

The Aging Process: An Update

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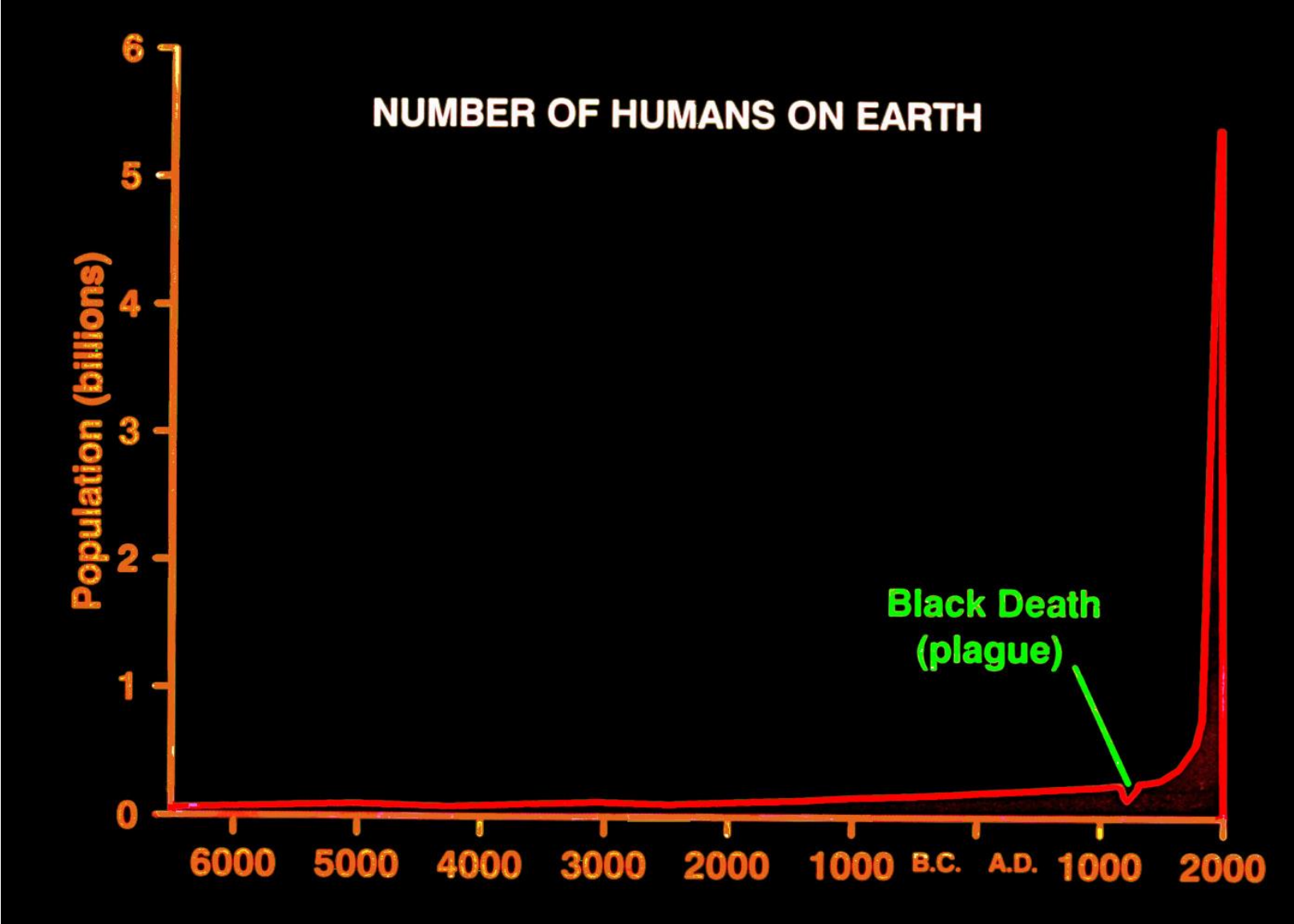
Institute of Health Sciences

