

This is the second article in a multi-part series on the aging process and its relationship to the mechanisms of oxidative stress, including: genetic endowment, lifestyle and diet.

# Modern Theories of Aging

“Aging is a disease. The human lifespan simply reflects the level of free radical damage that accumulates in cells. When enough damage accumulates, cells can't survive properly anymore and they just simply give up.”

— *Earl Stadtman*  
*National Institutes of Health*

Why do we age? Why do some people seem to age faster than others? Is there a limit to how old we can grow? These questions are pondered by each of us, as we examine our own mortality. They are usually framed in the context of a more fundamental question: what is it that I can do to extend the boundaries of my own existence?

Recent advances in molecular biology and genetics have uncovered some of the answers to these questions. Current research promises to unlock further mysteries of the dynamics that control the natural lifespan of the human organism.

We now know that aging, in large measure, is a consequence of oxidative stress acting on the basic unit of life - the cell. Damage at the molecular level, from the chemical processes of oxidation, cause the machinery of the cell to eventually malfunction. To put it in simplistic terms, our bodies are slowing “rusting” from within.

Managing the aging process, therefore, is a matter of reducing the rate of cumulative oxidative damage to the machinery of the cell. Managing oxidative stress is, in turn, a matter of lifestyle, diet and genetic endowment. To understand how the machinery of the cell operates, how it wears out and breaks down, is to identify the biochemical “trigger” for aging. To understand how the initial damage at the cellular level spreads outward - like ripples in a pond - to affect tissues, organs and, eventually, the organism itself, is to begin to understand the relationship between aging and degenerative disease.

Over the years, scientific researchers have put forth several theories of aging that show a common modality. These modern aging theories generally fall into two camps: structural damage theories and programmed obsolescence theories. Structural damage theories are concerned with the molecular damage that accumulates inside cells over time. Programmed obsolescence theories engage the concept that aging and death are the inevitable consequence of the workings of an internal biological clock, programmed at conception, that decides when cells can no longer operate and reproduce at a rate sufficient to maintain health.

## Structural Damage Theories

Structural damage theories of aging are based on the view that the molecular components of cells, over time, begin to malfunction and break down:

- **Wear and Tear Theory:** Posed by Dr. August Weismann (1882), the theory postulates that the daily grind of life, in particular abuse or overuse, literally wears the body out, leading to disease states. The degeneration of cartilage and eventual grinding of bone on bone is an example of the aging process on body joints, as wear and tear exceed the body's ability to repair.
- **Waste Accumulation Theory:** This theory proposes that, as we age, our cells accumulate waste products as a consequence of normal metabolic processes in the cells. It is believed that this build-up of toxic "sludge" eventually compromises normal cell functions. Lipofuscin pigments or liver spots, common on aging skin, are an example of this waste material. The brownish pigments consist of oxidized (rancid) fats that accumulate in the skin, as well as in the internal organs of our body, as we age.
- **Faulty Reconstruction Theory:** Throughout life the body is constantly re-building and repairing itself. The Faulty Reconstruction Theory argues that, as we age, the repair process begins to produce faulty reconstruction materials that compromise the repair job and weaken the cell - much like renovating a house with poor quality building supplies that diminish its final structure.
- **Immuno-suppression Theory:** It is well known that the thymus gland, or gland of youth, which is located at the base of the throat, declines in size from infancy (250 gm) to adulthood (3 gm) The thymus is known to play a role in the auto-immune system, the body's primary defence against disease. Age-related reduction in the size of the thymus appears to correspond to a reduction in our immune systems, suggesting that the thymus may play a significant role in the aging process;
- **Errors and Repair Theory:** According to this theory, the aging process is, in part, caused by damage to the genetic structure of the DNA, the genetic blueprint of our cells. Geneticist Bruce Ames of the University of California at Berkeley, states that, while the cell can repair over 99 percent of these point mutations, thousands of errors go un-repaired each day, leading to a life-long accumulation of molecular rubbish that, in turn, leads to errors in the manufacture of related proteins and helps accelerate the aging process.
- **Molecular Cross-linkage Theory:** Postulated back in 1942 by Johan Bjorksten, the theory advances the thought that molecular cross-linking between protein molecules, such as the collagen found in our skin, tendons and ligaments and the glycation (cross-linking) of other structural proteins and lipids (fats) with excess glucose, disrupts the functions of these molecules, leading to acceleration of the aging process. Glycation is one of the likely reasons that diabetics, who have chronically high levels of blood sugar (glucose), exhibit accelerated aging.
- **Mitochondrial Damage Theory:** Mitochondria are minute organelles that are the respiratory centres within the cells of our body. Think of them as the "powerhouses of the cell," miniature blast furnaces where the foodstuffs of the cell are converted into useable energy to drive the cell's metabolic machinery. The Mitochondrial Damage Theory postulates that the oxidative processes occurring deep within the mitochondrial membranes eventually damage the organelle, leading to a loss of function. Once mitochondria are lost to the cell, they cannot be replaced, leading to a gradual but inexorable loss of energy and function in cells over time.

