Aging and Its Theories

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Abstracts: Several factors (the lengthening of the average and, to a lesser extent, of the maximum human life span; the increase in percentage of elderly in the population and in the proportion of the national expenditure utilized by the elderly) have stimulated and continue to expand the study of aging. Recently, the view of aging as an extremely complex multifactorial process has replaced the earlier search for a distinct cause such as a single gene or the decline of a key body system. This mini review keeps in mind the multiplicity of mechanisms regulating aging; examines them at the molecular, cellular, and systemic levels; and explores the possibility of interactions at these three levels. The heterogeneity of the aging phenotype among individuals of the same species and differences in longevity among species underline the contribution of both genetic and environmental factors in shaping the life span. In this mini review, several theories are identified only briefly; a few (evolutionary, gene regulation, cellular senescence, free radical, and neuro-endocrineimmuno theories) are discussed in more detail, at molecular, cellular, and systemic levels [Jain P et al NJIRM 2012; 3(1) : 166-168]

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"..Genetic damage (particularly gene loss) is almost certainly a (or probably the) central cause of aging."

Aging is described as the process that reduces the number of healthy cells in the body; therefore, the body loses its ability to respond to a challenge to maintain homeostasis.

Background: Every cell in the human body contains approximately 30,000 genes[1]. While the majority of these genes are responsible for passing on hereditary traits to offspring, there is an extremely important group of about 4000 genes active in controlling, guiding and instructing of any particular cells function. When enough of these 4000 genes become weakened or damaged in any way, we then begin to expertise any of the multitudes of subtle health effects.[1,2,3,4,5]

Aging has been identified as occurring due to four major categories:[1,2,4,]

1) Gene repression: if any important gene is turned off temporarily, that cell will not be working at optimum efficiency for as long as the gene is turned off.

2) Intracellular communication and spatial rearrangements: There is an optimum spatial arrangement of the parts of a cell, tissue, organ

system or body with respect to each other. Any change in physical relationships or in barriers to diffusion, will result in some decrease in optimum function.

3) Accretional defects: The third contributing source of dysfunction during aging is the accumulation of waste materials composed of nonfunctioning or poorly functioning parts of the system.

4) Depletional defects: The final type of change that is responsible for the aging process is the physical loss of functioning parts.

The Neuroendocrine Theory: It was proposed by Professor Vladimir Dilman and Ward Dean. This theory elaborates on wear and tear by focusing on the neuroendocrine system. As we age, the secretion of many hormones declines and their effectiveness is also reduced due to the receptors down-grading[3].

The Genetic Control Theory: This planned-obsolescence theory focuses on the genetic

programming encoded within our DNA. We are born with a unique genetic code, a predetermined tendency to certain types of physical and mental functioning and that genetic inheritance has a great deal to say about how quickly we age and how long we live. When that clock goes off, it signals our bodies first to age and then to die.[14,15,16]

The Free Radical Theory : Now a very famous theory of aging was developed by Denham Harman in 1956. The term free radical describes any molecule that has a free electron, and this property makes it react with healthy molecules in a destructive way. Free radicals are known to attack the structure of cell membranes, which then create metabolic waste products. Such toxic accumulations interfere with cell communication, disturb DNA, RNA and protein synthesis, lower energy levels and generally impede vital chemical processes.[7, 21]

Waste Accumulation Theory: In the course of their life span, cells produce more waste than they can properly eliminate. This waste can include various toxins which when accumulated to a certain level, can interfere with normal cell function, ultimately killing the cell. The presence of a waste product called 'lipofuscin' leading to age pigment support this theory.[9]

Hayflick Limit Theory: Hayflick theorized that the aging process was controlled by a biological clock contained within each living cell.[6]

Death Hormone Theory (DECO): Dr. Donner Denckle speculated that as we age, the pituitary begins to release Decreasing oxygen consumption hormone (DECO) which inhibits the ability of cells to use thyroxine and accelerate the process of aging.