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Terminology

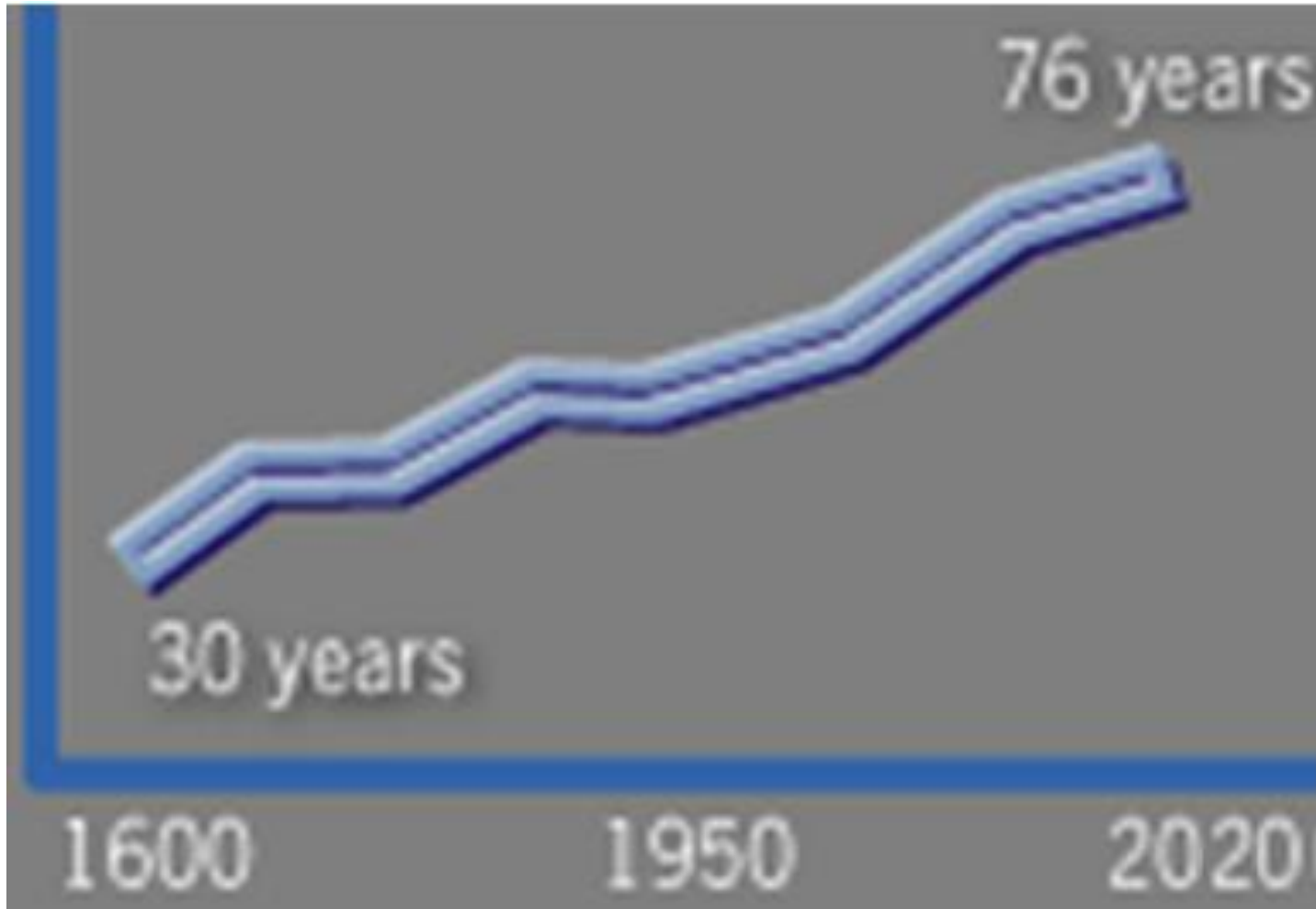
- **Gerontology (study of aging)**
- **Geriatrics (care of the elderly)**

