INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

A Review Article on Aging and Age-Related Disorders

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ARTICLE INFO

Published: 6 Nov 2026
Keywords:
Aging, age-related disorders, gerontology, senescence, oxidative stress, inflammation, healthy aging, geroscience, biological activity, mitochondrial dysfunction, cellular senescence, neurodegenerative diseases
DOI:
<DOI>

ABSTRACT

Aging is a complex, progressive biological process characterized by a gradual decline in physiological reserve, impaired ability to maintain homeostasis, and increased susceptibility to disease and death. It results from interacting molecular, cellular, genetic, environmental, and lifestyle factors rather than from a single mechanism. Modern aging biology describes interconnected hallmarks of aging, including genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, impaired autophagy, mitochondrial dysfunction, deregulated nutrient sensing, cellular senescence, stem-cell exhaustion, altered intercellular communication, chronic inflammation, and microbiome alterations. Age-related disorders include cardiovascular disease, stroke, cancer, osteoporosis, osteoarthritis, sarcopenia, diabetes, chronic respiratory disease, neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, sensory impairment, depression, frailty, falls, and other geriatric syndromes. Importantly, aging itself is not synonymous with disease: healthy aging focuses on preserving functional ability and quality of life, even when chronic diseases are present.

INTRODUCTION

Aging is a universal and lifelong phenomenon affecting virtually every organ system. At the biological level, it involves the accumulation of molecular and cellular damage together with declining physiological reserve. However, aging is highly heterogeneous: individuals of the same chronological age may have markedly different physical, cognitive, and functional capacities.

Population aging has become a major global health issue. The World Health Organization estimates that the number of people aged 60 years and older will increase from approximately 1 billion in 2020 to **1.4 billion by 2030 and 2.1 billion by 2050**. The fastest growth is occurring in low- and middle- income countries.

The importance of aging research therefore extends beyond increasing lifespan. The major objective is

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

increasingly **healthspan extension**—maintaining physical, cognitive, and social function for as much of life as possible

2. Definition of Aging

Aging can be defined as a **time-dependent, progressive deterioration of biological structure and function that reduces an organism's ability to maintain homeostasis and respond to stress**.

Aging should be distinguished from:

- **Chronological age:** number of years lived.
- **Biological age:** physiological and molecular state of an individual.
- **Healthy aging:** preservation of functional ability and well-being.
- **Age-related disease:** pathological conditions whose incidence or severity increases with age.

The WHO defines healthy aging as the process of developing and maintaining the **functional ability that enables well-being in older age**. Importantly, healthy aging does not require complete absence of disease.

3. Biological Mechanisms of Aging

Modern research views aging as a network of interacting processes rather than a single pathway.

3.1 Genomic instability

DNA is continuously damaged by:

- Reactive oxygen species
- Radiation
- Environmental toxins
- Replication errors
- Spontaneous chemical modifications

DNA repair mechanisms normally correct this damage. With advancing age, accumulated DNA damage and declining repair efficiency can lead to mutations, cellular dysfunction, senescence, and cancer.

3.2 Telomere attrition

Telomeres are repetitive DNA sequences at chromosome ends that protect chromosomes from degradation and inappropriate fusion.

During repeated cell division, telomeres progressively shorten. When they become critically short, cells may enter:

- Replicative senescence
- Apoptosis
- Genomic instability

Telomere biology is particularly important in tissues requiring continuous cellular renewal.

3.3 Epigenetic alterations

Aging is accompanied by changes in:

- DNA methylation
- Histone modification
- Chromatin organization
- Non-coding RNA regulation

These changes can alter gene expression without changing the DNA sequence itself.

Age-associated epigenetic changes are being investigated as potential biomarkers of biological age.

3.4 Loss of proteostasis

Proteostasis refers to maintenance of properly folded and functional proteins.

With aging, protein quality-control systems become less efficient. Misfolded or damaged proteins can accumulate, contributing to disorders such as:

- Alzheimer's disease
- Parkinson's disease
- Huntington's disease
- Amyloidosis

The decline involves impaired molecular chaperones, proteasomal degradation, and autophagy.

