Panel: Aging of hematopoietic system

Meltem Kurt Yüksel MD Prof

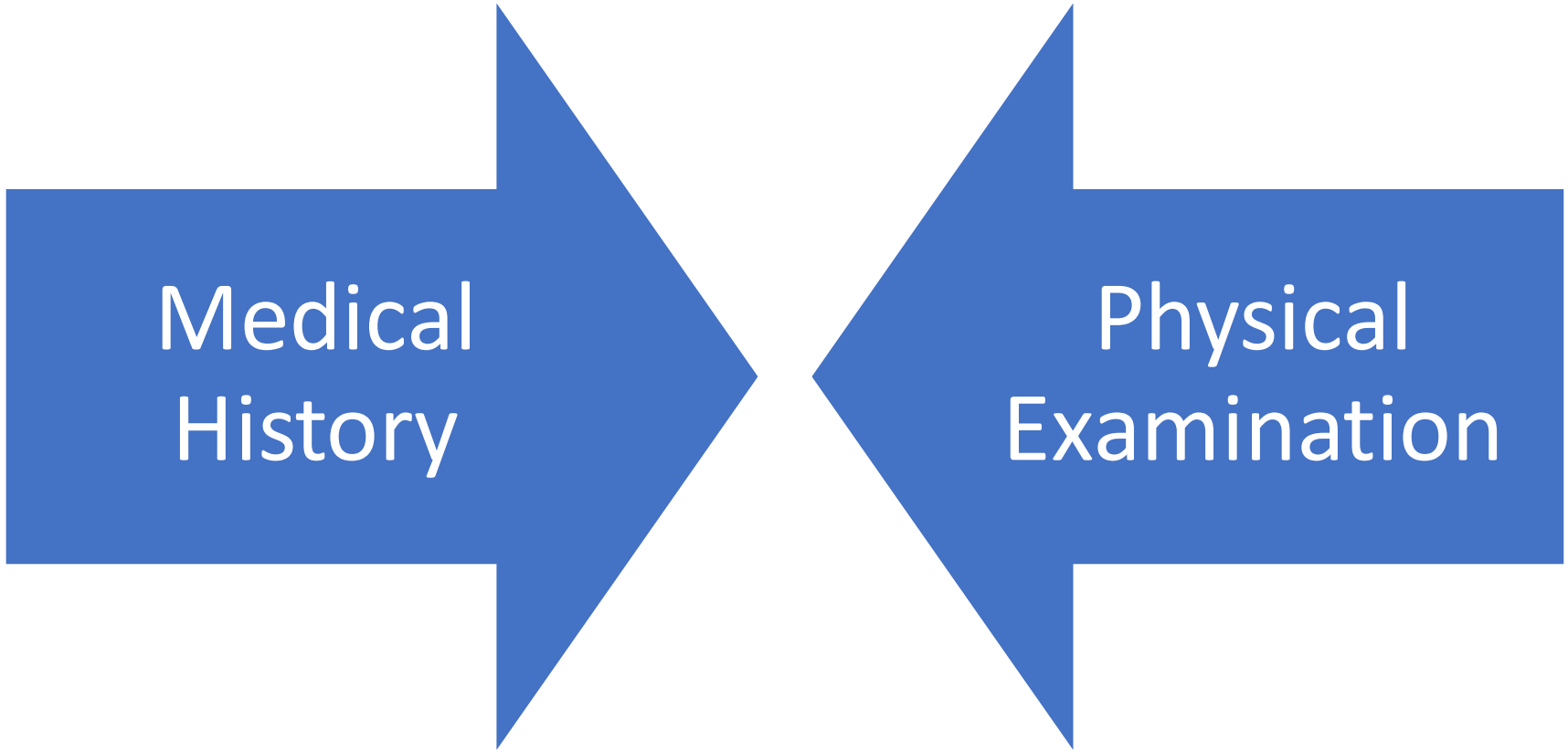
Division of Internal Medicine

Adult Hematology Department and Stem Cell Transplantation

2021-2022

Grade II AUFM

Initial Approach to the patient



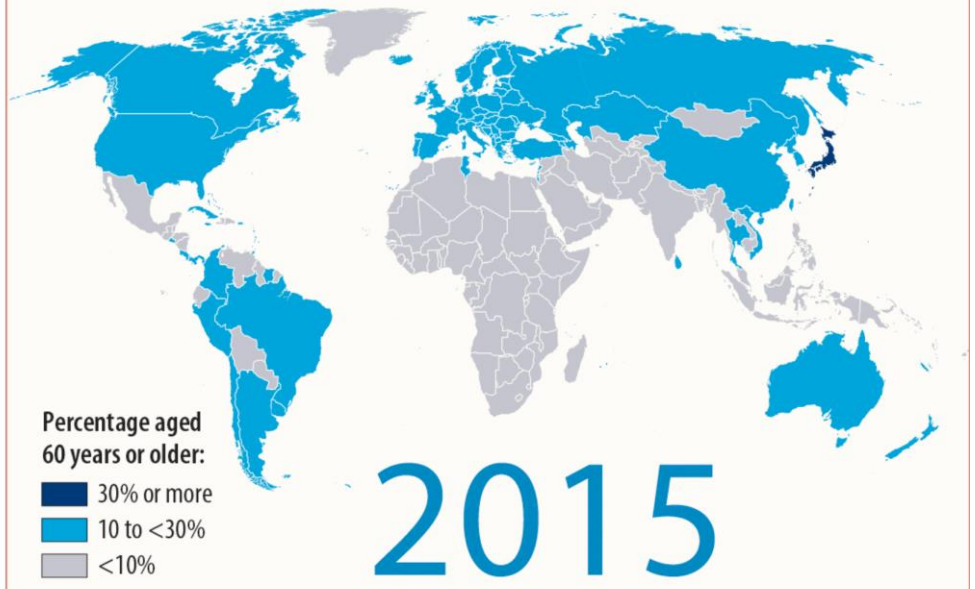
There is no “typical” older person

Definition

Geriatrics refers to medical care for older adults, an age group that is not easy to define precisely. “Older” is preferred over "elderly," but both are equally imprecise; > 65 is the age often used, but most people do not need geriatrics expertise in their care until age 70, 75, or even 80. Gerontology is the study of aging, including biologic, sociologic, and psychologic changes.