Humanity - J Population Curve

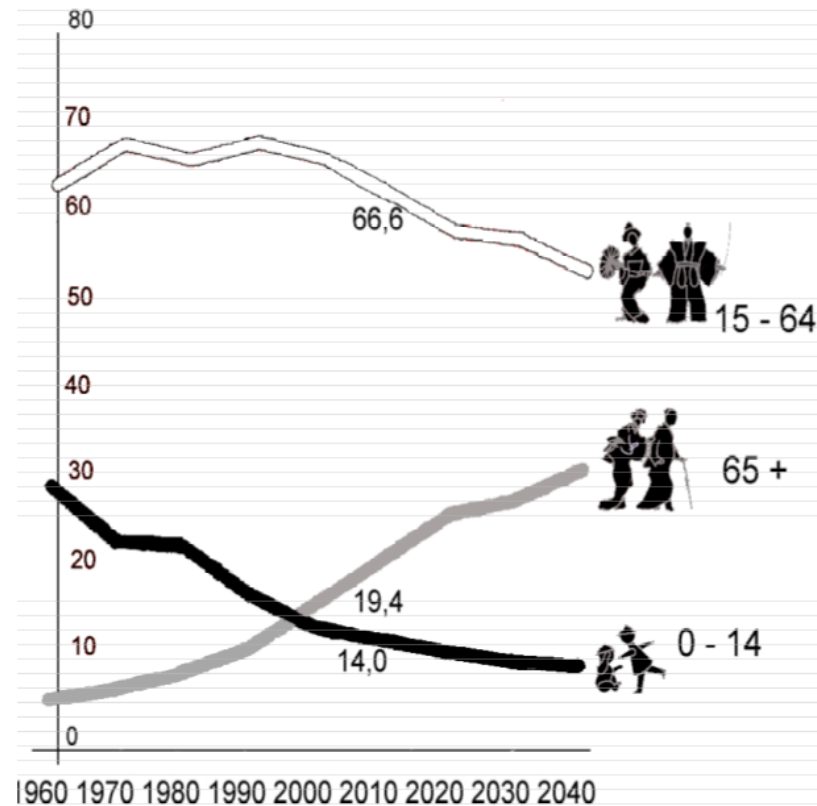


Life expectancy at birth

Longevity - the total number of years a newborn is expected to live

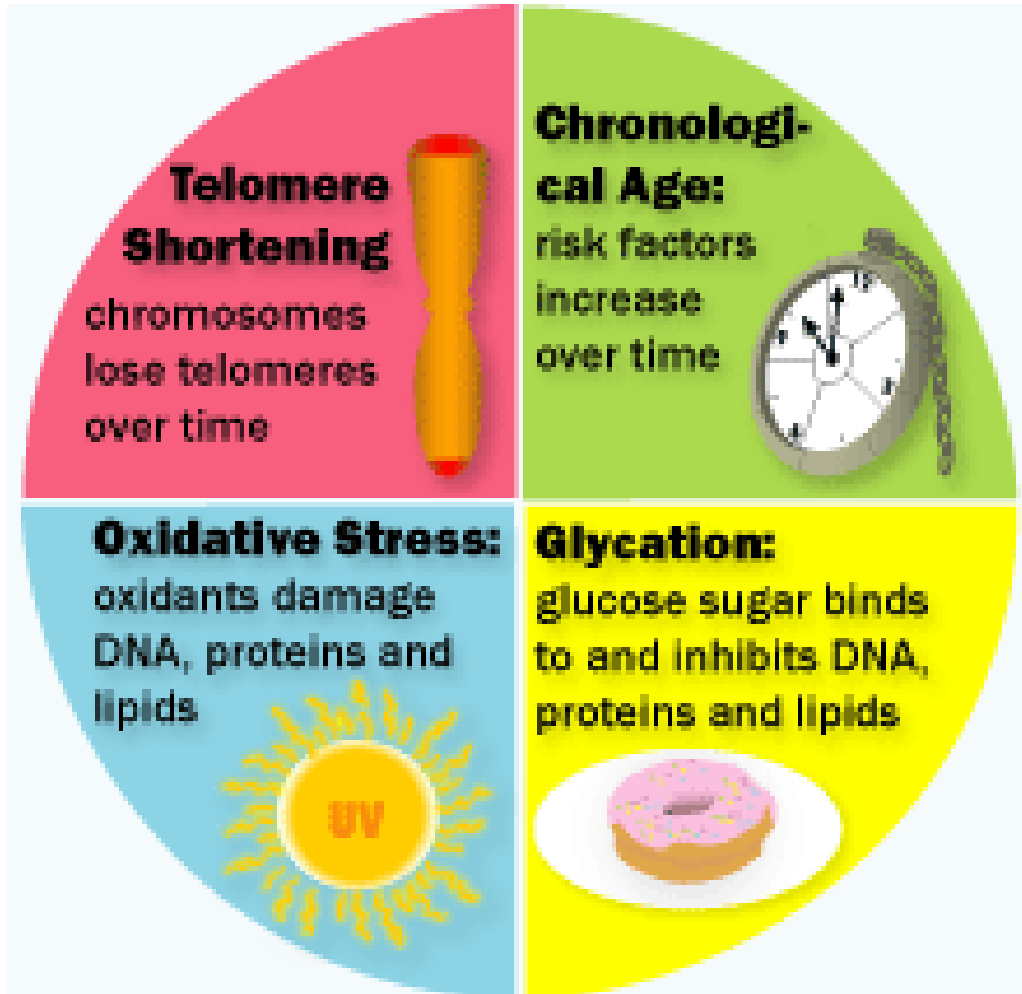


Population trends in Japan



With a rapidly growing number of elderly persons and an increase in life expectancy, research in geronto-areas has begun to flourish.

