but cataracts are a measurable and well-studied problem.

Here, we summarize the work of Paul F. Jacques and Allen Taylor in "Micronutrients and Age-Related Cataracts," which explores the role various nutrients play in reducing the risk of cataracts and protecting against

➤

TOO MUCH TENNIS? ARTHRITIS ACTING UP?

Have you tried natural Boswellia - many years of clinical research have revealed the potent anti-inflammatory properties of this Allovedic herb.

Don't let the minor aches and pains of exercise, tendinitis, bursitis or arthritis get you down. Try our tablets or our new Boswellia cream which combines Boswellia with natural capsaicin and vitamins. Get back in the swing of things!

AMERICA'S FINEST
800-350-3305

the oxidative processes that contribute to many aspects of the aging process.[34] As Jacques and Taylor point out, senile cataracts are "the leading cause of preventable blindness" in the world." Each year, some 400,000 people develop cataracts; in the United States alone, 20% of people between ages 65 and 75 and 45% of those over 75 suffer from cataracts and vision impairment.

As we age, both structural and biochemical events contribute to the formation of cataracts. The epithelial cells of the lens (which transmits and focuses light rays on the retina of the eye) form fiber cells throughout life. These cells start at the lens equator and travel inward. Eventually, say the authors, the old fibers become more dehydrated and compressed in the center of the lens. The gelatin-like substance of the lens has a refraction index that prevents light from scattering. This substance consists of 65% water and 35% protein. According to Jacques and Taylor, changes in the lens will alter the refraction index, allowing more light to scatter and the lens to become clouded. This opacity is called a cataract.

In studying cataracts, then, one must consider the elements that affect the protein in the lens, such as exposure to light, oxygen, the products of normal aging and environmental factors. These factors can cause protein aggregation and precipitation, both of which are linked to a greater level of water-insoluble protein in old lens or those with cataracts. When cataracts form, the process by which protein becomes insoluble seems to be accelerated, say the authors.

A number of risk factors have been associated with senile cataracts, which make up the majority of lens opacities. Among those factors are ultraviolet radiation and infrared, ionizing and microwave radiation. The risk of senile cataracts also has been correlated with demographic factors such as gender, blood pressure, blood sugar, education, occupation and vital capacity.

Beyond those basic risk factors, there is much research data relating the development of cataracts to reduced levels of certain micronutrients, according to Jacques and Taylor. The lens, for example, needs certain enzymes to help protect it against the effects of oxidation, which has been strongly correlated with cataract formation. In the young lens, the antioxidant defense mechanisms will keep free radicals and photooxidation in check. As we age, however, this activity may fall off and lead to the oxidation of lens proteins.

The lens depends on three enzymes for its protection against oxidation: the glutathione redox cycle (which includes tripeptide glutathione, glutathione peroxidase and glutathione reductase), SOD and catalase. SOD, for example, protects the lens against the highly reactive superoxide radical, while catalase may protect the lens from the less reactive hydrogen peroxide.

Glutathione peroxidase, for its part, eliminates hydroperoxide radicals. While glutathione is oxidized in the process, say the authors, it is restored with the help of glutathione reductase. Glutathione also can perform direct free radical-scavenging work and help to prevent the oxidation of proteins and the formation of disulfide bonds, which also contribute to cataracts.

A number of familiar nutrients help to fuel the glutathione enzyme system. These include vitamin C, vitamin E, vitamin B2 and selenium. Due to the link between cataracts and the process of oxidation, much of the research in this area has centered on these nutrients because they have antioxidant properties. What follows is a brief summary of experimental and epidemiological evidence that correlates the level of these nutrients with the risk of cataracts:

Vitamin C (ascorbate). This nutrient generates attention, say the authors, because the ascorbate concentration in the lens can be 30 times higher than that of plasma. Compared to normal lens, older lens and lens with cataracts have low ascorbate levels. In six animal studies conducted between 1978 and 1986, ascorbate was found to delay the formation of cataracts or protect the lens against various types of damage, including galactose-induced cataracts, glucocorticoid (which reduces glutathione levels), ultraviolet induced protein damage, photooxidative changes to the lens, and light-induced damage to the lens from photochemically produced superoxide.[35]

