What Causes Skin Aging?

by Dr. Diana Howard

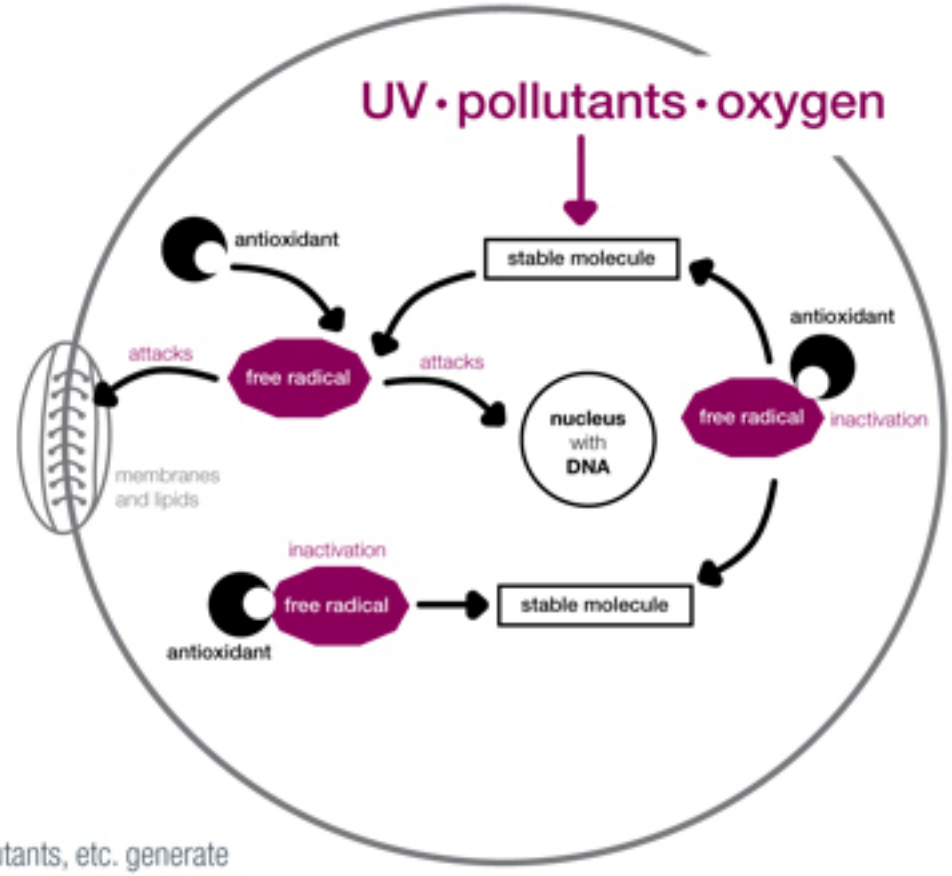
Wrinkles, altered pigmentation, loss of skin tone… we all associate these changes with skin aging. Age-related skin changes are the result of genetically programmed changes (intrinsic factors) and environmental wear-and-tear on the skin (extrinsic factors). While both influence the skin's structure and function, extrinsic factors cause more pronounced changes.

Estimates state that 80-99% of what we see on our skin as adults is the result of exposure to daylight, which is referred to as photoaging. Manifestations of photoaging include an increase in wrinkle formation, a loss of tension and elasticity, degeneration of the vascular supply and skin thickness, hyperpigmentation and other skin discoloration, dilated capillaries (Telangiectasis) and a reduction in the water-binding properties of the skin.

While scientists attribute the majority of these structural changes to exposure to ultraviolet (UV) radiation, it has only been in recent years that they have come to understand the actual biochemical triggers that instigate these changes. These are the chemical reactions that occur within the skin and include:

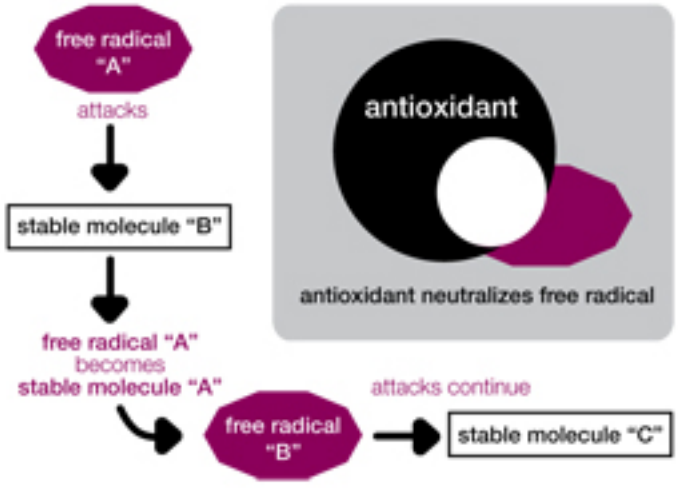
• Generation of Reactive Oxygen Species (ROS), also known as free radicals.
• Activation of Metalloproteinase enzymes (Matrix Metalloproteinase or MMPs) with a subsequent decline in collagen biosynthesis.
• Glycation leading to Advanced Glycation End-products (AGEs).