Main factors in aging

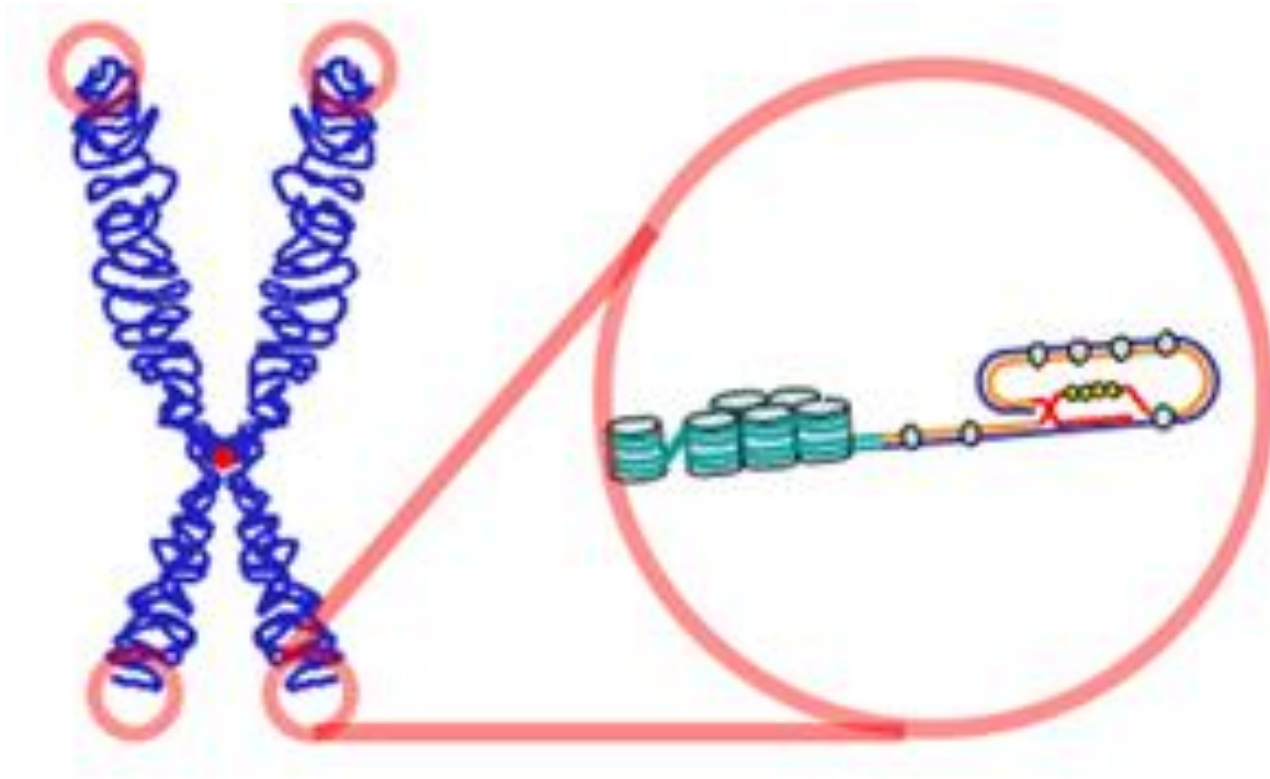


Theories of aging

- **Telomere theory - or replicative senescence**

Senescence may result from telomere loss.

TELOMERES



Each chromosome has 2 telomeres at its ends

Each human cell contains 92 telomeres

Each telomere is made up of 5 kbp

Each chromosome contains 130-150 Mbp

Telomeres

- **Cells normally can divide 50 to 70 times.**
- **Each time a cell divides, the telomeres get shorter by 30 to 200 base pairs.**
- **When they get too short, the cell no longer can divide and becomes inactive or "senescent" and it dies.**

- **Telomeres enable the cell to replicate chromosome ends, as the enzymes that normally replicate DNA cannot copy the extreme ends of chromosomes.**
- **Shorter telomeres are associated with shorter lives.**
- **In human blood cells, the length of telomeres ranges from 8,000 base pairs at birth to 3,000 base pairs as people age and as low as 1,500 in the elderly people.**

- **Among people older than 60, those with shorter telomeres were three times more likely to die from heart disease and eight times more likely to die from infectious disease.**
- **Once a person is older than 60, the risk of death doubles with every eight years of age. So, a 68-year-old has twice the chance of dying within a year compared with a 60-year-old.**

Telomeres

- **It is not yet known whether shorter telomeres are just a sign of aging - like gray hair - or actually contribute to aging.**
- **Differences in the telomere length account for only 4% of the increase in death risk. Another 6% is due just to chronological age.**
- **When the telomere length, chronological age, and gender are combined (women live longer than men), those factors account for 37% of the variation in the risk of dying over the age of 60.**

**What are the causes of the remaining
63 percent?**

Cellular senescence = Cell stress

- **Wear-and-tear** - gradual accumulation of random molecular injuries (increased expression of abnormal proteins – mutations)
- **Oxidation** - free radical effects
- **Apoptosis** - Programmed cell death due to genetic events
- **Metabolic insufficiency**
- **Chronic hypoxia**
- **Immunity issue**
- **Psycho-distress**

Oxidative stress

- **A major cause of aging is "oxidative stress." It is the damage to DNA, proteins and lipids (fatty substances) caused by oxidants and free radicals, which are highly reactive substances containing oxygen.**
- **These oxidants are produced normally when we breathe, and also result from inflammation, infection, and consumption of alcohol and cigarettes.**