3.5 Impaired autophagy

Autophagy is a cellular recycling system that removes damaged proteins and organelles.

Reduced autophagic activity may result in accumulation of:

- Damaged mitochondria
- Misfolded proteins
- Cellular debris

Consequently, impaired autophagy is strongly linked with metabolic, neurodegenerative, and age-related disorders.

3.6 Mitochondrial dysfunction

Mitochondria produce cellular energy in the form of ATP.

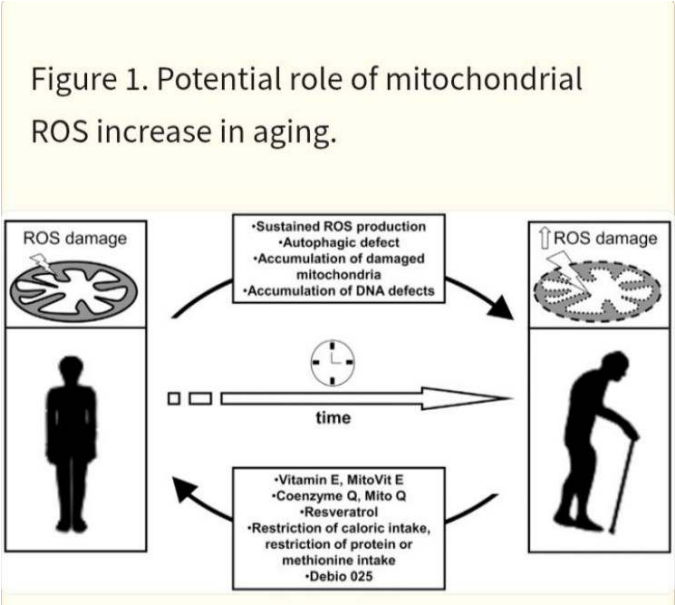


Figure 1. Potential role of mitochondrial ROS increase in aging.

Aging is associated with:

- Reduced mitochondrial efficiency Accumulation of mitochondrial DNA damage
- Abnormal reactive oxygen species production
- Altered mitochondrial dynamics
- Impaired mitophagy

These changes are particularly important in tissues with high energy requirements, including the brain, heart, and skeletal muscle.

3.7 Deregulated nutrient sensing

Several interconnected pathways regulate cellular responses to nutrients and energy:

- Insulin/IGF-1 signaling
- mTOR
- AMPK
- Sirtuins

Abnormal regulation of these pathways can affect metabolism, growth, autophagy, and longevity.

This area has attracted considerable interest because experimental manipulation of nutrient-sensing pathways can influence lifespan in several model organisms. However, translating these findings into safe human anti-aging therapies remains an active research area.

3.8 Cellular senescence

Cellular senescence is a state in which cells permanently stop proliferating but remain metabolically active.

Senescent cells can release inflammatory and tissue-remodeling molecules collectively called the **senescence-associated secretory phenotype (SASP)**.

Accumulation of senescent cells may contribute to:

- Chronic inflammation
- Tissue dysfunction
- Fibrosis
- Impaired regeneration
- Cancer biology
- Age-related diseases

This has led to research into **senolytics**, drugs designed to selectively eliminate senescent cells.

Human clinical applications remain investigational.

3.9 Stem-cell exhaustion

Stem cells maintain tissue regeneration throughout life.

Aging can reduce:

- Stem-cell number
- Self-renewal capacity
- Differentiation potential
- Tissue regenerative capacity

This contributes to impaired healing, muscle loss, reduced blood-cell production, and degeneration

of several organs.

3.10 Chronic inflammation — "inflammaging"

Low-grade, persistent systemic inflammation increases with age and is often termed **inflammaging**.