Let's look at these individually and see how they are interrelated.



1. UV light, oxygen, pollutants, etc. generate Reactive Oxygen Species (ROS), otherwise known as free radicals, from stable molecules. Free radicals attack lipids, membranes and DNA in the nucleus in an attempt to steal an electron to stabilize themselves. When this happens they form new free radical molecules from other stable molecules. The resultant free radical cascade causes damage to the cell which leads to inflammation, cross-linking of collagen and disease.

2. Antioxidants quench free radicals, neutralizing them and returning them to a stable state.



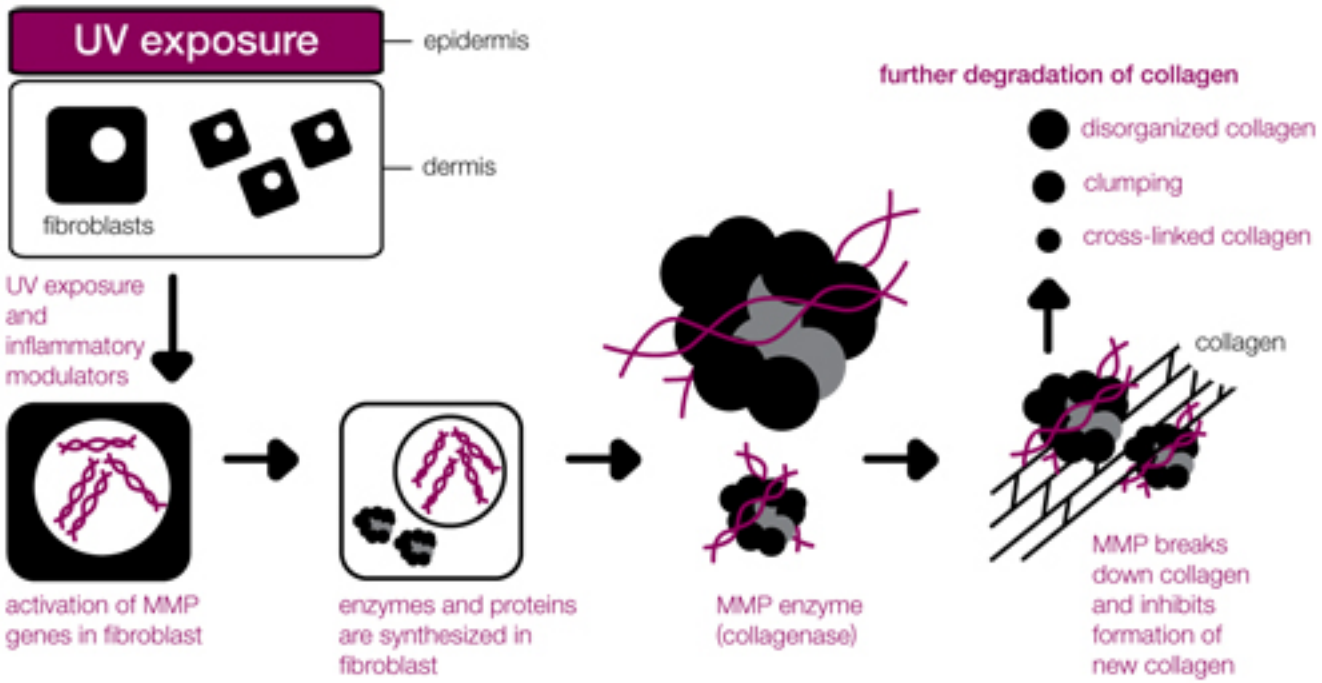
Generation of Reactive Oxygen Species (ROS)

Reactive Oxygen Species (ROS) include oxygen ions, free radicals and peroxides. ROS are generally very small molecules and are highly reactive due to the presence of unpaired electrons. They form as a natural by-product of the normal metabolism of oxygen. During times of environmental stress, ROS levels can increase dramatically, causing significant damage to cell structures. This is known as oxidative stress, which is the major cause of degenerative disorders

including aging and disease. Studies have shown that UV-induced damage to the skin is in part caused by Reactive Oxygen Species. Lipid peroxidation also results from ROS damage to cell membranes, leading to premature aging, skin cancer and cell death.

Activation of Matrix Metalloproteinases (MMPs)

Matrix Metalloproteinases are enzymes that, when activated, control tissue degradation in the dermis. MMPs include collagenase that specifically decomposes particular collagens or other proteins in the extracellular matrix of the dermis. Collagenase is really a group of enzymes that are responsible for breaking down the different types of collagen and elastin. For example, collagenase-1, or MMP-1, acts on collagens I, II, III, VII and X. MMP-1 cleaves the triple helix strand of collagen into smaller fragments that spontaneously denature into gelatinous peptides that are further degraded by other MMPs. This activity makes the MMPs critical for the remodeling of connective tissue, which is an integral part of aging and wound healing.

