# DOWNLOAD PDF BIOLOGICAL THEORIES OF AGING

## Chapter 1 : Biological Aging Theories

*The programmed theories imply that aging follows a biological timetable, perhaps a continuation of the one that regulates childhood growth and development. This regulation would depend on changes in gene expression that affect the systems responsible for maintenance, repair and defense responses.*

Ageing versus immortality[ edit ] Immortal Hydra, a relative of the jellyfish Human beings and members of other species, especially animals, necessarily experience ageing and mortality. Fungi, too, can age. Early life forms on Earth, starting at least 3. Such organisms prokaryotes, protozoans, algae multiply by fissioning into daughter cells; thus do not age and are innately immortal. The sexual organism could henceforth pass on some of its genetic material to produce new individuals and could itself become disposable with respect to the survival of its species. A number of characteristic ageing symptoms are experienced by a majority or by a significant proportion of humans during their lifetimes. Dementia becomes more common with age. Furthermore, many types of memory decline with ageing , but not semantic memory or general knowledge such as vocabulary definitions, which typically increases or remains steady until late adulthood [41] see Ageing brain. Intelligence declines with age, though the rate varies depending on the type and may in fact remain steady throughout most of the lifespan, dropping suddenly only as people near the end of their lives. Individual variations in rate of cognitive decline may therefore be explained in terms of people having different lengths of life. Senescence year-old woman holding a five-month-old boy At present, researchers are only just beginning to understand the biological basis of ageing even in relatively simple and short-lived organisms such as yeast. A model organism for studying of ageing is the nematode C. Programmed factors follow a biological timetable, perhaps one that might be a continuation of the one that regulates childhood growth and development. This regulation would depend on changes in gene expression that affect the systems responsible for maintenance, repair and defence responses. Damage-related factors include internal and environmental assaults to living organisms that induce cumulative damage at various levels. It is likely that most of these pathways affect ageing separately, because targeting them simultaneously leads to additive increases in lifespan. For example, numerous perennial plants ranging from strawberries and potatoes to willow trees typically produce clones of themselves by vegetative reproduction and are thus potentially immortal, while annual plants such as wheat and watermelons die each year and reproduce by sexual reproduction. In it was discovered that inactivation of only two genes in the annual plant Arabidopsis thaliana leads to its conversion into a potentially immortal perennial plant. In laboratory settings, researchers have demonstrated that selected alterations in specific genes can extend lifespan quite substantially in yeast and roundworms , less so in fruit flies and less again in mice. Some of the targeted genes have homologues across species and in some cases have been associated with human longevity. The strong effect of age on DNA methylation levels has been known since the late s. DNA methylation age of blood predicts all-cause mortality in later life. This resetting into a juvenile state was experimentally achieved by activating the four Yamanaka DNA transcription factors â€" Sox2 , Oct4 , Klf4 and c-Myc which have previously been routinely used for producing young animals from cloned adult skin cells. In humans and other animals, cellular senescence has been attributed to the shortening of telomeres at each cell division ; [76] when telomeres become too short, the cells senesce and die or cease multiplying. Sirtuin in turn inhibits mTOR. When organisms restrict their diet, mTOR activity is reduced, which allows an increased level of autophagy. This recycles old or damaged cell parts, which increases longevity and decreases the chances of being obese. This is thought to prevent spikes of glucose concentration in the blood, leading to reduced insulin signalling. This has been linked to less mTOR activation as well. Therefore, longevity has been connected to caloric restriction and insulin sensitivity inhibiting mTOR, which in turns allows autophagy to occur more frequently. It may be that mTOR inhibition and autophagy reduce the effects of reactive oxygen species on the body, which damage DNA and other organic material, so longevity would be increased. Many have argued that life span, like other phenotypes , is selected. Traits that benefit early survival and reproduction will be selected for even if they contribute to an earlier death. Such a genetic effect is called the antagonistic pleiotropy effect when referring to a gene