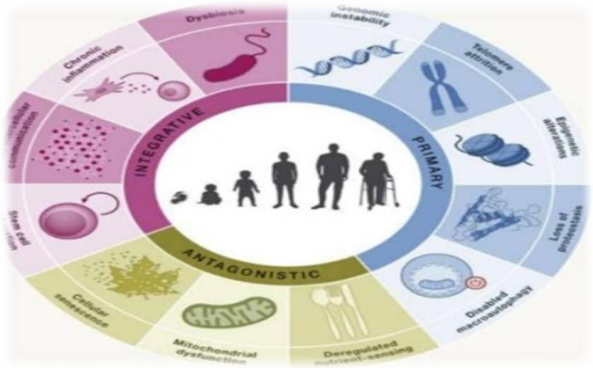
Potential contributors include:

- Cellular senescence
- Damaged cells
- Altered gut microbiota
- Obesity
- Chronic infections
- Immune-system dysregulation

Inflammaging has been associated with cardiovascular disease, neurodegeneration, diabetes, frailty,

and other chronic conditions.

3.11 Altered intercellular communication



As people age, communication between cells and organs becomes altered through changes in:

- Hormones
- Cytokines
- Neurotransmitters
- Immune signaling
- Extracellular vesicles

This can disturb coordination between tissues and contribute to systemic decline.

3.12 Gut microbiome alterations

The intestinal microbiome changes with age.

Factors contributing to dysbiosis include:

- Diet
- Medications
- Reduced physical activity
- Chronic disease
- Changes in immune function

Altered microbiota may influence inflammation, metabolism, immune function, and brain health.

Dysbiosis is now included among the expanded hallmarks of aging.

4. Major Age-Related Disorders

Aging increases vulnerability to multiple chronic diseases. Older adults frequently have

multimorbidity, meaning two or more chronic conditions simultaneously. WHO identifies hearing

loss, cataracts, osteoarthritis, chronic respiratory disease, diabetes, depression, dementia, and other

conditions as common problems in older age.

4.1 Cardiovascular diseases

Major cardiovascular disorders include:

- Hypertension
- Coronary artery disease
- Heart failure
- Atherosclerosis
- Stroke
- Peripheral arterial disease

Mechanisms

Age-related vascular changes include:

- Arterial stiffening
- Endothelial dysfunction
- Atherosclerotic plaque accumulation
- Increased vascular inflammation
- Reduced cardiovascular reserve

Cardiovascular disease remains one of the most important causes of morbidity and mortality in older

adults.

5. Neurodegenerative Disorders

5.1 Alzheimer's disease

Alzheimer's disease is the most common cause of dementia.

Important pathological features include:

- Amyloid-β accumulation
- Tau pathology
- Synaptic dysfunction
- Neuroinflammation
- Neuronal loss

Clinical manifestations include progressive impairment of:

- Memory
- Language
- Executive function
- Orientation
- Activities of daily living

Age is the strongest major risk factor, although genetics, vascular health, education, physical activity,

and other factors also influence risk.

5.2 Parkinson's disease

Parkinson's disease is characterized by degeneration of dopaminergic neurons, particularly in the

substantia nigra.

Typical manifestations include:

- Bradykinesia
- Resting tremor
- Rigidity
- Postural instability

Non-motor symptoms may include:

- Depression
- Sleep disorders
- Constipation
- Autonomic dysfunction
- Cognitive impairment

5.3 Stroke

Stroke occurs when cerebral blood flow is interrupted or a blood vessel ruptures.

Risk factors that become increasingly important with age include:

- Hypertension
- Diabetes
- Atrial fibrillation
- Dyslipidemia
- Smoking

• Atherosclerosis

Stroke may cause permanent disability affecting movement, speech, cognition, and independence.

6. Musculoskeletal Disorders

6.1 Osteoporosis

Osteoporosis is characterized by reduced bone strength and increased fracture risk.

Common consequences include:

• Hip fractures

• Vertebral fractures

• Wrist fractures

Risk increases with aging because of changes in bone remodeling, hormonal changes, reduced

physical activity, nutritional factors, and other influences.

6.2 Sarcopenia

Sarcopenia is age-associated loss of skeletal muscle mass, strength, and/or physical performance.

Contributing mechanisms include:

• Reduced physical activity

• Motor-neuron loss

• Anabolic resistance

• Hormonal changes

• Mitochondrial dysfunction

• Chronic inflammation

• Inadequate protein intake

Sarcopenia contributes to:

• Falls

• Frailty

• Disability

• Loss of independence

• Increased hospitalization risk

6.3 Osteoarthritis

Osteoarthritis is a degenerative joint disorder involving cartilage, bone, synovium, and surrounding

tissues.

