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LEARNING OBJECTIVES

- Summarize the process of inflammaging from the molecular, hormonal level to manifestation as disease.
- Correlate the potential impact of immunosenescence and inflammaging in COVID-19 outcomes.
- Cite the function of exercise and lifestyle in promoting health and well-being.

Inflammation + Aging = Inflammaging?

By Lilith Bailey-Kroll

Aging is an integral part of living and brings with it exponential risk factors for disease. It affects every living organism from yeast to humans. Aging is often described as the progressive accumulation of deleterious changes over time leading to a loss of physiological aptitude and fertility, an increased susceptibility to disease, and ultimately to death. In the last 100 years many humans in some parts of the world have been able to extend their lifespans and as a result are sick longer and coping with multiple chronic diseases simultaneously. Medical research historically has targeted each disease separately, but the emerging field of geroscience has recognized the highly intertwined processes of disease and defined seven factors of aging: (1) decreased adaptation to stress, (2) epigenetic dysregulation, (3) macromolecular damage, (4) derangement of metabolism, (5) loss of proteostasis (protein homeostasis), (6) exhaustion of stem cells, and (7) inflammation.[1]

The question of whether a common biology links cancer, degenerative diseases, and aging has led to the current working hypothesis of "inflammaging." The term, a contraction of *inflammation* and *aging,* was coined by Italian researcher and expert on aging and immunology Claudio Franceschi in 2000. Inflammaging refers to the low-grade, chronic inflammation that characterizes aging. This process may partially explain why some people become much more ill with COVID-19. An understanding of inflammaging can also point yoga therapists toward shaping their work to target the damaging cellular effects of aging.

A Molecular Process

Cellular Aging

The mechanisms of inflammaging appear to begin at the molecular level. It has been proposed that cells have an evolutionary design called *senescence* or *permanent cell cycle arrest.* Simply put: Cells don't die but instead stop dividing. This design has its advantages, as it limits the malignant progression of tumor cells and stops the proliferation of damaged or dysfunctional cells. Senescence allows the cell to respond to damage or stress and contributes to optimal wound healing in normal tissue. Unfortunately, as we age, senescent cells accumulate and secrete numerous proinflammatory cytokines, which drives aging and age-associated pathologies.[2]

Among the best-studied inflammatory mediators of inflammaging are interleukin-6 (IL-6), interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP).[3] Specifically, IL-6 is a common marker across age-related pathologies that have strong chronic inflammatory components.[4] Secretion of these cytokines (small cell-signaling proteins) is important because they change the neighboring tissue microenvironment and alter the function of nearby cells, creating an optimal environment for tumorigenesis (tumor formation) and chronic inflammatory diseases.[5,6] A longitudinal study on a cohort of 1,018 elderly Italian people demonstrated that higher circulating levels of inflammatory mediators were associated with the occurrence of a higher number of chronic conditions, including hypertension, diabetes, ischemic heart disease, congestive heart failure, stroke, chronic obstructive pulmonary disease, cancer, Parkinson's disease, hip fracture, lower-extremity joint disease, anemia, kidney disease, peripheral artery disease, and cognitive impairment.[7]

Immune System Effects

Additionally, as we age, a gradual deterioration of the immune system results in a reduced ability to fight new infections, diminished vaccine immunity, and reduced tumor clearance.[8] *Immunosenescence,* the aging of immune cells, refers to structural changes and decreased function in these particular cells. Immunosenescence is thought to be the other side of inflammaging[9] and is a consequence of the progressive atrophy of the thymus gland. This lymphoid organ of the immune system is located behind the sternum and in front of the heart and facilitates the maturation of protective T cells. (The T stands for thymus-derived.) As we age, the thymus declines in its capacity to eliminate self-reactive T cells and to produce naïve (considered immature) T cells; this reduces the diversity of the T cells that assist in defense against various invaders and disrupts the cells' homeostasis.[10] As a result, the aging thymus becomes less capable of protecting our bodies.

Nearly two decades after the inflammaging theory was put forward, Franceschi added "garb-aging" to the theory of aging. Garb-aging links chronic stress, the microbiota-gut-brain axis, and an

increased inflammatory state into a unified body-brain-mind framework that can be used to understand aging and age-related diseases.[11] In short, our aging cells stop replicating, have impaired ability to clean up debris and damage (garbage), stop going through apoptosis (cell death), and start secreting proinflammatory markers. At the same time, our immune system becomes weaker at warding off harmful bacteria, viruses, and cancer.