Ageing and Health #yearsahead

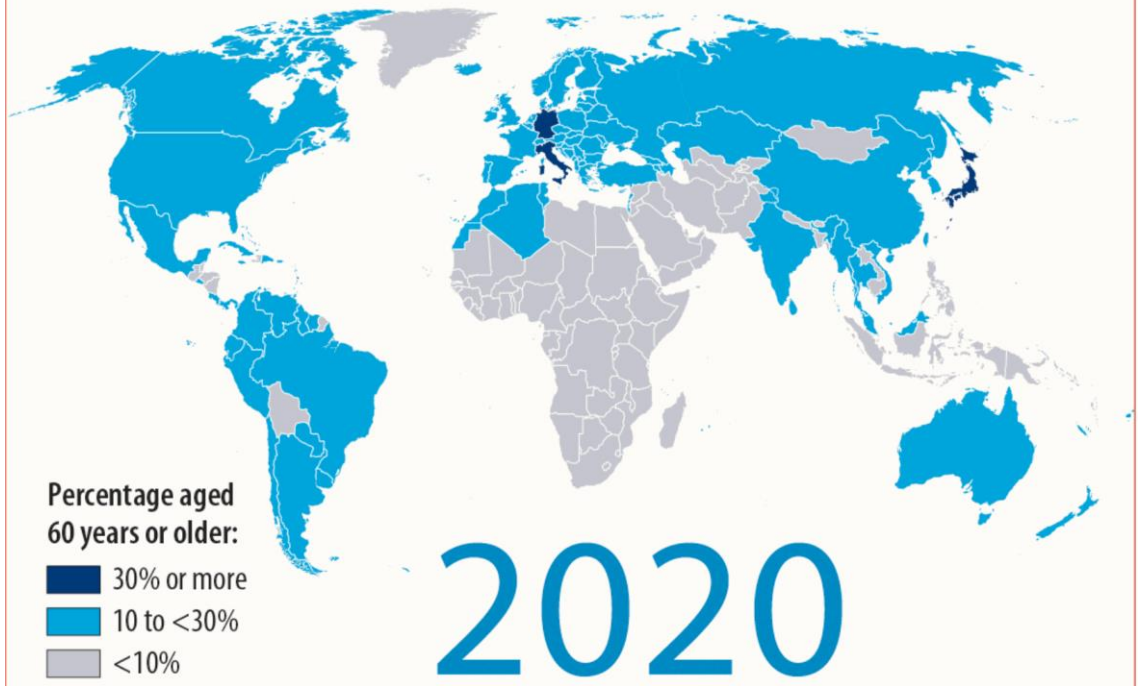
Populations are getting older



World Health Organization

Ageing and Health #yearsahead

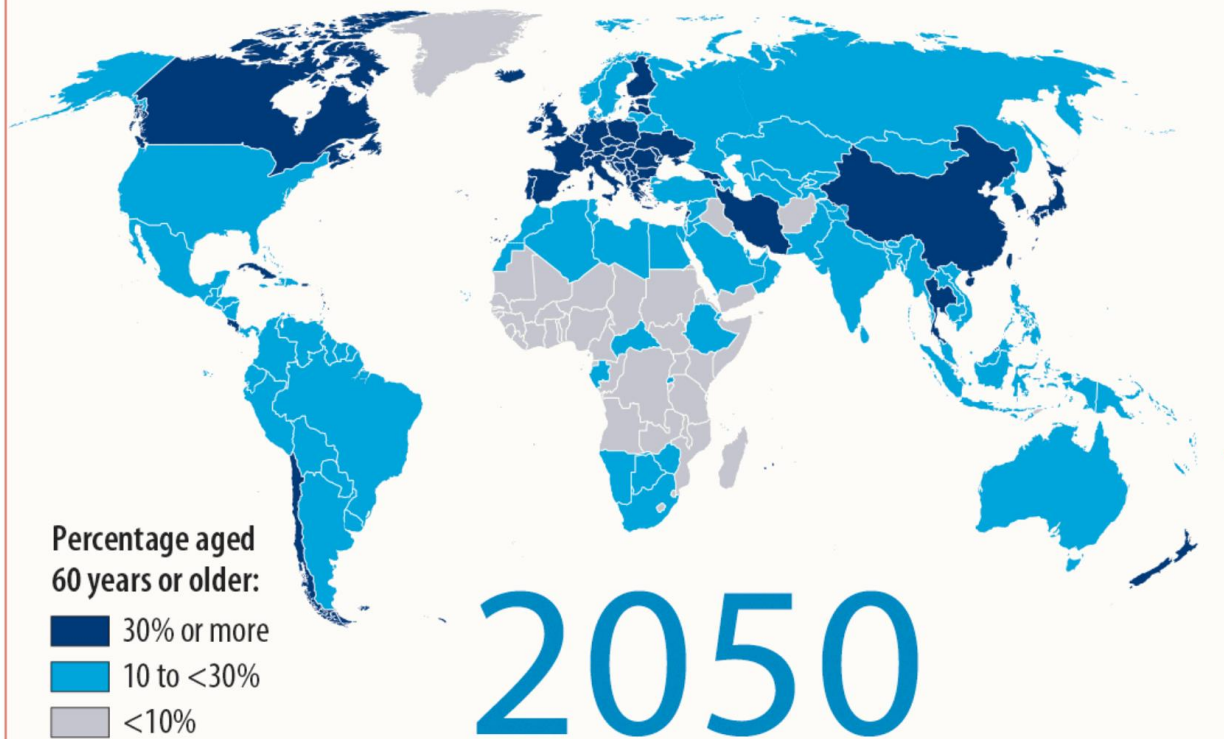
Populations are getting older



World Health Organization

Ageing and Health #yearsahead

Populations are getting older



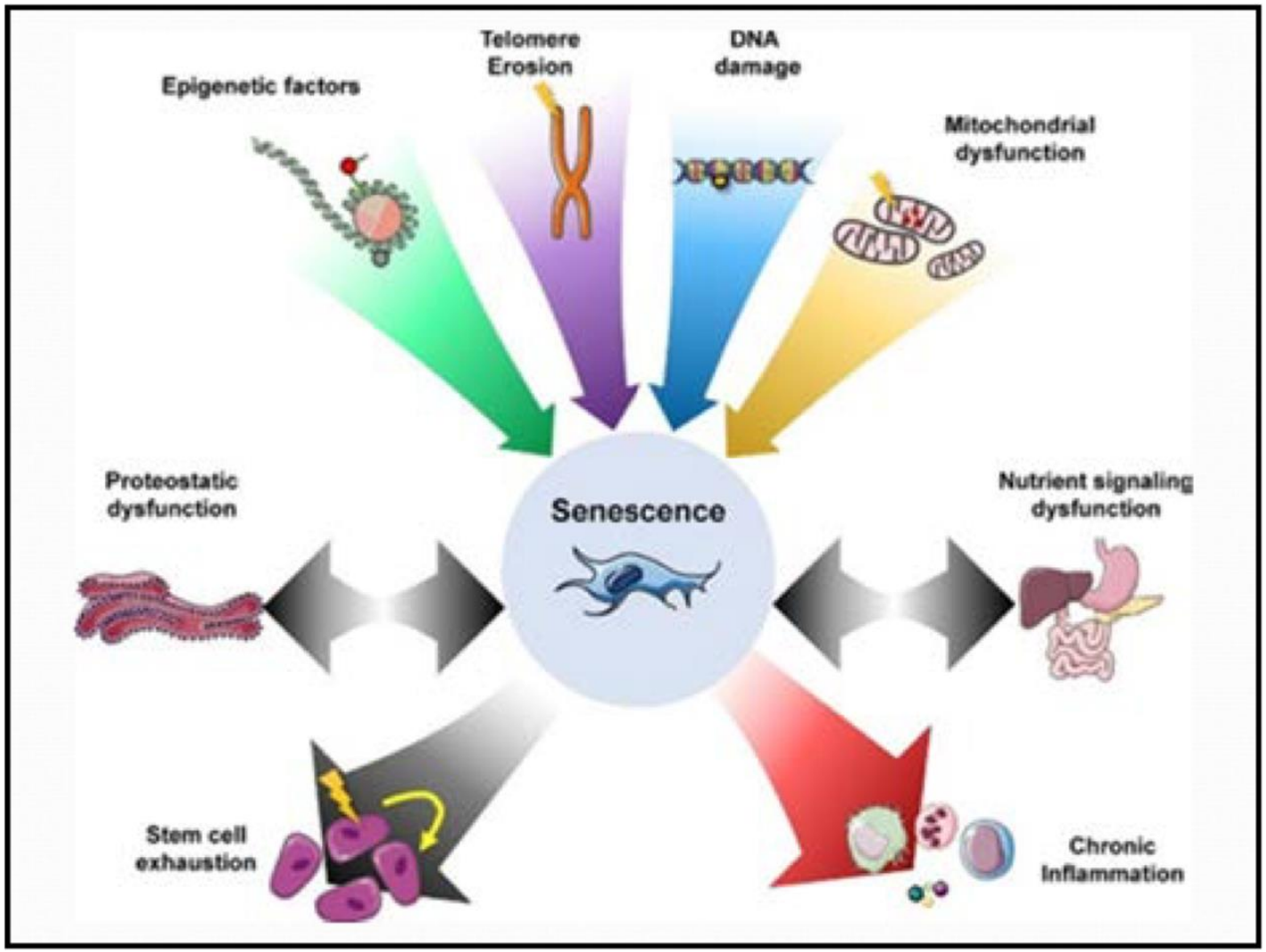
World Health Organization

TABLE 9–2. Anemia Prevalence in the Elderly Using the WHO* Criteria

Study	Age (Years)	Population	Prevalence
Guralnik, 2004[127]	≥65	Community-dwelling elderly American	10.6%
Ferrucci, 2007[299]	≥70	Community-dwelling elderly Italian	11%
Denny[300]	≥71	Community dwelling	24%
Joosten[128]	≥65	Hospitalized	24% (defined as hemoglobin <11.5 g/dL)
Artz[126]	Most ≥65	Nursing home	48%
Robinson[182]	≥65	Nursing home	59.6%

*World Health Organization anemia criteria; hemoglobin <13 g/dL for adult men and <12 g/dL for adult women.

Mechanisms


Telomere
Erosion
DNA
damage
Epigenetic factors
Mitochondrial
dysfunction
Proteostatic
dysfunction
Senescence