Common symptoms include:

• Joint pain

• Stiffness

• Reduced mobility

• Functional limitation

Knee, hip, hand, and spine involvement is common.

7. Metabolic Disorders

7.1 Type 2 diabetes mellitus

Aging is associated with increased risk of insulin resistance and impaired pancreatic β-cell function.

Diabetes can lead to:

• Cardiovascular disease

• Kidney disease

• Neuropathy

• Retinopathy

• Poor wound healing

Lifestyle factors such as physical inactivity, obesity, and unhealthy diet can substantially influence

risk. WHO identifies tobacco, alcohol, unhealthy diet, high BMI, and insufficient physical activity as

important shared risk factors for chronic diseases in older age.

8. Sensory Disorders

8.1 Cataract

A cataract involves progressive opacity of the eye's lens and may cause:

• Blurred vision

• Glare

• Reduced contrast

• Difficulty seeing at night

Cataract is one of the most common causes of visual impairment in older adults.

8.2 Age-related hearing loss

Presbycusis is progressive sensorineural hearing loss associated with aging.

It can contribute to:

- Communication difficulties
- Social isolation
- Reduced quality of life
- Increased functional dependence

WHO identifies hearing loss and visual disorders among common health problems in older age.

9. Cancer and Aging

Cancer incidence generally increases with age because cancer development requires the

accumulation of genetic and epigenetic alterations over time.

Important cancers in older adults include:

- Breast cancer
- Colorectal cancer
- Lung cancer
- Prostate cancer
- Skin cancers

Aging can also influence cancer treatment because older individuals may have:

- Reduced physiological reserve
- Multiple comorbidities
- Polypharmacy
- Increased treatment toxicity

Therefore, cancer management in older adults should consider **functional status and individual**

goals, not chronological age alone.

10. Geriatric Syndromes

Some important problems in older adults do not fit neatly into a single organ-system diagnosis.

These are known as **geriatric syndromes**.

Major examples include:

Frailty

A state of increased vulnerability to stressors caused by reduced physiological reserve.

Falls

Multifactorial events associated with:

- Muscle weakness
- Poor vision
- Balance impairment
- Medications
- Neurological disease
- Environmental hazards

Delirium

An acute disturbance of attention and cognition, often triggered by infection, medications, metabolic

abnormalities, surgery, or hospitalization.

Urinary incontinence

Loss of bladder control that can substantially affect quality of life.

Pressure injuries

Localized tissue damage associated particularly with immobility and prolonged pressure.

WHO specifically identifies frailty, urinary incontinence, falls, delirium, and pressure ulcers as

important geriatric syndromes.

11. Psychological and Social Disorders

Aging is also associated with important mental-health challenges.

These include:

- Depression
- Anxiety
- Loneliness
- Social isolation
- Cognitive impairment
- Dementia
- Sleep disorders

However, these should not be considered inevitable consequences of aging.

Social environment, socioeconomic conditions, physical activity, cognitive stimulation, relationships,

and access to health services can substantially influence later-life health.

12. Risk Factors for Age-Related Disorders

Age-related disease results from interactions between biological aging and environmental/lifestyle factors.

Modifiable factors

- Tobacco use
- Excessive alcohol consumption
- Physical inactivity
- Unhealthy diet
- Obesity
- Poor sleep
- Uncontrolled hypertension
- Diabetes
- Dyslipidemia
- Social isolation

Non-modifiable factors

- Chronological age
- Genetic susceptibility
- Sex
- Early-life exposures
- Family history

Importantly, aging trajectories are influenced throughout the **life course**, not just during old age.

WHO emphasizes that nutrition, education, living conditions, employment, environment, and health behaviors can influence health in later life.

13. Prevention and Healthy Aging

The goal should not simply be to increase lifespan but to increase the proportion of life spent in good health.

