PONDERING AGING

Of the 30 theories of aging, the free radical theory may explain why the body ages and diseases occur.

By Charlene DeHaven, MD, FACEP

AS OUR AVERAGE LIFE expectancy increases, researchers ponder various theories of aging. The National Institutes of Health now recognizes up to 30 theories of aging, some more supported by scientific research than others.

Among the more supported is the free radical theory. This theory postulates that accumulated free radical damage and oxidative stress make the body's biochemical and cellular processes do "incorrect" things. Most free radical damage occurs during times of active metabolic turnover, which occurs in early puberty.

At this time, however, we also possess the most physiologic reserve. But as damage accumulates, our physiologic reserve diminishes. Thus, a 20-year-old faced with trauma or biochemical assault can recover faster than an 80-year-old, whose physiologic reserve has been depleted.

Another theory—the neurohumoral theory of aging—says our biochemical processes, especially enzymatic and other hormonal reactions, begin to give incorrect or incomplete messages as we age. This increases over time as damage accumulates. Many experts believe that free radical damage is the cause of this biochemical decline. Thus, this theory may be viewed as a subset of the free radical theory, which is gaining more acceptance in the scientific community.

The Cause of Disease

Diseases begin to develop as increasingly more oxidative stress accumulates in one organ system. When a critical amount of damage occurs, diseases strike, such as diabetes, atherosclerosis, stroke, cancer, etc. These "diseases of aging" typically aren't seen with any frequency in younger people. But, as our average lifespan increased, we began to develop these diseases, all of which are caused by free radical damage.

Inflammation may contribute to the problem. As free radicals damage cells and tissues, the organism attempts to clear away the damaged cells. To do this, the body activates various inflammatory pathways. The body's own cells are sent to the site of damage to "clean up." These cells release various chemicals that cause inflammation. The inflammation further destroys and liquefies the damaged tissue so it may be removed.

However, inflammation is never restricted only to the damaged cells, but spills over to involve surrounding healthy tissue. More research is being published about limiting oxidative stress and inflammation as a way to protect functional tissue.

Sources of Free Radical Damage

By far, most free radical damage comes from the cell's own metabolism. Our cells take the oxygen inspired by the lungs and use it in enzymatic reactions to burn fuel (glucose, fat or protein) and create energy. Each cell uses its energy to perform its own individual function. But nature didn't make us totally efficient in using created energy.

Each cell makes extra energy to ensure that it can perform its function. As energy is created, radicals (very high energy molecules) are created. More are generated than needed. The extra ones "spin off" into the interior of the cell, combining with whatever structure they strike, damaging it. These extra packets of energy are termed "free radicals" because they're not committed to any particular ongoing biochemical reaction. Thus, free radical damage can be thought of as a consequence of living and breathing in an oxygen-rich environment.

The skin, as the body's first environmental defense, is exposed to other sources of free radical damage. Still, the vast majority of each cell's damage comes from its own internal metabolic creation of energy.

The Lifespan Curve

Each species has a "species-specific maximum lifespan," which is the age at which the mitochondria inside the organism's cells shut down and stop producing energy. For humans, the maximum lifespan is 120 years. For some types of parrots, it's about 105 years. For chimpanzees, it's about 45 years and for rats, it's about three.

Interestingly, some species don't really age, such as the Galapagos tortoise and the rockfish. These species don't seem to get older; they simply get bigger. Of course, they have a high rate of death from predation and natural events.

The lifespan/survival curve, above, illustrates these principles. Each species has a species-specific maximum lifespan, or the longest any member of the species can live before its mitochondria shut down, cellular energy production stops and the organism dies.

Curve A is for Neanderthal Man who, on average, lived about 17 years. This was old enough for men and women to reach puberty, mate and produce offspring, thus passing on the genetic material of the species. Infant mortality was very high, as were death rates from predation, accidents and infections.

Curve B depicts the average life span of humans in 1900. Sewers and household plumbing helped increase the average lifespan of humans to 45 at the turn of the 20th century.

Curve C is our present survival curve. Since 1900, we have developed antibiotics. Work has become less hazardous, and other social developments have prolonged life.