Metabolic

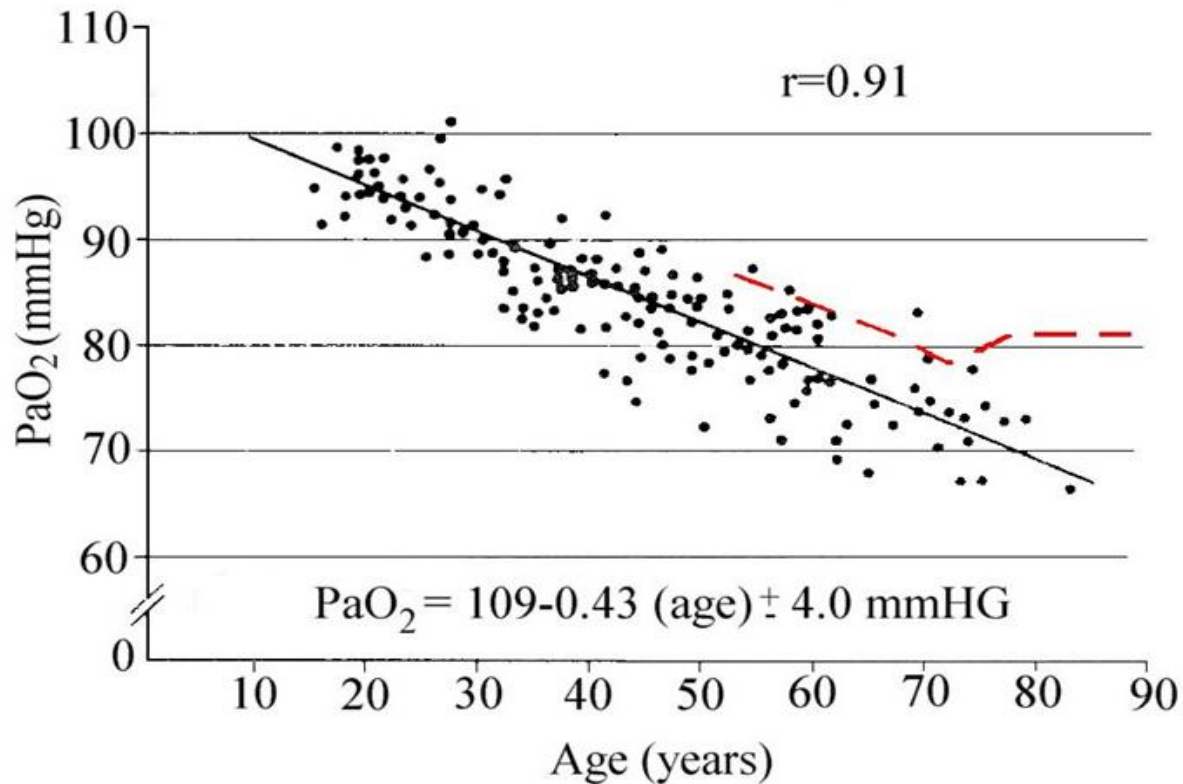
Amount of metabolic potential is genetically fixed for an individual

live fast – dye young

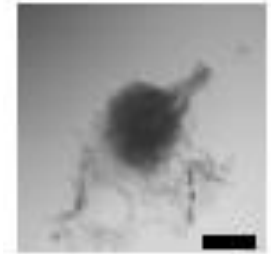