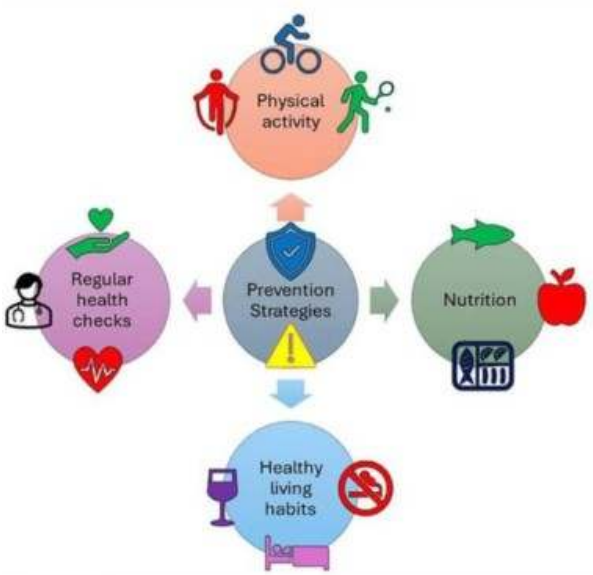
Physical activity

Regular exercise should combine:

- Aerobic activity
- Resistance training
- Balance exercises
- Flexibility/mobility work

Resistance exercise is particularly important for preserving muscle strength and functional independence.

Nutrition



A balanced dietary pattern should provide:

- Adequate protein
- Fruits and vegetables
- Whole grains
- Healthy fats
- Adequate calcium and vitamin D where appropriate
- Sufficient hydration

Nutritional needs should be individualized, particularly in frail or chronically ill adults.

Cardiovascular risk reduction

Control of:

- Blood pressure
- Blood glucose
- Lipids
- Body weight

can reduce the risk of cardiovascular and cerebrovascular disease.

Cognitive and social engagement

Maintaining social relationships, meaningful activities, learning, and cognitive stimulation may support psychological and cognitive health.

Prevention of falls

Interventions include:

- Strength and balance training
- Vision assessment
- Medication review
- Appropriate footwear
- Home safety modifications
- Management of contributing medical conditions

14. Diagnosis and Geriatric Assessment

Traditional disease-specific assessment is often insufficient in older adults because multiple conditions interact.

A **Comprehensive Geriatric Assessment (CGA)** evaluates:

1.Medical conditions

2.Medications

3.Functional status

4.Cognitive status

5.Psychological health

6.Nutrition

7.Mobility and falls

8.Social support

9.Living environment

10.Goals and preferences

WHO's Integrated Care for Older People (ICOPE) approach similarly emphasizes maintaining intrinsic capacity and functional ability through person-centered, coordinated care.

15. Pharmacological Considerations

Older adults are particularly vulnerable to medication-related problems because of age-associated changes in:

- Renal function
- Hepatic metabolism
- Body composition
- Drug distribution
- Drug sensitivity

Polypharmacy can increase the risk of:

- Drug interactions
- Falls
- Delirium
- Hypotension
- Adverse drug reactions

Therefore, medication review and individualized prescribing are essential components of geriatric care.

16. Emerging Anti-Aging Strategies

Aging research is increasingly moving from treating individual diseases toward targeting biological mechanisms shared by multiple age-related conditions.

Research areas include:

Senolytics

Agents intended to remove senescent cells.

mTOR modulation

Targeting nutrient-sensing pathways involved in growth, metabolism, and aging.

NAD^+ metabolism

Investigating whether restoration of cellular NAD^+ availability can improve age-associated dysfunction.

Autophagy enhancement

Strategies aimed at improving removal of damaged cellular components.

Mitochondrial interventions

Approaches designed to improve mitochondrial quality and function.

Epigenetic interventions

Attempts to modify age-associated changes in gene regulation.

Anti-inflammatory strategies

Targeting chronic age-associated inflammation.

Vaccination and immune modulation

An emerging area of research aimed at preventing or modifying age-associated diseases. Recent reviews have explored vaccines as potential tools for targeting aging-related processes and diseases.

It is important to emphasize that many proposed "anti-aging" interventions remain experimental.

Evidence from animal models does not automatically establish safety or effectiveness in humans.