Curve D is the "ideal" lifespan curve for man. Here, all members of the species would reach the maximum lifespan of 120 years. To do this, disease would have to be eliminated. Finding cures for all diseases can alternately be described as curing aging or curing the diseases of aging It also probably involves considerable lifestyle modification.

Getting past Curve D and increasing the maximum lifespan involves genetic manipulation.

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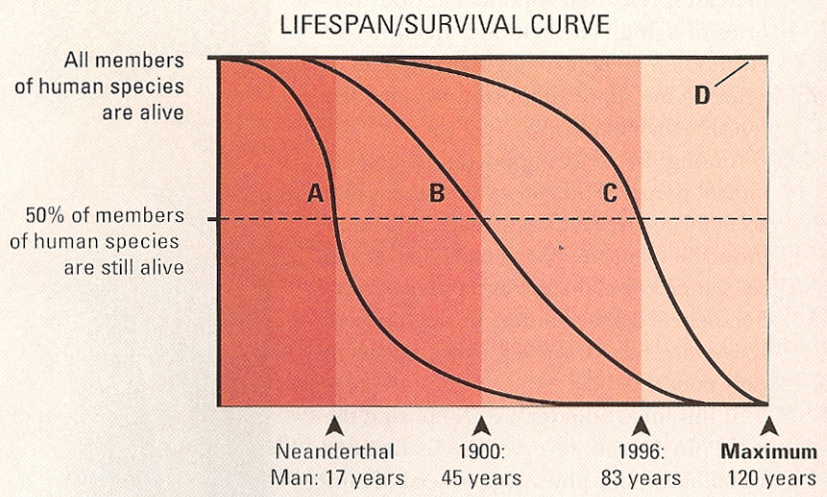

Other sources of free radical damage to the skin include solar damage, ozone, pollutants, applied substances (for example, some sunscreens) and other toxins. Smoking is highly damaging to cells and tissues as well. Every puff of cigarette smoke contains enough free radicals for a "free radical hit" to every cell of the body.

The Importance of Antioxidants

The abbreviated chemical reactions below illustrate the accumulation of free radical damage and oxidative stress. For our first free radical, we'll use the oxygen radical, written with an asterisk, indicating it contains very high energy. The O* is of such high energy that it immediately combines with whatever structure it touches first. In combining with this structure, it damages it and, in the process, creates another free radical. This second free radical, which also possesses very high energy, combines with the first structure it touches. The process continues as shown below.

O* + cell membrane → damaged cell membrane + A* (cell membrane protects integrity of cell)

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A* + mitochondria → damaged mitochondria + B* (mitochondria produces energy for the cell)

B* + DNA → damaged DNA + D* (DNA is the genetic mechanism of the cell that directs all cellular function and reproduces itself to create another cell. Damaged DNA leads to a malignant cell.)

D* + cellular protein/collagen/elastin → damaged elastic tissue (wrinkles) + E*

This process continues forever as cellular structures are damaged by free radicals, and more free radicals are created. However, an antioxidant combines with O* at the beginning of this process, neutralizing this entire cascade and preventing all of the ensuing damage. For this reason, antioxidants are crucial to maintaining cellular function as we age.

Lipid (fat) soluble antioxidants exist, such as vitamin E, which targets the lipid-rich (fat-containing) parts of cells, such as cell membranes. Aqueous or water-soluble antioxidants also exist, such as vitamin C, which protects the water-containing interior liquid portions of cells. Extrinsic antioxidants can be ingested or applied.

Intrinsic antioxidants exist inside the cells as well. These intrinsic antioxidants, which help protect the cells, include superoxide dismutase, glutathione, catalase and peroxidase.