Beyond that, two epidemiological studies have found an increased risk of cataracts in people with low ascorbate levels. In one of these studies, for example, researcher J. Robertson compared the risk of senile cataracts among people who took regular ascorbate acid supplements (300 - 600 mg. per day) and those who did not. The cataract risk for supplement users was only 30% of that for non-supplement users.[36]

The authors note, however, that a large study in India reported mixed results on the ascorbate/cataract connection. With a given increase in the plasma ascorbate level, there was a 90% jump in the risk of posterior subcapsular and nuclear cataracts. But at the same time, lower levels of an antioxidant index that factored in plasma ascorbate increased the risk of these same cataracts.[37]

Vitamin E (tocopherol). This nutrient, which is the primary fat-soluble antioxidant, prevents photoperoxidation of the lens lipids. As with other parts of the body, the integrity of the cell membranes in the lens must be preserved. Tocopherol seems to stabilize and protect cell membranes. A number of studies also show that this nutrient will retard cataract-like changes to the lens by various cataractogenic agents, including glucose, galactose, sorbitol, ionizing radiation and steroids and other cataractogenic drugs.[38]

In Robertson's study on the relationship between vitamin C status and cataracts, it was also found that people who took an average of 400 IU of vitamin E each day had 40% of the risk of senile cataracts as those who did not take supplements. A study by Jacques, however, did not find any difference in the cataract risk for people with low, moderate or high levels of tocopherol in the plasma.

Vitamin B2 (riboflavin). As a cofactor for glutathione reductase, riboflavin may indirectly affect the antioxidant mechanisms in the lens. According to Jacques and Taylor, research indicates that people who took riboflavin supplements or thyroxine, had higher glutathione reductase activity in the lens epithelia than did people who did not take such

supplements. While the clarity of the lens depends on riboflavin, however, there is no firm link between this nutrient and senile cataracts.[39]

In a 1981 study of people with cataracts, researchers found that 34% of those over the age of 50 had a riboflavin deficiency, compared to none of the study's control subjects. In a later study of malnourished subjects, 81% of those with cataracts (and 12% of controls) were riboflavin deficient.[40,41] According to the authors, these studies and others suggest a link between riboflavin deficiency and senile cataracts. "However, in populations where riboflavin status is adequate, there is no evidence to suggest that riboflavin supplementation can provide any additional protection against cataract," they state.

Selenium. As a cofactor in the glutathione redox cycle selenium may help to protect against injury from the oxidation process. The authors note, however, that an increased risk of experimental cataract has been linked to both a deficiency and an excess of selenium. Meanwhile, the only epidemiological data that links a low selenium level to cataract formation found that the correlation was only marginally significant.[42]

Based on their research, Jacques and Taylor conclude that senile cataracts are a common problem among the aged population, but not an inevitable one. The formation of cataracts appears to stem, in part, from damage to the lens proteins by the process of oxidation. And research shows that antioxidant nutrients can slow down various types of cataract-like injuries. As a result, they say, the existing data establishing a connection between the risk of senile cataract and micronutrient intake provides a foundation for future work in this area.

Please direct correspondence to the *Townsend Letter*.

