

Aging theories

김 태 수

Department of Physical education, Korea Univ.

❖ Scientists Bet Half-A-Billion On 150-Year Lifespan

Lifespan is the maximum number of years that a human can live (~130 years-unchanged).

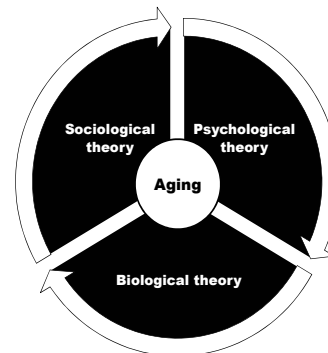


Olshansky



Austad

❖ Categorization of aging theories



❖ characteristic on aging theory

- ◆ Many theories have been proposed to explain the process of aging, but neither of them appears to be fully satisfactory. Jin (2010).
- ◆ There are now more than 300 theories of ageing and the number continue to grow. Medvedev (1990).
- ◆ The history of modern aging study is not more than 70 years.
- ◆ aging is very diffuse and affects many different systems and tissues.
- ◆ Human aging is a long-term process. Goldsmith (2014).

❖ Many classifications of biological theories

1. Era or decade.
e.g. tradition, 50-60's etc.
2. Units of human anatomy.
e.g. molecule, cell, system, etc.
3. inheritance.
e.g. Genetic vs. non Genetic.
4. Modern theory(other terms as same meaning).

Programmed theory.	Non programmed theory.
Non-Stochastic.	Error/damage, Stochastic, Random event.

❖ Classifications of modern aging theories

1. Goldsmith (2014).

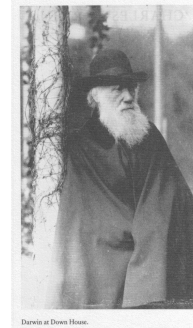
Modern programmed aging theory.	Modern non-programmed theory.
biological suicide mechanism, Program.	Mechanical wear, oxidation, other damage.

2. Jin (2010).

Programmed theory.	damage or error theory.
Programmed Longevity, Endocrine Theory, Immunological Theory.	Wear and tear theory, Rate of living theory, Cross-linking theory, Free radicals theory, Somatic DNA damage theory.

❖ Darwin' s Theory of Evolution

- ◆ Population variation in body structure and behavior.
- ◆ Method of reliable inheritance – Mendel's genes.
- ◆ Natural selection for fitness among variants – too many offspring, depends on reproductive success.



❖ Mutation accumulation theory

- ◆ Recurrent, deleterious, GERM LINE mutations occur.
- ◆ Fewer bearers survive to express later-acting mutations. e.g. cancer.

Lubuncic, & Reznick. (2009).



Peter Medawar
Nobel Laureate for the discovery of immune tolerance

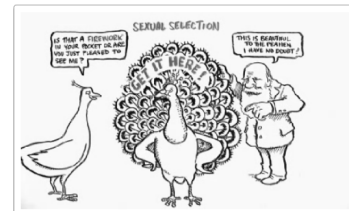


❖ Antagonistic pleiotropy(trade-off) theory

- ◆ Suppose there are mutations are beneficial in youth, but at the price of a higher rate of ageing. Lubuncic, & Reznick. (2009).
- e.g. high testosterone in gorilla leads to arteriosclerosis; large attractive feathers of male peacocks limits their ability to escape predators.



George Williams
American evolutionary biologist



❖ Wear & Tear Theory



Weismann¹ speculated that "death takes place because a worn-out tissue cannot forever renew itself, and because a capacity for increase by means of cell division is not everlasting but finite".

❖ Wear & Tear Theory

Ordinary insults and injuries of daily living accumulate, and over time decrease the organism's efficiency.

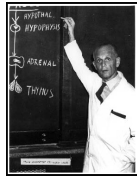
- years of damage to cells, tissues and organs.
- preprogrammed process: biological clock.
- preprogrammed amount of energy → used up.



Human body like your car engine.

❖ Wear & Tear Theory

Hans Selye: The Discovery of Stress (1936)



General Adaptation Syndrome (G.A.S.)

Alarm reaction
childhood

Resistance
adulthood

Exhaustion
senescence



if the duration of stress is sufficiently long, the body eventually enters a stage of exhaustion, a sort of aging "due to wear and tear"

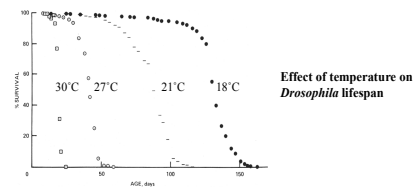
❖ The Rate-of-Living Theory



Raymond Pearl

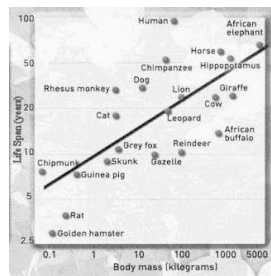
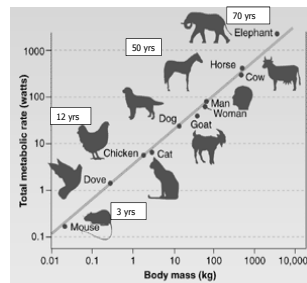
"...the duration of life varies inversely as the rate of energy expenditure ... the length of life depends on the rate of living"

Loeb and Northrop (1916, 1917): increasing temperature reduces *Drosophila* lifespan.



