

## *Age-related biological and physical decline*

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Aging is a complex process. Over years of living, accumulative, multiple impairments present across different organs as components of age-related biological and physical decline. Age is the main risk factor for cardiovascular disease<sup>(5)</sup>, neurodegenerative diseases<sup>(17)</sup>, decline in muscle mass, strength, and function<sup>(7)</sup>, and biological senescence characterized by chronic inflammation<sup>(8)</sup>. Results of the aging process are characterized by decreased physiological reserves and an increase in vulnerability to corporeal stressors. The biological decline that accompanies aging attenuates physical wellbeing. Age-related changes involve cell integrity, muscle mass, bone density, brain integrity, and gradual loss of vascular homeostasis<sup>(2)</sup>.

Structural and functional changes presage aging. Structural changes occur in many body systems. Aging bones increase in porosity, become less dense, weaker and easier to break in an accidental fall. Apoptosis (programed cell death) which is the aging and death of osteocyte bone cells impedes tissue maintenance and repair<sup>(13)</sup>. Changes in the vertebra include a decline in fluid cushions between the disks causing compression and shortening. Aging cartilage thins from years of wear and tear. Ligaments which bind joints, and tendons which bind muscle to bone, loose elasticity. This makes the joints stiff and tight. The older body is less flexible, more prone to injury, and once injured, heals more slowly.

Aging conveys a decline in physical performance as body mass and strength diminish. However it does not have to interfere with activities of daily living or participation in vigorous sporting exercises. Muscle loss is usually not severe unless influenced by illness or sedentary lifestyle. Major loss of muscle mass can lead to frailty, affect balance, gait, and overall performance, decreasing well-being. Sarcopenia is the progressive, degenerative loss of skeletal muscle tissue. The quantitative/qualitative bi-directional nature of sarcopenia is characterized by losses of muscle mass, strength/power, and physical performance<sup>(16)</sup>.

Changes occur in body systems, organs, and cells. The aging human immune system functions as an accelerator for other age-related pathologies<sup>(19)</sup>. Aging is the primary risk factor for many common chronic syndromes which can cascade into

concurrent and confounding illness and disabilities. The accumulation of senescent cells with advancing age negatively affects tissue structure and function, ultimately leading to tissue pathology<sup>(11)</sup>. Physiological changes associated with aging involve mutations in genetic material, and a variety of cellular senescence<sup>(11)</sup>, and apoptosis<sup>(14)</sup>. Aging manifests increased arterial stiffness and decreased telomere length<sup>(9)</sup>. When the artery walls thicken you experience a loss in elasticity and resulting arterial stiffness. The immune system also undergoes dramatic aging-related changes. By continuously progressing to a state of ‘immunosenescence’, the aging immune system loses its ability to support appropriate wound healing and protect against infections<sup>(19)</sup>.

As the body ages, so does the brain. Aging brings about an increased incidence of cerebrovascular dysfunction and microcirculatory damage seen in the pathogenesis of many types of elderly dementia<sup>(15)</sup>. Buchman, et al (2014) notes the association between physical frailty, cognition, aging and brain pathology. Primarily consisting of myelinated axons, white matter with its extended fibers connect the various gray matter centers of the brain and spinal cord to form communication networks, quickly relaying messages from one section to another. Cognition occurs in the gray matter of the brain which is made up of neuron cell bodies, dendrites, and unmyelinated axons. Neuroimaging research reveals that even in the absence of specific neurological disease, incoherent white-matter increases with age<sup>(3)</sup>. Brain pathology contributes to the simultaneous change in physical frailty and cognition in old age, which may be partly due to a shared common pathologic basis<sup>(6)</sup>. The amalgamation of dysregulated cellular signaling pathways, shortened essential telomeres on chromosomes and destructive oxidative stress induces cellular senescence.

With aging, there is a thickening of the arterial walls in vascular structures. Arterial stiffness increases with age even in healthy adults<sup>(9, 12)</sup>. The risk of developing acute and chronic cardiovascular diseases increases with age. Cardiovascular aging is evidenced by the increasing prevalence of vessel wall thickening and reduction of nitric oxide<sup>(2)</sup>. Vascular stiffness and occurrence of hypertension occur more frequently in the elderly population<sup>(10)</sup>. Most vascular changes are related to age and cardio-unhealthy lifestyles that become accelerated in the presence of related cardiovascular risk factors<sup>(9)</sup> such as high blood pressure, diabetes, smoking, lack of exercise, and an unhealthy diet.

Age-related changes occur throughout the body and in virtually all organ systems. Age-related molecular changes are associated with cell autophagy, mitochondrial decline, apoptosis, senescent cell development, and necroptosis (18). Aging brings on the increased need for the body to eliminate dysfunctional cellular components. Autophagy mediates the accumulation of cells damaged by oxidative stress. “Failure to eliminate dysfunctional mitochondria by autophagy could lead to further accumulation of oxidative damage and induction of cellular apoptosis” (14). The problem is that aging portends inefficient autophagy. Reduced efficiency in cellular autophagy means less robust healthy cells in the body.

Most cells can only divide a limited number of times before dying. As endcap structures on chromosomes, telomeres are made of up repetitive DNA sequences, preventing degradation and maintaining genomic integrity<sup>(1)</sup>. However over time, cellular senescence decreased cellular metabolic activity, mitochondrial dysfunction and another host of factors result in shortened telomeres and telomere dysfunction. Every time a cell divides, the telomeres shorten, eventually becoming so short that the cell can no longer divide<sup>(4)</sup>. Death is inevitable.

Aging is a consequence of gradual life-long accumulation of molecular and cellular damage. Attendant to cellular changes associated with aging are interrelated extracellular, molecular alterations. Extracellular changes are those which occur outside the cells. For example, the extracellular fluid moving between the cells, providing structural and biochemical support, are essential to physical scaffolding. Degradation and loss of interstitial material contributes to physical decline.

In spite of all this negativity, there is a positive association between physical activity and having better or improved vascular structure and function, strong bones, and a healthy brain. Do not adopt a sedentary lifestyle. But if you are currently a couch potato, don't lose hope or give up. Get up and get out. Exercise is key to good health along with an omega-3 rich—calorie restricted diet for improving your quality of the life no matter what your age or current health status.

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