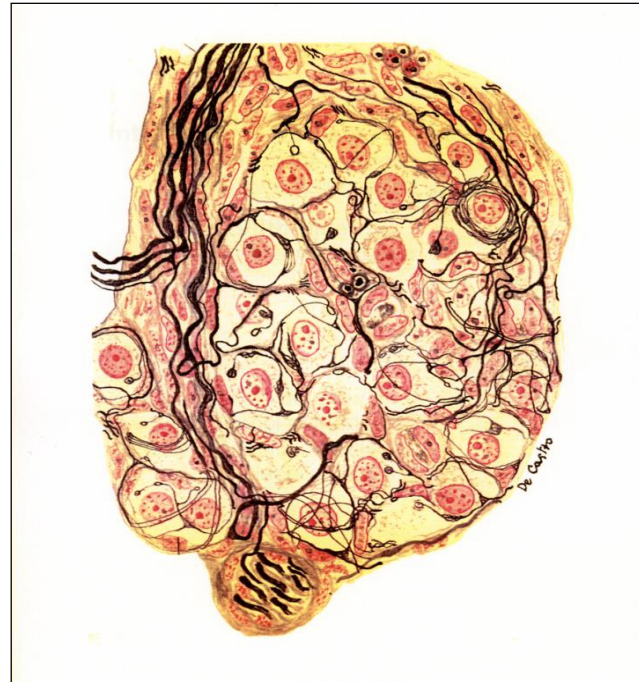
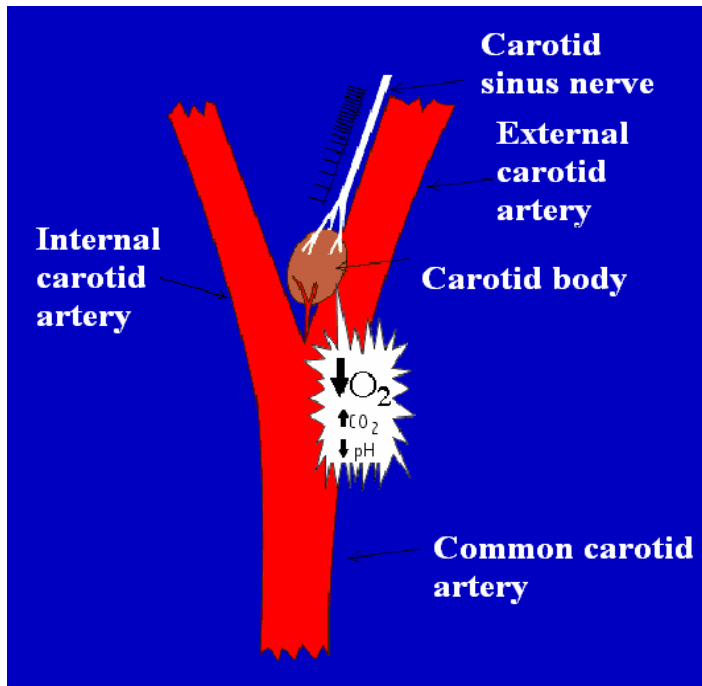
Food consumption, most often regarded as metabolic fueling, does not extend longevity.