References

1. Richard A. Passwater, Ph.D., *The Antioxidants: The Nutrients That Guard Us Against Cancer, Heart Disease. Arthritis and Allergies-And Even Slow the Aging Process*, Keats Publishing Inc., New Canaan, Conn., 1985, p. 2.
2. Derrick Lonsdale, M.D., "Free Oxygen Radicals and Disease," *1986/A Year in Nutritional Medicine Monograph*, Keats Publishing Co., New Canaan, Conn., 1986, p. 5-6.
3. William A. Pryor, "Free Radical Biology: Xenobiotics, Cancer, and Aging," *Annals New York Academy of Sciences*, 1992, p. 2-5.
4. Jeffrey Bland, Ph.D., "The Nutritional Effects of Free Radical Pathology," *1986/A Year in Nutritional Medicine Monograph*, Keats Publishing Co., New Canaan, Conn., 1986, p. 1.
5. A. Bendich, "Antioxidant Micronutrients and Immune Responses," *Micronutrients and Immune Functions*, A. Bendich and R.K. Chandra (eds.) Annals New York Academy of Sciences, New York, 1990, p. 168.
6. 0da, T. et. al. as cited in Bendich, p. 169.
7. Anthony T. Diplock, "Antioxidant Nutrients and Disease Prevention," *Am. J. Clin. Nutr.*, 1991, 53:189S-193S.
8. Ibid, p. l90S.
9. P.A. Southorn and G. Powis, "Free Radicals in Nature: Chemical Nature and Biologic Reactions," *Mayo Clin. Proc.*, April 1988, vol. 63, p. 381-389.
10. Bendich, p. 171.
11. Bendich, p. 175
12. Diplock, p. l90S.
13. Passwater, p. 2.
14. Bland, p. 12-13.
15. Diplock, p. l90S.
16. Bland, p. 14.
17. Passwater, p. 19.
18. Lonsdale, p. 5-6.
19. Bendich, p. 170.
20. R. Bradford and H. Allen, Antioxidant Enzymes, Agents and Mechanisms, Robert W. Bradford Research Institute, Chula Vista, Calif.
21. Majid Ali, M.D., "Intravenous Nutrient Protocols in Molecular Medicine," adapted from the forthcoming book, *Nutritional Medicine: Principles and Practice*, Institute of Preventive Medicine, Denville, N.J., 1991.
22. D. Harman and D.E. Eddy, "Free Radical Theory of Aging: Effects of Adding Antioxidants to Maternal Mouse Diet on the Life Span of Their Offspring, Second Experiment," *Age*, 1978, 1:162.
23. J. Tolmasoff, T, Ono and R. Cutler, "Superoxide Dismutase: Correlation With Life Span and Specific Metabolic Rate in Primate Species," *Pro. Nat. Acad. Sci.*, 1980, 77:2777.
24. J. Miquel et al., "Economos AC, Arch Geriatral," *Geriatr.*, 1982, 1:159.
25. R.G. Culter, "Peroxide-Producing of Tissues: Inverse Correlation with Longevity of Mammalian Species," *Pro. Nat. Acad. Sci.*, 1985, 82:4798.
26. C.E. Cross et al., *Intern Med.*, 1987, 107:526.
27. Majid Ali, M.D., "Molecular Basis of Environmental Illness," Syllabus of the AAEM, Denver, Colo., 1991.
28. Ali, p. 17-19.
29. C. Gordon et al., "Abnormal Sulphur Oxidation in Systemic Lupus Erythematosus," 339:25, 1992.
30. P. Olumu et al., "High Incidence of Poor Suphoxidation in Patients with Pirmary Biliary Cirrhosis," *N. Eng. J. Med.*, 318:1089, 1988.
31. P. Emery et al., "D-Penicilline Induced Toxicity in Rheumatoid Arthritis: The Role of Sulphoxidation Status and HLA-DR 3," *J. Rheumatol.*, 11:626, 1984.
32. Ali, Intravenous Nutrient Protocols in Molecular Medicine, p. 27.
33. Ibid, p. 64-65.
34. Paul F. Jacques and Allen Taylor, "Micronutrients and Age Related Cataracts," *Micronutrients in Health and in Disease Prevention*, Marcel Dekker, N.Y., p. 359-379.
35. Ibid, p. 367.
36. J. Robertson, A.P. Donner and J.R. Trevithick, "Vitamin E Intake and Risk of Cataracts in Humans," *Ann. NY Acad. Sci.*, 1989, 570:372-382.
37. M. Mohan et al., "India-US Case-Control Study of Age-Related Cataracts," *Arch. Ophthalmol.*, 1989, 107:670-676.
38. Jacques, p. 368-369.
39. Ibid, p. 370.
40. H.W. Shalka and J.T. Prchal, "Cataracts and Riboflavin Deficiency," *Am. J. Clin. Nutr.*, 1981, 34:861-63.
41. K.S. Bhat, "Nutritional Status of Thiamine, Riboflavin and Pyridoxine in Cataract Patients," *Nutr. Rep. Int.*, 1987, 36:685-92.
42. P.F. Jacques et al., "Nutritional Status in Persons With and Without Senile Cataracts: Blood Vitamin and Mineral Levels," *Am. J. Clin. Nutr.*, 1988, 48:152-158.

◆