Effect of temperature on *Drosophila* lifespan

❖ The Rate-of-Living Theory



This theory explains why most larger animals live longer than most smaller animals.

- ♦ rapid metabolism = shortest life spans.
- ♦ slower metabolic rates = tend to have longer life spans.

❖ The Hay-flick Limit

- ♦ there is a limit to the number of times cell can divide.
- ♦ cells reach a predefined limit (Hay-flick Limit) replicative
- ♦ senescence causes a non-dividing state.
- ♦ inability to divide represents aging.



Figure 1 | Leonard Hayflick in 1965. Photograph Peter Aronson

- ♦ cells from older organisms divide proportionately fewer times than cells from younger ones.



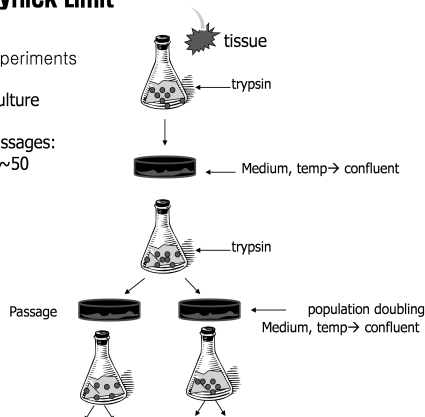
Debunked Carrel (1940): cultured cells were immortal (HeLa Cells)

❖ The Hayflick Limit

Hayflick's experiments

In vitro cell culture

Finite # of passages:
Hayflick Limit~50



❖ The Hayflick Limit

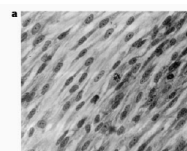


Figure 2 | Young and old human diploid cells (strain WI-38). a) Young cells in phase II at population doubling 20. b) Old cells in phase III at population doubling 55.

Rats : PD ~ 10

3.5



Humans : PD ~ 50

122




Galapagos tortoises : PD ~110

200



Fibroblasts

❖ **Free Radical Theory of Aging**

- ◆ Aging is a result of oxidative damage caused by free radicals generated by the metabolic system.
 - ◆ Free radicals are unstable organic molecules that appear as a by-product of oxygen metabolism in cells.
 - ◆ Free radicals are any number of chemical species that are highly reactive because they possess an odd number of electrons and seek to combine with other molecules to pair off their free electron.
 - ◆ **Damage:** lipids, protein, carbohydrates, nucleic acids, various other cell components
- 



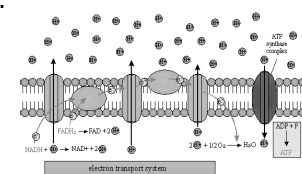
Denham Harman, Ph.D, M.D,

❖ **Free Radical Theory of Aging**

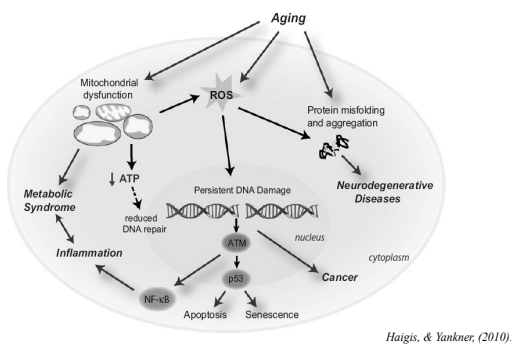
Reactive oxygen species (• = unpaired electrons)				
$\ddot{\text{O}}:\ddot{\text{O}}:$	$\cdot\ddot{\text{O}}:\ddot{\text{O}}:$	$\cdot\ddot{\text{O}}:\ddot{\text{O}}\cdot$	$\cdot\ddot{\text{O}}:\text{H}$	$\cdot\ddot{\text{O}}:\text{H}$
Oxygen O_2	Superoxide anion $\text{O}_2^{\cdot-}$	Peroxide $\text{O}_2^{\cdot-2}$	Hydroxyl radical $\cdot\text{OH}$	Hydroxyl ion OH^-

ROS

Oxygen-derived radicals are generated constantly as part of normal life (2–3 % of O_2).



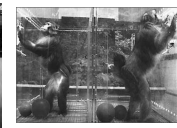
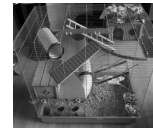
❖ Free Radical Theory of Aging



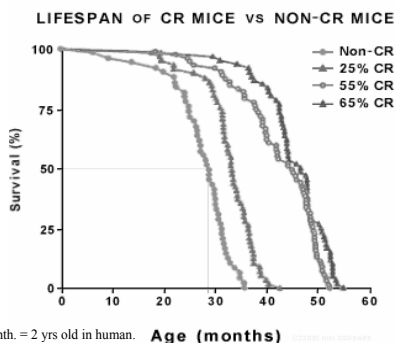
Haigis, & Yankner, (2010).

