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AGING OF THE BODY. THE MAIN LAWS AND MECHANISMS

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Aging is a universal, progressive, and multifactorial phenomenon in which the ability to resist, repair, and respond to disease systematically decreases over time.

The underlying mechanisms centre on a framework of closely intertwined hallmarks, including genomic instability, telomere shortening, epigenetic change, proteostatic failure, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication.

These mechanisms can be understood as an expression of pathological reactivity, wherein normal benign functions such as senescence, inflammation, or metabolism gradually turn against the organism, culminating in the syndrome of inflamm-aging and multimorbidity.

Cellular senescence initially serves as a protective mechanism that halts division in response to stress, thereby preventing malignant transformation. However, with advancing age, senescent cells accumulate in tissues and adopt a senescence-associated secretory phenotype, releasing cytokines, chemokines, and proteases that disrupt the surrounding microenvironment.

This chronic secretory activity shifts senescence from a tumour-suppressive safeguard into a driver of systemic decline, fuelling persistent low-grade inflammation and tissue damage.

Mitochondrial dysfunction plays a central role as well, with deteriorating mitochondria producing less ATP and more reactive oxygen species. The resulting oxidative damage affects DNA, proteins, and lipids, while impaired energy metabolism weakens cellular resilience and accelerates apoptosis and metabolic disorders.

Loss of proteostasis further contributes by impairing chaperone function, the proteasome, and autophagy pathways, allowing misfolded and aggregated proteins to accumulate. This accumulation is a defining feature of neurodegenerative diseases such as Alzheimer’s and Parkinson’s and directly contributes to cognitive decline and systemic frailty.

Stem cell exhaustion reduces regenerative capacity across multiple tissues, leading to anaemia, impaired immune responses, osteoporosis, and skeletal fragility. Altered intercellular communication, including dysregulated endocrine signalling and chronic immune activation, reshapes the internal environment and amplifies age-related deterioration.

Inflamm-aging – the persistent, low-grade inflammatory state that develops with age – exemplifies maladaptive immune reactivity. Unlike acute inflammation, which resolves after injury, this chronic baseline activation erodes tissue homeostasis and accelerates atherosclerosis, neurodegeneration, and cancer.

The exposome, or the totality of environmental exposures across the lifespan, interacts with genetic predispositions to influence aging trajectories. Air pollution, diet, psychosocial stress, and climatic conditions can accelerate molecular damage, alter DNA methylation patterns, and exacerbate hallmarks such as mitochondrial dysfunction and epigenetic drift. Epigenetic clocks based on these methylation patterns now provide measurable indices of biological age.

Recent theoretical frameworks, including the Protein-Homeostasis-System hypothesis, the inflamm-aging model, and the mitochondrial-ROS hypothesis, view aging as a consequence of impaired quality control and chronic inflammatory reactivity. These hypotheses integrate molecular damage, immune activation, and epigenetic regulation, positioning aging as a dynamic pathological process that bridges basic biology and clinical medicine.