Thymic-Stimulating Theory: It suggests that disappearance of the thymus contributes to the aging process by weakening the body's immune system. [23]

The Mitochondrial Decline Theory: Due to free radical damage, mitochondria lack most of the defences, and as we age, it becomes less efficient and fewer in number. Thus ATP production declines and there is aging.[14,19]

Errors and Repairs Theory: If DNA repair processes for errors that is sometimes done by body, does not exist, scientists estimate that enough damage would accumulate in cells in one year to make them non-functional.[15]

Cross-Linkage Theory: Developmental aging and cross-linking were first proposed in 1942 by Johan Bjorksten. He applied this theory to aging diseases such as sclerosis, a declining immune system and the most obvious example of cross-linking is loss of elasticity in the skin. With age however the number of cross-links increases, causing the skin to shrink and become less soft and pliable. It is thought that these cross-links begin to obstruct the passage of nutrients and waste between cells.[4]

Autoimmune Theory: The immune system is the most important line of defence against foreign substances that enter the body. With age, the system's ability to produce necessary antibodies that fight disease declines, as does its ability to distinguish between antibodies and proteins. In a sense, the immune system becomes self-destructive and reacts against itself.[5,18]

Gene Mutation Theory: In the 1940s, scientists investigated the role of mutations in aging. Mutations are changes that occur in the genes which are fundamental to life. Evidence supporting this idea came from experiments with radiation. It was observed that radiation not only increased animal's gene mutation but it also accelerated their aging process as well.[13,15]

The Rate of Living Theory: Max Rubner who discovered the relationship among metabolic rate, body size and longevity, first introduced this theory in 1908. It simply states that we are each born with a limited amount of energy. If we use this energy slowly, then our rate of aging is slowed. If the energy is consumed quickly, aging is hastened. [12, 24]

Order to Disorder Theory: Dr. Leonard Hayflick states, directing most of our energies to fulfilling a genetically determined plan for the orderly production and arrangement of an enormous number and variety of molecules." After sexual maturation, however, these same energies start to diminish efficiency. Disorder occurs in molecules in

turn causing other molecules to produce errors and so on. These chaotic changes in cells, tissues and organs cause aging.

The Telomerase Theory of Aging: Discovered by scientists at the Geron Corporation. Telomeres are sequences of nucleic acids extending from the ends of chromosomes. Telomeres act to maintain the integrity of our chromosomes. Every time our cells divide, telomeres are shortened, leading to cellular damage and cellular death associated with aging. Telomerase appears to repair and replace telomeres manipulating the "clocking" mechanism that controls the life span of dividing cells. Future development of "telomerase inhibitor" may be able to stop cancer cells from dividing and presumably may convert them back into normal cells.[11,12,13]

The DNA and Genetic Theories: Our DNA is the blue-print of individual life obtained from our parents. It means we are born with a unique code and a predetermined tendency to certain types of physical and mental functioning that regulate the rate at which we age. But this type of genetic clock can be greatly influenced with regard to its rate of timing. For example, DNA is easily oxidized and this damage can be accumulated from diet, lifestyle, toxins, pollution, radiation and other outside influences. Thus, we each have the ability to accelerate DNA damage or slow it down. [11]

The Membrane Theory of Aging: This theory described by Professor Imre Zs.-Nagy. According to this theory, it is the age-related changes of the cells ability to transfer chemicals, heat and electrical processes that impair it. As we grow older, the cell membrane becomes less lipidous. This impedes its efficiency to conduct normal function and in particular there is a toxic accumulation. This cellular toxin is referred to as lipofuscin. It is known that Alzhemier disease patients have much higher levels of lipofuscin deposits than compared to their healthy controls. [12, 24, 25]

Thus, it is clear that some of these theories of aging may be a result of other theories and most of these theories are interlinked.

Finally, approaching any one or a combination of these theories with a specialized treatment protocol will assist the aging problem on different levels, and help to slow down and eradicate some of the so called "pillars of aging".[16, 17]

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