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Global Journal of
Medical and Clinical Case Reports
OPEN ACCESS JOURNAL

ISSN: 2455-5282 Journal DOI: https://dx.doi.org/10.17352/gjmccr

Mini Review

The Evolution of Aging: Implications for Human Health and Geriatric Research

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Submitted : 27 April, 2026
Accepted : 29 April, 2026
Published : 30 April, 2026

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Keywords: Senescence; lifespan; Accumulation; Extrinsic mortality; Fitness; Negative senescence; Mutation accumulation; Antagonistic pleiotropy; Geriatric relevance; Gene editing; Telomerase

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Abstract

Aging, or senescence, is not a uniform phenomenon among living organisms. Some organisms experience progressive physiological decline while others show negligible or negative senescence. This review examines diverse aging patterns across taxa, focusing on evolutionary mechanisms such as antagonistic pleiotropy and mutation accumulation. We argue that extrinsic mortality rates shape the force of natural selection across all ages, resulting in different evolutionary trajectories of senescence. Importantly, this review highlights the relevance of these evolutionary theories to human geriatric research, including potential therapeutic interventions.

Introduction

Aging refers to the progressive decline of physiological functions over time [1]. Although aging is common across many species, it is not universal [2]; some organisms show little or no physiological deterioration with age, while others, including humans, experience significant decline in fitness—an individual's ability to survive and reproduce. Extrinsic mortality, caused by environmental factors such as accidents and diseases, reduces the likelihood of surviving to old age [3]. However, some species exhibit negative senescence, where fertility or mortality improves with age [4]. This variation raises key questions: Why do some species age while others do not? Why do mammals, particularly humans, experience progressive health decline? And if natural selection improves survival and reproduction, why does aging evolve at all? This review focuses on translating evolutionary theories of aging into human geriatric contexts.

History of the concept of Aging

In 1891, August Weismann proposed that aging eliminates worn-out members from a population [5]. Later, Fisher and Haldane argued that aging arises because natural selection has a weaker impact on survival and reproduction at old age [6,7]. Hamilton, Medawar, Rose, and Williams extended these ideas, emphasizing that extrinsic mortality weakens selection against late-acting deleterious mutations [8,9]. By the mid-20th century, evolutionary biologists formulated a theory of aging based on population genetics: the force of natural selection declines with age, allowing deleterious mutations that manifest later in life to accumulate. Thus, aging is not an adaptive benefit to species but a non-adaptive consequence of declining selection efficacy with age [10,11].

Is the Concept of Aging Universal?

Patterns of aging differ across species. Some show clear senescence, others negligible senescence (little or no decline of fitness), and a few exhibit negative senescence (improved performance with age) [12,13]. For example, *Hydra* displays negligible senescence under laboratory conditions [3]. About 95% of angiosperms show no clear signs of aging, and many trees live on for centuries [14]. Aging tends to evolve in species

Citation: Yeboah R, Appiah P. The Evolution of Aging: Implications for Human Health and Geriatric Research. Glob J Medical Clin Case Rep. 2026:13(4):47-51. Available from: https://dx.doi.org/10.17352/gjmccr.000245

with a clear germline-soma distinction and age structure [12,15]. Thus, aging is not a universal phenomenon.

Mechanisms of Aging

The evolutionary theory of aging is founded on three fundamental mechanisms: mutation accumulation, antagonistic pleiotropy, and the disposable soma theory [11,16].

Mutation accumulation

Proposed by Medawar (1952), this mechanism argues that rare, deleterious mutations accumulate at higher frequencies because natural selection weakens with age [8]. Senescence results from a build-up of older tissues that are not removed by selection, leading to age-related conditions such as inflammation and cancer [8]. Medawar went on to define aging, or senescence, as a change in the faculties and senses of the body, which render the individual more likely to die from extrinsic or accidental incidences [8]. According to him, the most unfavorable hereditary conditions are withheld or postponed until a later time in life (old age), with most conditions delaying their manifestations until later in life when clinical symptoms begin to show up [8]. Because hereditary factors express themselves at a particular age, natural selection tends to act in a way to postpone the expression of these unfavorable conditions to a later period in life [12].

Antagonistic pleiotropy

Williams came up with the mechanism of antagonistic pleiotropy [17], which is when a single gene has multiple effects, enhancing fitness early in life but reducing it later [18]. Such alleles are favored because early benefits outweigh late costs [18]. For example, cellular senescence aids the healing of wounds early in life but later contributes to pro-inflammatory cells [17,19]. In humans, this mechanism helps explain why genes that promote reproductive fitness may also predispose individuals to age-related diseases such as cancer or neurodegeneration.