Nutrient signaling
dysfunction
Stem cell
exhaustion
Chronic
Inflammation

Genetic Effects

That genetic controls are involved seems obvious when one considers that lifespan is highly species-specific. For example, mice generally live approximately 30 months and humans approximately 90 years. However, the aging phenomenon is not necessarily a direct consequence of primary DNA sequence. For example, mice and bats have 0.25 percent difference in their primary DNA sequence, but bats live for 25 years, 10 times longer than mice. Thus, regulation of gene expression seems likely to be the major source of species longevity differences.

Progeria Syndromes Gerontologists have long been intrigued by the concept of accelerated aging and by examining those rare individuals who are so affected. From work with invertebrate models a number of genes have been identified that associate with longevity. Yet, the identification and functional analysis of analogous genes in humans remains elusive. With regard to genetic examples of accelerated aging, two syndromes have been well characterized: Hutchison-Guilford syndrome (early-onset progeria) and Werner syndrome (adult-onset progeria).[41,42] Although neither these nor other progeria syndromes manifest a complete phenotype of advanced age, the identification of the genes responsible for these particular syndromes is beginning to pay dividends by providing clues to the molecular mechanisms involved in the aging process. For example, Werner syndrome is now defined by mutations in a single gene on chromosome 8 that encodes a protein containing a helicase-like domain.[43,44] The activity of the Werner protein helps to maintain telomere structure and homology-dependent recombination.[45] Similarly, a mutation in the lamin A *(LMNA)* gene localized to chromosome 1 has been causally related to the Hutchison-Guilford syndrome.[46] The product of the mutated *LMNA* gene (termed *progerin*) accumulates, producing a variety of nuclear distortions of which telomere dysfunction and associated replicative senescence are notable.[47]