Cell Structure

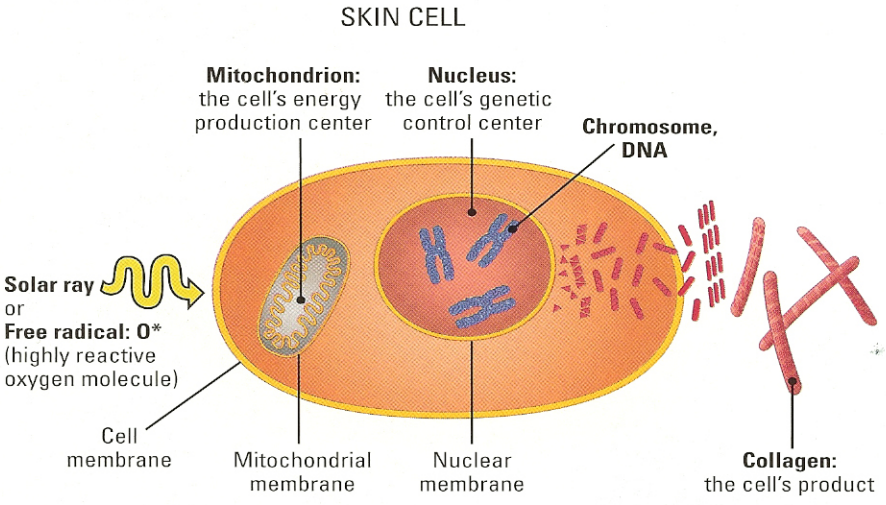
Following are a few additional facts about the structure of the cell as it pertains to oxidative damage and antioxidants:

All membranes are designed to enclose a part of the cell (as mitochondria, nucleus) or the cell itself. Membranes are lipid-soluble (fat-soluble). If they become damaged, they have difficulty protecting their interior structures, as well as letting the right substances in and keeping other substances out of cellular components. Lipid-soluble antioxidants protect these and all other lipid-containing structures. An example of a lipid-soluble antioxidant is vitamin E, although many other lipid-soluble antioxidants exist as well, such as CoQ10 and phosphatidylserine.

The interior of cellular structures, including the interior of the cell itself, contains much water. Therefore, aqueous (water-soluble) antioxidants protect these areas. Vitamin C is an example of an aqueous antioxidant.

The DNA portion of the cell in the chromosomes of the nucleus not only directs the cell's function, but it also directs the reproduction of the cell so that other similar cells can be made. In the case of the above example, making collagen is the cell's function. If the DNA is damaged, it may direct the formation of collagen containing "mistakes." Biochemically inaccurate collagen would be unable to function properly. It might have poor elasticity (causing wrinkles) or it might be unable to bind with other collagen chains, causing wrinkles, loss of resilience, improper scarring, etc.

If the mitochondria are damaged, the cell can't produce energy, which it needs to function. In producing energy, the mitochondria create radicals as energy sources. Nature designed us to make extra energy, and this unused energy creates cellular damage inside the cell's boundaries.



A simple drawing of a skin cell illustrates the location of the cellular components. Any of the body's cells could be used to illustrate these general principles. But a skin cell, which is near the body's surface, is bombarded with additional environmental stressors, which fail to reach other cells deep in the body.

Antioxidant Protection

As soon as any free radical—solar rays, oxygen free radicals, radicals from smoking—touches the cell, the cascade of free radical damage begins. Antioxidants can quench free radicals before they touch the cell. Antioxidant protection should exist at all cellular layers because it's impossible to stop all free radicals at the surface. Many of them get through the initial skin barrier or come from inside the cell itself via cellular metabolism.

Antioxidants can be ingested or applied topically to the skin. Of ingested antioxidants, only about 1 percent reach the surface of the skin. To increase antioxidant protection, we should apply effective topical antioxidants to the skin.

Good antioxidants for the skin must be of high quality, stability, purity and effectiveness. The skin's primary function, simply put, is to keep some substances in and to keep other environmental agents out. This makes designing topical antioxidants particularly challenging. To attain maximum effectiveness, topical antioxidants must penetrate the skin barrier to the interior of the cell and their site of action. Yet it still must maintain its chemical functionality in the cell's interior.

If we want to age gently, we must modulate the progression of oxidative stress and free radical damage. In so doing, we will maintain a greater physiologic reserve into our later years. Simply put, this means living healthy, longer. Maintaining health into our older years benefits all parts of our bodies, including our skin. ■

For a list of resources, go to www.advanceweb.com/healthyaging and click on the references toolbar.

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Disclosure: Dr. DeHaven indicates that she has an ownership position and holds patents with IS Clinical.

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