Hypoxia

Arterial oxygen content change with age



Carotid Body



0.5 mm
In the rat

In 1938 Heymans got a Noble Prize for the discovery of carotid body function.

Immunology

- **Decline of immune function and immune dysregulation with aging results in an increased incidence of infectious and autoimmune diseases.**

Cellular immunity

- Interrelationship of aging, immunity, and infections was recognized by Elie Metchnikoff at the turn of the 19/20th century.
- He created the concept of phagocytosis – a major defence mechanism of cell-mediated immunity.
- That theory started the popularity of fermented milk products, particularly yogurt, to counteract the aging process and extend longevity – **intestinal microbiota involvement !!**

Geriatric infections at age > 65 years	Mortality rate when compared with young adults
Pneumonia	3
Urinary tract infection	5
Renal infections	10
Infective endocarditis	2-3
Bacterial meningitis	3
Tuberculosis	10
Sepsis	3
Cholecystitis	2-8
Appendicitis	15-20

Modified from Yoshikawa; J Infect Dis, 1997

Geronto-immunology

- **Aging has its greatest impact on cell-mediated immunity, with a lesser effect on humoral immune function.**
- **Cytokine synthesis, activity, and receptors are affected.**
- **There is an increase in cytokine antagonists resulting in a reduced production of IL-2, which decreases T cell proliferation.**

Geronto-immunology

- **Response to pyrogenic cytokines is low – no fever or lower fever than in younger persons.**
- **Temperature fails to reach the criterion for “fever”, i.e., 38°C.**
- **Seniors have a lower-than-normal baseline core body temperature.**
- **It has been recommended that a rise in body temp by 1°C should be a criterion for fever rather than a sheer temp. level in the elderly persons .**

Geronto-pharmacology

- In elderly patients, β -lactam antibiotics should be considered as first-line therapy:
 - effective
 - favorable pharmacokinetics (high serum levels and infrequent dosing)
 - no need for measuring serum concentrations,
 - safe

Vaccinations

- **Immunizations with tetanus toxoid, influenza, COVID-19, RSV (respiratory syncytial virus), herpes zoster, and pneumococcal vaccines are recommended for the elderly persons.**

Geronto-psychology

- **Distress defined as the imposed demands that are perceived as exceeding the ability to cope with (Lazarus & Folkman, 1984).**
- **Stressful events put the elderly at risk of disease.**

Dementia

- **Dementia is not a specific disease. It's an overall term that describes a wide range of symptoms associated with a decline in memory and other mental skills that are severe enough to reduce a person's ability to perform everyday activities.**
- **Dementia is often incorrectly referred to as "senility" or "senile dementia" as it is not a normal part of aging.**