Biology of aging

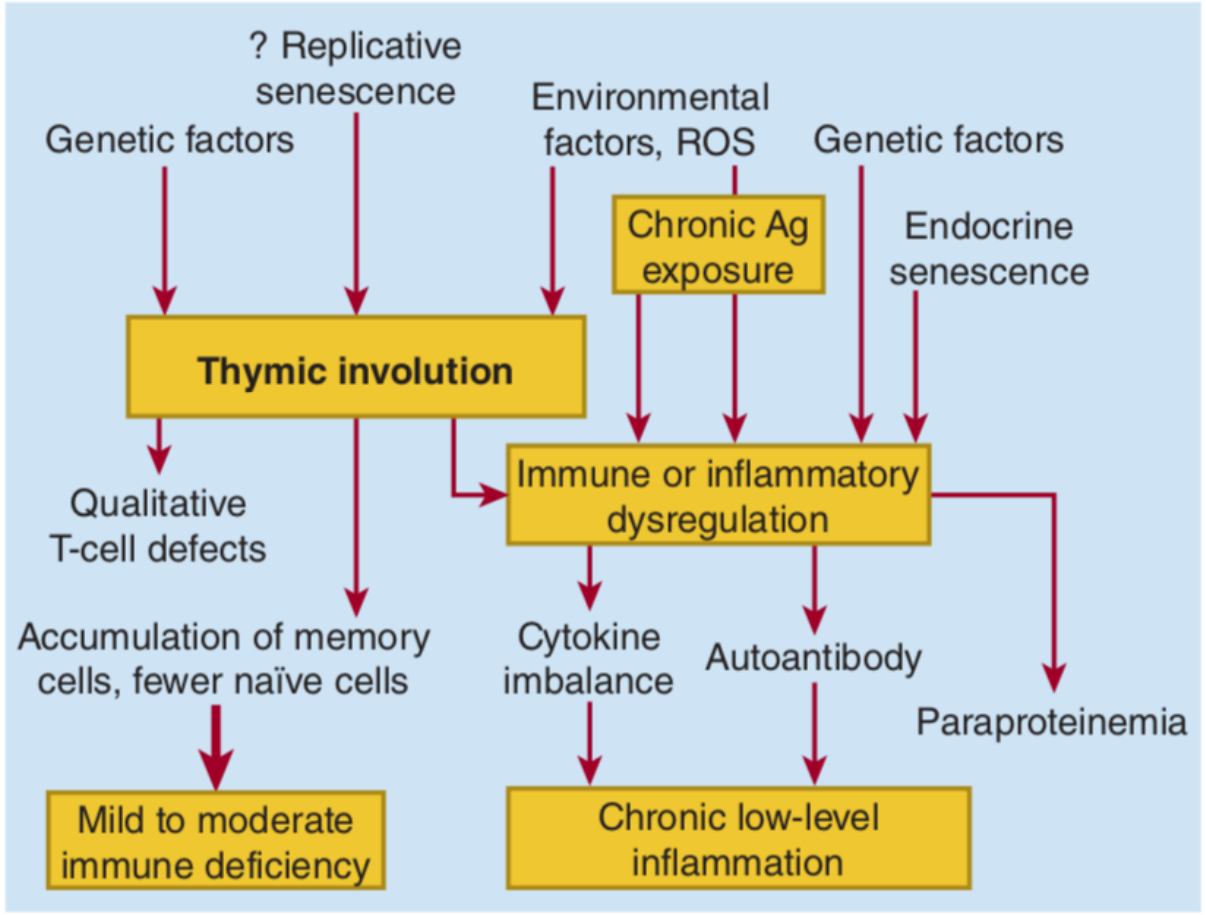
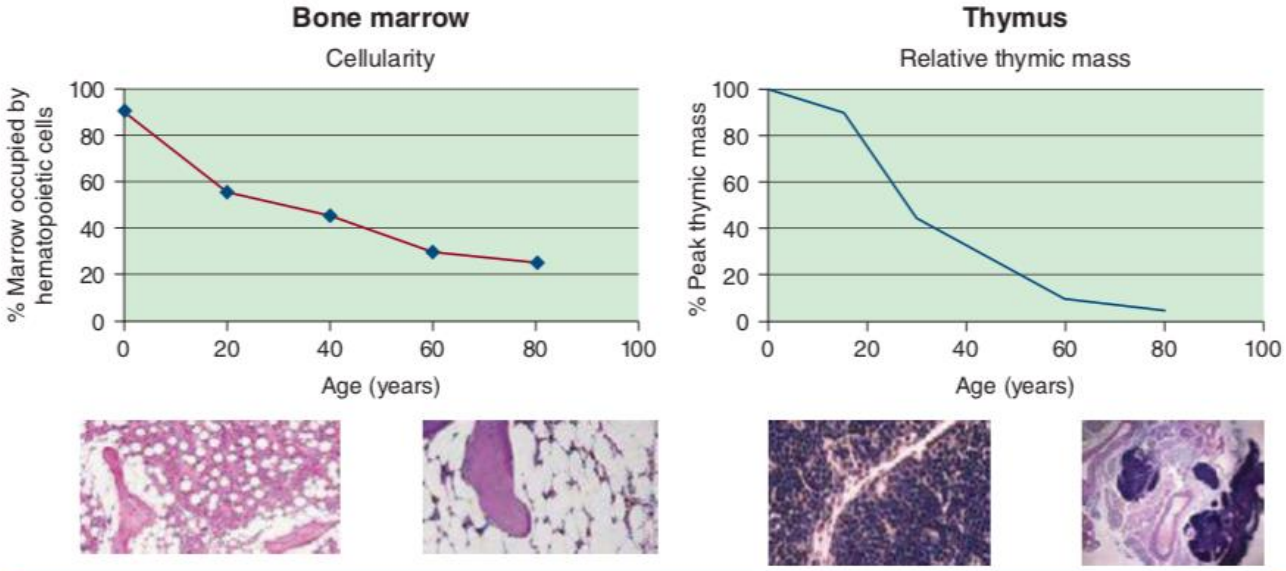