❖ **Calorie-Restricted theory**National Institute
on Aging ■ ◆ ★ ✨

George Roth, Ph.D.
Long-term study
Began in 1987.



"Until 1987, caloric restriction was never tried in a controlled way with animals that live longer than three years," says Roth. A decade later, we're finally accumulating information on how caloric restriction affects primates.

❖ **Calorie-Restricted theory**

Mice: 1 mth. = 2 yrs old in human. **Age (months)**

❖ **Calorie-Restricted theory**

Okinawan Elders



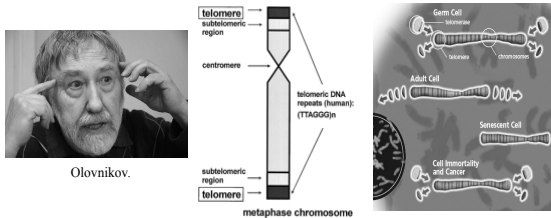
40% fewer calories than Americans and 17% fewer calories than the Japanese average.

Compared to Americans, Okinawan elders
get 80% fewer breast and prostate cancers.
get 50% fewer ovarian and colon cancers .
have 50% fewer hip fractures.
have 80% fewer heart attacks

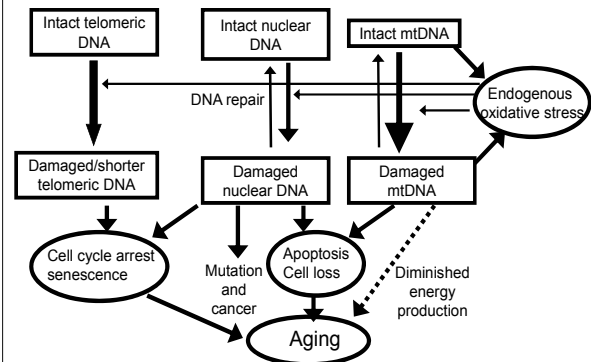
Retrieved from : http://www7.nationalgeographic.com/ngm/0511/sights_n_sounds/index.html

❖ Telomere Hypothesis

- ◆ Telomeres are sequences of all human chromosomes.
- ◆ End pieces of DNA (the tail of DNA).
- ◆ Every time cells divide, telomeres shorten.
- ◆ Once the telomeres become too short, cell division slows and finally ceases and the cell will die.

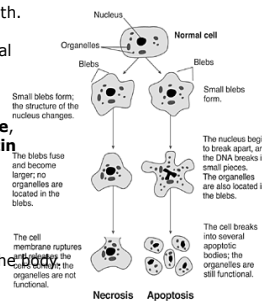


❖ Genomic Alterations with Aging



❖ Apoptosis theory

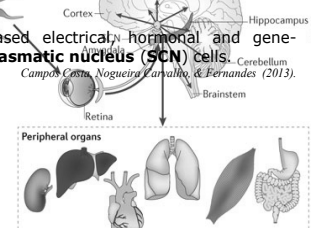
- ◆ **Apoptosis** is programmed cell death.
- ◆ **Necrosis** may occur due to external or internal factors.
e.g. mechanical trauma etc.
- ◆ Apoptosis occurs by **cell shrinkage, protein fragmentation, chromatin condensation, DNA degradation and collapse of cell.**
- ◆ Apoptosis is an important process in that it prevents diseases and controls unnecessary cells within the body.



Apoptosis is defective process.

❖ Bio-clock, circadian rhythm

- ◆ **Circadian rhythms** are generated by an intrinsic cellular mechanism that controls of physiological and metabolic processes.
Orocco-Solis & Sassone-Corsi (2014).
- ◆ **circadian clock** disruption has been shown to increase the ageing rate in mice.
- ◆ Age is associated with decreased electrical, hormonal and gene-expression activity of **supra-chiasmatic nucleus (SCN)** cells.



❖ Reference

- ◆ Campos Costa, I., Nogueira Carvalho, H., & Fernandes, I. (2013). Aging, circadian rhythms and depressive disorders: a review. *Am J Neurodegener Dis*. 2(4), 228-246.
- ◆ Goldsmith, T.C. (2014). *An Introduction to Biological Aging Theory* (Rev. ed). Crownsville, MD: Azinet Press.
- ◆ Jin, K. (2010). Modern biological theories of aging. *Aging and Disease*. 1(2), 72-74.
- ◆ Haigis, M.C., & Yankner, B.A. (2010). The aging stress response. *Mol. Cell*. 40, 333-344.
- ◆ Lubuncic, P., & Reznick, A.Z. (2009). The evolutionary theories of aging revisited-A mini-review. *Gerontology*, 55, 205-216.
- ◆ Medvedev, Z.A. (1990). An attempt at a rational classification of theories of ageing. *Biol Rev Camb Philos Soc*. 65(3), 375-398.
- ◆ Orocco-Solis, R., & Sassone-Corsi, P. (in press). Circadian clock: linking epigenetics to aging. *Curr Opin Genet Dev*. Retrieved from: doi: 10.1016/j.gde.2014.06.003.

*Everyman desires to live long,
but no man would be old.*