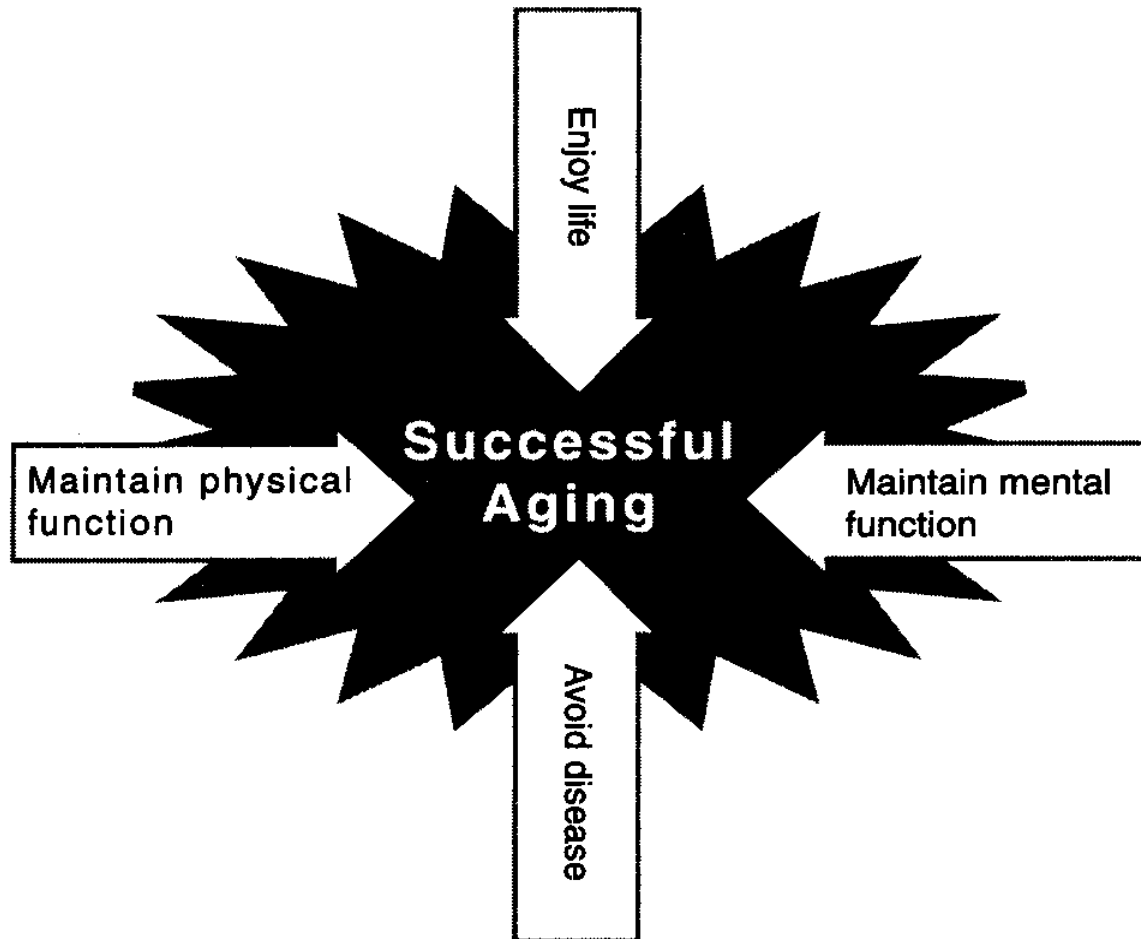
Challenges for the future

- **Training programs should include a curriculum on:**
 - **biology of aging**
 - **geriatric pharmacology**
 - **unique aspects of elderly clinic (epidemiology, clinical manifestations, treatment, prognosis, and prevention).**
- **Continuing medical education and research on the process of aging.**

The time has come for clinicians, educators, and researchers, as well as professional organizations to take a more proactive role in addressing the issues involved with the population aging.

Successful Aging

“No treating illness but supporting wellness”





Pietro BELLOTTI
Parca Lachesi

1625–1700