Figure 9–2. Immunity and aging. A variety of factors have been associated with thymic involution, the consequence of which is a mild to moderate immune deficiency. Dysregulated inflammatory pathways are also observed with advancing age and these may be of greater clinical importance. Ag, antigen; ROS, reactive oxygen species.

Senescence of the bone marrow and thymus



Clinical consequences*	
Mild anemia (unexplained)	Mild immune deficiency
?Increased GVHD as marrow donor	Increased susceptibility to herpes zoster
	Tuberculosis reactivation
	?Predisposition to cancer

*Consequences of aging in the bone marrow and thymus in the absence of disease.

Figure 9–1. Aging of marrow and thymus. Marrow cellularity declines from birth in a manner comparably to thymic mass. This is reflected histologically by the increased presence of fat. The clinical consequences of these age-associated changes, in the absence of disease, are a mild anemia and immune deficiency. The latter is reflected by an increased predisposition to certain infections (e.g., herpes zoster or reactivation of latent tuberculosis) and possibly to the increased predisposition to cancer. GVHD, graft-versus-host disease.

TABLE

Close

Selected Physiologic Age-Related Changes

Affected Organ or System	Physiologic Change	Clinical Manifestations
Body composition	↓ Lean body mass ↓ Muscle mass ↓ Creatinine production ↓ Skeletal mass ↓ Total body water ↑ Percentage adipose tissue (until age 60, then ↓ until death)	Changes in drug levels (usually ↑) ↓ Strength Susceptibility to dehydration
Cells	↑ DNA damage and ↓DNA repair capacity ↓ Oxidative capacity Accelerated cell senescence ↑ Fibrosis Lipofuscin accumulation	↑ Cancer risk
CNS	↓ Number of dopamine receptors ↑ Alpha-adrenergic responses ↑ Muscarinic parasympathetic responses	Tendency toward stiffer muscles, less flexibility, impaired balance, and loss of spontaneous movements (eg, ↑ muscle tone, ↓ arm swing)
Ears	Loss of high-frequency hearing	↓ Ability to recognize speech
Endocrine system	↑ Insulin resistance and glucose intolerance	↑ Incidence of diabetes
	Menopause, ↓ estrogen and progesterone secretion ↓ Testosterone secretion ↓ Growth hormone secretion ↓ Vitamin D absorption and activation	Vaginal dryness, dyspareunia ↓ Muscle mass ↓Bone mass ↑ Fracture risk

Related Changes), the decline may be critical during stress, but it usually has little or no effect on daily activities. Therefore, disorders, rather than normal aging, are the primary cause of functional loss during old age.