The disposable soma theory

The disposable soma theory, proposed by Thomas Kirkwood, suggested that organisms encounter a trade-off in allocating limited metabolic resources between reproduction and somatic maintenance [20]. It predicts a decrease in investments in somatic maintenance after reproductive events and explains a gradual decline in physiological functions over time [20]. Because extrinsic mortality ensures that no individual lives indefinitely, natural selection tends to invest resources into early reproduction rather than costly, long-term somatic repair. Consequently, somatic tissues accumulate damage over time, leading to aging. This theory complements mutation accumulation and antagonistic pleiotropy by explaining why maintenance is evolutionarily limited [Table 1].

Table 1: Summary of Evolutionary Mechanisms of Aging.

Mechanism	Key proponent	Core idea	Human Geriatric Relevance
Mutation Accumulation	Medawar (1952)	Accumulation of late-acting deleterious mutations	Explains late-onset genetic diseases (e.g., Huntington's)
Antagonistic Pleiotropy	Williams (1957)	Early benefits, late costs	Genes for inflammation may protect against infection in youth but drive diseases like arthritis in old age.
Disposable Soma	Kirkwood (1977)	Trade-off between reproduction and repair	Caloric restriction mimics resource allocation to repair

Empirical validation: Cross-Species and CRISPR Evidence

Recent comparative studies across species have quantified the relationship between extrinsic mortality and senescence. Species with higher extrinsic mortality (e.g., small fish, rodents) exhibit rapid senescence with mortality rates exceeding 50%, while low-extrinsic-mortality species (e.g. elephants) exhibit slower aging [21,22]. Bats provide a particularly striking case: despite their small body size, many bat species have very low extrinsic mortality due to flight and nocturnal habits, and they exhibit exceptional longevity—some live up to 40 years with minimal age-related decline. Comparative genomics has revealed that long-lived bats have evolved enhanced DNA repair pathways and reduced inflammatory signaling, consistent with the disposable soma theory's prediction that reduced extrinsic mortality favors investment in somatic maintenance [22].

While comparative studies reveal correlations, CRISPR-Cas9 gene editing has enabled direct, causal tests of genes known to mediate trade-offs between early fitness and late-life decline. CRISPR-Cas9 gene-editing experiments in model organisms have also tested causal roles of aging-related genes. For example, CRISPR-mediated knockdown of IGF-1R in mice extends lifespan, supporting antagonistic pleiotropy [18]. These experiments provide the strongest empirical support for antagonistic pleiotropy and mutation accumulation and present stronger causal evidence than observational studies alone [Table 2].

Does aging always come with deterioration?

Although aging is mostly associated with the deterioration of physiological functions, laboratory environments can alter their expression. Dietary restrictions (reducing food intake without malnutrition) rather extend the lifespan of laboratory animals and delay age-related diseases in many vertebrates and invertebrates [1,23]. In rhesus monkeys, caloric restrictions reduce insulin and triglyceride levels, limiting diabetes and cardiovascular diseases [23]. However, it is important to note that protein restriction, rather than overall caloric reduction, may drive many benefits in rodents and primates [24]. Translation to humans remains uncertain; current evidence does not justify recommending protein restriction for longevity without further research.

Trade-offs with life

Trade-offs between reproduction and longevity are common; bats that produce more offspring have a shorter lifespan than those that produce fewer offspring [25]. Social

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insects like termites and bees also show unusual aging patterns: queens living longer than workers, despite their high fertility [26], likely due to protection from extrinsic mortality and social structures, rather than from an absence of aging.

Human lifespan extension: Possibilities and interdisciplinary perspectives

Ongoing research aims to extend human lifespan by studying slow-aging species. Naked mole rats exhibit negligible senescence and cancer resistance [13]. Planarian flatworms possess pluripotent stem cells capable of regenerating aged tissues [27]. Although no species is truly immortal, these models reveal mechanisms that slow aging. In humans, clinical interventions include the use of metformin (originally for diabetes), which improves cognitive function and slows brain aging in male monkeys [28,29]. Senotherapy, which targets senescent cells, has also proven its efficiency, improving conditions like osteoporosis and reducing chronic inflammation [2,4].