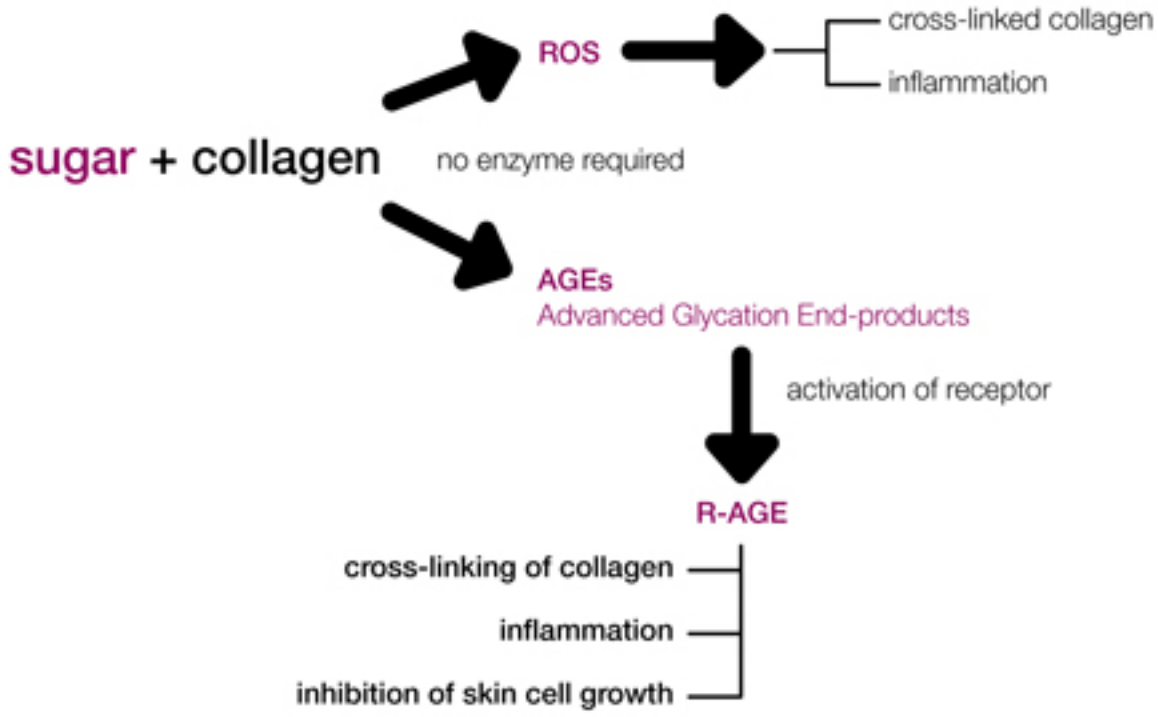


1. MMP enzymes are activated within the fibroblast nucleus by UV light or inflammatory modulators.
2. MMPs, such as collagenase, are synthesized in the fibroblast.
3. MMPs (collagenase) break down collagen and inhibit formation of new collagen.
4. Collagen is degraded into gelatinous peptides that are further degraded by other MMPs. Cross-linking of collagen also occurs, causing wrinkling and stiffening of skin.

Advanced Glycation End-products (AGEs)

How does photoaging lead to cross-linking of collagen and elastin in our skin? Exciting new research has contributed to our understanding of this critical step in aging. We now know that collagen and elastin proteins are highly susceptible to an internal chemical reaction within the body called glycation. This is a non-enzyme mediated reaction that takes place between free amino groups in proteins and a sugar such as glucose. The same glucose that provides energy for our cells can react with proteins (such as collagen), resulting in the formation of Advanced Glycation End-products and Reactive Oxygen Species; these contribute to cross-linking of protein fibers, the loss of elasticity and changes in the dermis associated with the aging process.

When AGEs form in the skin, they activate a receptor site and form a complex known as Receptor-AGE (R-AGE) that signals cellular processes related to inflammation and subsequent disease. Why is this so important? Because we now know that inflammation is the catalyst critical to the aging process and many diseases. For example, diabetics have characteristically high levels of sugar in their blood and suffer from numerous health issues (including cataracts, atherosclerosis, etc.), which emanate from the formation of AGEs in the body. Hence, diabetes is considered a disease of accelerated aging due to the inflammation that arises from the formation of AGEs. This is not restricted to diabetes; muscle weakness, heart disease and many diseases of the brain are associated with glycation. Scientists now believe that reducing glycation is a means of slowing the aging process and disease formation.



1. When sugar comes in contact with a protein (such as collagen), it immediately reacts. This generates Reactive Oxygen Species (ROS – free radicals), which leads to a cross-linking of collagen and inflammation.

2. Advanced Glycation End-products (AGEs) are formed, and bond with a Receptor on the cell to form Receptor-AGE (R-AGEs).

3. This causes inflammation, inhibits skin cell growth and contributes to cross-linking of collagen.

The Biochemical Phenomena

While free radical formation and the activation of Matrix Metalloproteinase enzymes have been

studied quite extensively over the past decade, the formation of Advanced Glycation End-products is now one of the hottest areas of research for understanding not only how the skin ages, but for determining the mechanism of disease formation in the human body. At The International Dermal Institute, we maintain that it is the combination of these three phenomena that are responsible for the aging skin condition. While it may seem like these three biochemical phenomena are isolated occurrences in the skin, it is important to note their connection and the influence they have on each other.