Reviews have also highlighted limitations in current approaches for determining whether an intervention truly slows biological aging rather than merely extending lifespan or affecting an individual disease.

17. Relationship Between Aging and Disease

A useful conceptual model is:

Aging mechanisms → cellular dysfunction → tissue dysfunction → reduced physiological reserve → increased disease susceptibility → multimorbidity → frailty/disability

For example:

Mitochondrial dysfunction + inflammation + muscle inactivity → muscle loss → sarcopenia → falls → fractures → immobility → further muscle loss and frailty

Similarly:

Vascular aging + hypertension + metabolic dysfunction → atherosclerosis → cardiovascular

disease/stroke → disability

Thus, age-related disorders should not always be considered isolated diseases. They frequently share

common biological pathways.

18. Aging, Healthspan and Lifespan

Three concepts should be distinguished:

- **Lifespan:** total duration of life.
- **Healthspan:** period of life spent in relatively good health and functional independence.
- **Disease burden:** period characterized by chronic illness, disability, or dependency.

The ideal outcome is to **compress morbidity**—maintain function for longer and postpone severe disability toward the end of life.

WHO similarly emphasizes functional ability rather than simply absence of disease as the central goal

of healthy aging.

19. Future Perspectives

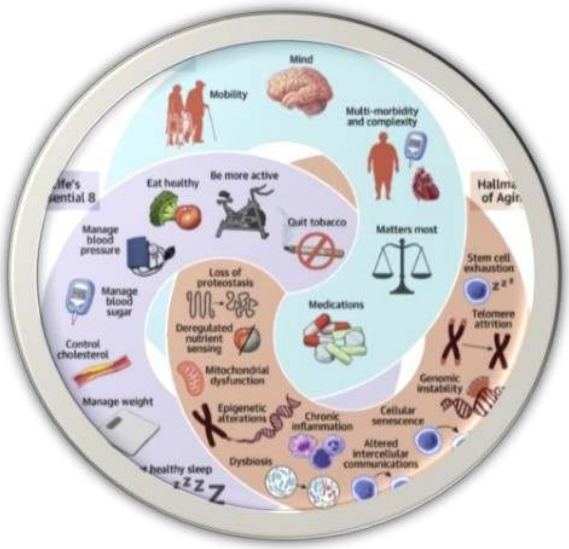
Future aging research is likely to focus on:

1.Biomarkers capable of accurately measuring biological age.

2.Early identification of individuals at risk of frailty and dementia.

3.Personalized interventions based on biological and functional profiles.

4.Combination therapies targeting multiple aging mechanisms.



5.Prevention rather than treatment of advanced age-related disease.

6.Integration of geriatric medicine with precision medicine.

7.Development of interventions that extend healthspan rather than merely lifespan.

CONCLUSION

Aging is a multifactorial biological process involving progressive changes in genomic stability, epigenetic regulation, protein homeostasis, mitochondrial function, nutrient sensing, cellular senescence, stem-cell activity, immune signaling, inflammation, and the microbiome. These interconnected mechanisms progressively reduce physiological reserve and increase susceptibility to chronic diseases.

Age-related disorders encompass cardiovascular, neurological, metabolic, musculoskeletal, sensory, respiratory, oncological, psychological, and geriatric conditions. However, **aging should not be equated with inevitable disease or disability**. Significant differences exist between individuals of the same chronological age.

The modern approach to aging therefore emphasizes **healthy aging, prevention, preservation of functional ability, early detection of frailty and disease, person-centered care, and extension of healthspan**. As research into the biology of aging progresses, interventions targeting fundamental aging mechanisms may eventually complement conventional disease-specific treatments. At present, however, the strongest practical strategy remains comprehensive prevention and management of modifiable risk factors combined with appropriate medical, functional, psychological, and social care.

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HOW TO CITE: Sudarsanam Nagarjuna, Dr. B. Thangabalan, *K. Sravani*, *M. Beula*, *K. Pravallika*, Sk. Naziya, *J. Dwaraka*, Leishangthem. Dibiya Devi, S. Mohan, A Review Article on Aging and Age-Related Disorders, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 11, 1333-1344. https://doi.org/<DOI>