Recent discoveries in molecular biology have provided unprecedented insight into the cellular mechanisms that govern aging, with telomerase regulation emerging as a central player [5]. Telomeres—protective DNA repeats at chromosome ends—shorten with each cell division due to the end-replication problem. When telomeres become critically short, cells enter senescence or apoptosis, contributing to tissue dysfunction, inflammation, and age-related disease [22]. Telomerase, the enzyme that elongates telomeres, is tightly regulated in somatic cells but active in germ cells, stem cells, and many cancers. Ecologically, species with lower extrinsic mortality (e.g., birds, bats) tend to have longer telomeres and higher telomerase activity, supporting an evolutionary link between environment and molecular aging mechanisms [5,30-35] [Table 3].

Future directions: Translational implications and gene editing

The translational implications of evolutionary aging theories are vast. Gene-editing technologies such as CRISPR-Cas9 offer potential therapeutic strategies to delay human aging. For example, editing pro-aging genes (e.g., PCSK9) for cardiovascular health, or targeting senescent cells via CRISPR-based knockout of BCL-2 family members) is being explored in preclinical models. However, ethical considerations and off-target effects remain barriers. Future research should therefore prioritize:

- Large-scale human cohort studies linking evolutionary predictions to clinical outcomes
- CRISPR-based screens to identify geroprotective gene variants
- Clinical trials of senolytics and metformin in diverse populations

Moreover, interdisciplinary integration of molecular biology, ecology, and clinical gerontology will be quite essential to translating evolutionary theories into safe and effective human therapies.

Table 2: Cross-Species Evidence Linking Extrinsic Mortality to Senescence.

Species / Group	Extrinsic Mortality Rate	Senescence Pattern	Lifespan (max, years)	Support for Theory
Wild mice	Very high (>70%/yr)	Rapid senescence	1–2	Mutation accumulation
Bats (e.g., *Myotis*)	Very low (<10%/yr)	Negligible senescence	30–40	Disposable soma
Naked mole rat	Very low (protected burrows)	Negligible senescence	30+	Multiple mechanisms
Birds (general)	Moderate (flight reduces predation)	Slower aging than similar-sized mammals	10–20	Reduced extrinsic mortality

Table 3: Comparing Aging Patterns Across Species.

Species	Aging Pattern	Key Mechanism	Human Relevance
Hydra	Negligible senescence	High regenerative capacity	Insights into stem cell maintenance
Naked mole rat	Negligible senescence, cancer resistance	High DNA repair, low oxidative stress	Cancer prevention strategies
Planarian flatworm	Regeneration-based rejuvenation	Pluripotent stem cells	Regenerative medicine
Humans	Progressive senescence	Telomere shortening, cellular senescence	Direct therapeutic targets

Conclusion

The evolution of aging is a complex subject in evolutionary biology and varies across different taxa. Natural selection acts more strongly on early-life traits, leading to fitness decline with age in humans. Rather than viewing aging as inevitable, research should focus on ecological and genetic factors that shape aging patterns. Clinical interventions are promising but may present side effects; their benefits must outweigh risks. Nevertheless, extrinsic factors (accidents, infections) remain difficult to control and cut lives short before old age. A pragmatic goal is to reduce age-related disease burden and extend health span.

Author contributions

The author conceptualized the study, conducted the literature review, drafted the manuscript, and contributed to data interpretation and manuscript revision. Philip Appiah contributed to the scientific review, critical revision of the manuscript, interpretation of evolutionary and geriatric concepts, and final approval of the submitted version. Both authors read and approved the final manuscript.

Acknowledgements

I would like to thank Dr. Peer for reviewing this paper.

Funding Statement

The authors received no specific financial support, grant, or funding from any public, commercial, or non-profit funding agency for the preparation, research, authorship, or publication of this manuscript.

Citation: Yeboah R, Appiah P. The Evolution of Aging: Implications for Human Health and Geriatric Research. Glob J Medical Clin Case Rep. 2026:13(4):47-51. Available from: https://dx.doi.org/10.17352/gjmccr.000245

Conflict of interest statement

The authors declare that there are no conflicts of interest regarding the publication of this manuscript. The authors have no financial, personal, institutional, or commercial relationships that could influence the work reported in this study.

Ethical considerations

This manuscript is a narrative review based exclusively on previously published literature and publicly available scientific sources. No human participants, animals, clinical samples, or confidential patient data were directly involved in this study. Therefore, ethical approval and informed consent were not required. The authors have ensured that all referenced studies were appropriately cited and discussed in accordance with academic and ethical publishing standards.

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