How COVID-19 Fits into the Picture

Immunosenescence and inflammaging could be predisposing conditions that allow COVID-19 to escape the body's immune surveillance and lead to the more serious COVID-19-related conditions.[12] Severe COVID-19 disproportionally affects those with inflammaging—older people with multiple comorbidities, including hypertension, diabetes, and obesity—as well as children with severe multisystem inflammatory syndrome.[13] An increase of IL-6 levels predicts adverse outcomes of COVID-19, underscoring inflammaging as an ally of SARS-CoV-2 (the coronavirus that causes COVID-19). In both mild and severe cases of COVID-19, increased levels of IL-6 are typical, whereas asymptomatic patients do not demonstrate this increase.[14]

Setting the Stage for Health

How, then, can yoga therapists use this scientific knowledge to help clients age well?

The research points to the overarching goals of lowering the levels of proinflammatory compounds and promoting an ideal homeostatic equilibrium between proinflammatory and anti-inflammatory responses.[15] Unsurprisingly, findings support a balanced approach of lifestyle and dietary modifications combined with exercise. The following two-pronged strategy suggests some approaches to help create meaningful anti-aging practices.

Exercise

As yoga therapists, we deeply understand and work with the multidimensional aspects of yoga. On a rudimentary level, when we practice yoga asana we contract muscles, which leads to the release of IL-6. When IL-6 is released from muscle fibers during muscle contraction it behaves very differently: Instead of provoking an inflammatory response, it acts as an anti-inflammatory. When released from a muscle, IL-6 is considered a *myokine* (a muscle-derived cytokine) and acts peripherally in several organs in a hormone-like fashion.[16] Acute physical exercise induces release of IL-6 in skeletal muscles, which in turn triggers the repair of muscle fibers and the production of anti-inflammatory cytokines such as IL-10 while inhibiting the proinflammatory cytokine TNF-α.[17] This paradigm illuminates on the molecular level how muscles communicate with organs and cells to downregulate inflammation.

Lifestyle

Metaflammation refers to chronic global low levels of inflammation most often caused by diet. It is well-established in scientific literature that high nutrient intake and obesity are linked to chronic inflammation and involve different tissue and organs, in particular adipose tissue.[18] Adipocytes are large fat cells that require more oxygen and are less vascularized, making them susceptible to cell death.[19] When they die, the body treats them as it would a wound, and the cells release proinflammatory cytokines, debris (remember garb-aging?), and excess fatty acids, thus fueling the inflammatory cascade.[18] (See my previous *YTT* article for a more in depth explanation of inflammatory cascades.[20]) Recent studies indicate that high-fat diets induce a dramatic increase of senescent cells in visceral tissue; that alone triggers both metaflammation and inflammaging.[11]

Although dietary consultation is outside the scope of practice for yoga therapists without additional education in the topic, it is

important to note the current scientific findings. Numerous studies in humans have demonstrated that calorie restriction (CR)—without malnutrition—exerts widespread effects on physiological, hematological, hormonal, biochemical, and inflammatory parameters.[21–23] There is scientific consensus that CR promotes the downregulation of insulin, insulin-like signaling, and glucose signaling, all of which have implications for type 2 diabetes (an inflammation-related condition). The effects of CR on aging are not simply the result of the reduced amount of calories consumed—these benefits are also determined by diet composition and can be achieved without a complete lack of food intake.

A Boon for Yoga Therapy

By understanding the basic science of aging and inflammation we can better promote clients' health and well-being. As part of the wellness economy, our profession is charged with supporting clients in navigating its options. According to 2018 figures from the Global Wellness Institute (globalwellnessinstitute.org), the wellness economy is valued at $4.5 trillion. And wellness expenditures represent more than half of total global health expenditures ($7.8 trillion, based on WHO data). There is ample space for our services here.

Yoga therapists can use information like that presented in this article to create marketing materials and structured practices that reduce the damaging cellular effects of aging and increase quality of life for clients. If you are new to the biological concept of inflammation, I recommend reading my previous *Yoga Therapy Today* article as a primer.[20] For more information or to discuss this in greater depth, I encourage you to reach out to me. YTT

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Additional Resources

The research cited in this article regarding muscle contraction and IL-6 originates from the Danish National Research Centre of Inflammation and Metabolism. For more information, visit https://inflammation-metabolism.dk/

Valter Longo's research on calorie restriction and intermittent fasting (https://valterlongo.com/) provides a pivotal understanding of how to decrease the biomarkers associated with inflammaging and cellular death. An additional resource to help you learn more about epidemiological studies and basic scientific research organized around specific types of foods is www.eattobeat.org

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