▸ WHAT INFLUENCES HEALTH IN OLDER AGE

▸ WHAT IS NEEDED FOR HEALTHY AGEING

A change in the way we think about ageing and older people

Creation of age-friendly environments

Alignment of health systems to the needs of older people

Development of systems for long-term care

Healthy Ageing...being able to do the things we value for a long as possible
#yearsahead

AGEING and HEALTH

World Health Organization

Between 2000 and 2050, the number of people aged 60 and over is expected to double

In 2050, more than 1 in 5 people will be 60 years or older.

By 2050, 80% of older people will be living in low– and middle–income countries.

▸EVERY OLDER PERSON IS DIFFERENT

Some have the level of functioning of a 30 year old.

Some require full time assistance for basic everyday tasks.

Health is crucial to how we experience older age.

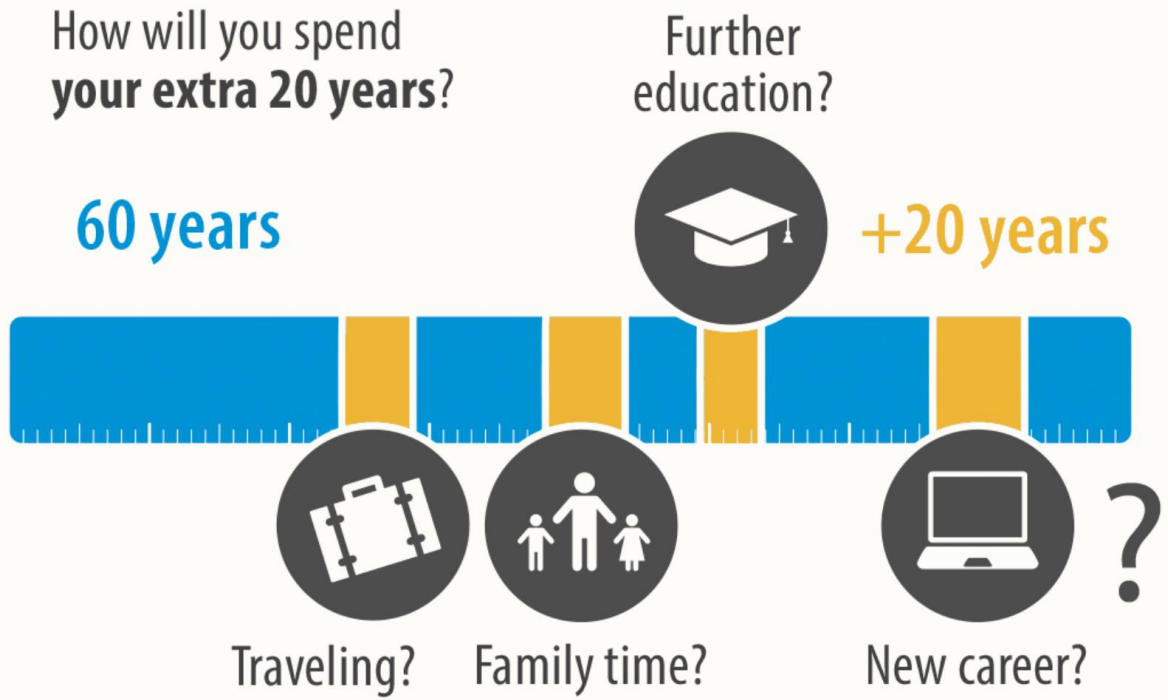
People live on average 20 years longer than 50 years ago

60 years

World Health Organization

Ageing and Health #yearsahead

People live on average 20 years longer than 50 years ago



World Health Organization

Thank you very much….