These damage-based theories all speculate that the initial damage moves from the molecular level outward to the tissues and organs of the body, eventually taking the form of degenerative diseases such as: heart disease, cancer, diabetes, arthritis, senile dementia, Alzheimer's disease and other life-ending processes.

But, the most widely accepted structural damage theory - and the one theory that encompasses all of the previous theories - is the Free Radical Theory of aging.

## Free Radical Theory of Aging

The Free Radical Theory of Aging was proposed in 1954 by University of Nebraska biochemist and professor emeritus of medicine, Dr. Denham Harman. Like most bold scientific theories, Harmon's ideas were largely ignored - even derided - until several investigations in the late 1960's overwhelmingly validated his brilliant insight.

According to Harmon, aging occurs when cells become permanently damaged from the life-long and unrelenting attack of charged molecular fragments, known as free radicals. The cellular damage inflicted by this uncontrolled oxidative stress inexorably spreads outward to the level of tissues and organs, where it eventually manifests itself as some form of degenerative disease.

Over 80 degenerative diseases are now known to be linked to free radical-induced oxidative stress. According to Harmon, such diseases are not really separate entities, but rather different forms of expression of the aging process, influenced by genetic endowment and environmental factors. An estimated 80 to 90 percent of all degenerative diseases are now believed to involve free radical activity. Which disease wounds you mortally depends much on the roll of the genetic dice, cast upon your conception, as well your individual lifestyle and life-long dietary choices.

Let's investigate free radicals in a little more detail, to find out why these molecular species are so damaging to our cells.

## Free Radicals - the Roguish Bachelors

Free radicals are atoms, molecules and molecular fragments with unpaired electrons. They are powerful oxidizing agents, created by the cell's own metabolic reactions and also present in the environment around us. The free radicals most critical to the aging process include: superoxide ion, hydrogen radical, singlet oxygen, hydrogen peroxide and hypochlorous acid. In general, free radicals are extremely unstable, short-lived and very reactive chemically, inflicting substantial damage and changing the chemical nature of structural molecules within the cell.

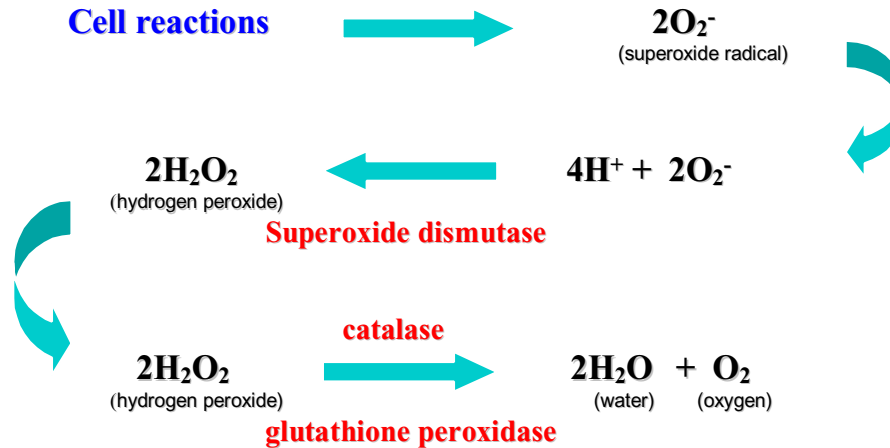
Think of free radicals as roguish bachelors, who steal away with electrons from other molecules and initiate destructive chain reactions that multiply and quickly spread throughout the cell. Free radical agents found in our environment include: industrial wastes, chemical residues, pesticides and herbicides, automobile exhaust, cigarette smoke, sunlight and other forms of ionizing radiation, to name a few. Even certain foods, particularly processed and preserved meats, and beverages, such as coffee and alcohol, are loaded with potent free radical generators.

Free radicals are so reactive they can attach to and damage molecules that usually don't take part in any reactions, such as the DNA in the nucleus of the cell, structural and enzymatic proteins and cell membranes. They disrupt the structure of such molecules, destroy their function and generally create a molecular Hell with in the cell.

# Antioxidant Enzymes

The first line of defence against free radicals consists of three protective enzyme systems within the cell: superoxide dismutase (SOD), catalase and glutathione peroxidase.

These natural defence mechanisms quench free radical damage by stopping the culprits in their tracks and changing them to harmless substances, such as water. Here's an example of how they do their thing.



Under the prodding of the antioxidant enzyme superoxide dismutase, toxic and damaging oxygen free radicals, generated from ongoing cellular reactions, are combined with hydrogen ions to form hydrogen peroxide. To rid itself of hydrogen peroxide, itself a toxic free radical generator, the cell then employs the talents of two more antioxidant enzyme systems, catalase and glutathione peroxidase. Working together, these enzyme proteins cleave the two remaining hydrogen peroxide molecules, to produce harmless water and molecular oxygen.

It is now believed that, when people age, their ability to make these important functional proteins starts to falter. Once cells can no longer make sufficient amounts of these antioxidants, or produce faulty copies that don't work very well (a result of oxidative damage to the genes that contain the molecular code to manufacture these proteins), then free radicals begin to accumulate and oxidative damage, the genesis of the aging process, ensues.

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