pleiotropy signifying the gene has a double function â€" enabling reproduction at a young age but costing the organism life expectancy in old age and is called the disposable soma effect when referring to an entire genetic programme the organism diverting limited resources from maintenance to reproduction. Also, it has been suggested that some of the genetic variants that increase fertility in the young increase cancer risk in the old. Such variants occur in genes p53 [95] and BRCA1. Moreover, the hormones that regulate reproduction also regulate cellular metabolism, explaining the increases in fat deposition during pregnancy through to the deposition of centralised adiposity with the dysregulation of the HPG axis following menopause and during andropause Atwood and Bowen, This theory, which introduced a new definition of ageing, has facilitated the conceptualisation of why and how ageing occurs at the evolutionary, physiological and molecular levels. However, while inflammation is very much evident in old mammals, even completely immunodeficient mice raised in pathogen-free laboratory conditions still experience senescence. In , it was demonstrated that acetylation levels of AMP-activated protein kinase change with age in yeast and that preventing this change slows yeast ageing. DNA damage is thought to be the common basis of both cancer and ageing, and it has been argued that intrinsic causes of DNA damage are the most important drivers of ageing. DNA damage causes the cells to stop dividing or induces apoptosis , often affecting stem cell pools and hence hindering regeneration. However, lifelong studies of mice suggest that most mutations happen during embryonic and childhood development, when cells divide often, as each cell division is a chance for errors in DNA replication. In heart muscle cells, dogs annually lose approximately 3. These numbers are close to the ratio of the maximum longevities of the two species years vs. The comparative percentage is also similar between the dog and human for yearly DNA loss in the brain and lymphocytes. As stated by lead author, Bernard L. A buildup of waste products in cells presumably interferes with metabolism. For example, a waste product called lipofuscin is formed by a complex reaction in cells that binds fat to proteins. This waste accumulates in the cells as small granules, which increase in size as a person ages. The situation, however, has been complicated by the identification that autophagy up-regulation can also occur during ageing. The very general idea that changes associated with ageing are the result of chance damage that accumulates over time. The idea that ageing results from chance events that escape proof reading mechanisms, which gradually damages the genetic code. The idea that ageing results from accumulation of cross-linked compounds that interfere with normal cell function. The authors propose that mtDNA mutations lead to respiratory-chain-deficient cells and thence to apoptosis and cell loss. They cast doubt experimentally however on the common assumption that mitochondrial mutations and dysfunction lead to increased generation of reactive oxygen species ROS. Damage by free radicals , or more generally reactive oxygen species or oxidative stress , create damage that may give rise to the symptoms we recognise as ageing. Notwithstanding the similarly low calorie intake, the diet composition differed between the two studies notably a high sucrose content in the Wisconsin study , and the monkeys have different origins India, China , initially suggesting that genetics and dietary composition, not merely a decrease in calories, are factors in longevity. Once these factors are accounted for, the optimal body weight above age 65 corresponds to a leaner body mass index of 23 to People who live the longest report sleeping for six to seven hours each night. Evidence in both animals and humans suggests that resveratrol may be a caloric restriction mimetic. Of particular note, the treatment began in mice aged 20 months, the equivalent of 60 human years. DePinho and his colleagues published research in mice where telomerase activity was first genetically removed. Then, after the mice had prematurely aged, they restored telomerase activity by reactivating the telomerase gene. As a result, the mice were rejuvenated: Shrivelled testes grew back to normal and the animals regained their fertility. Other organs, such as the spleen, liver, intestines and brain, recuperated from their degenerated state. However, activating telomerase in humans could potentially encourage the growth of tumours. As of [update] , the record for lifespan extension in C. However, the benefits may not be proportional; longevity gains are typically greater in C. One explanation for this is that mammals, being much longer-lived, already have many traits which promote lifespan. Prizes for extending lifespan and slowing ageing in mammals exist. The Methuselah Foundation offers the Mprize. It is a research incentive prize to encourage teams from all over the world to compete in an all-out effort to "hack the code" that regulates our health and lifespan. It was founded by Joon Yun. An elderly man Different cultures

express age in different ways. The age of an adult human is commonly measured in whole years since the day of birth. Arbitrary divisions set to mark periods of life may include: More casual terms may include "teenagers," " tweens ," "twentysomething", "thirtysomething", etc. Most legal systems define a specific age for when an individual is allowed or obliged to do particular activities. These age specifications include voting age , drinking age , age of consent , age of majority , age of criminal responsibility , marriageable age , age of candidacy , and mandatory retirement age. Admission to a movie for instance, may depend on age according to a motion picture rating system. A bus fare might be discounted for the young or old. Each nation, government and non-governmental organisation has different ways of classifying age. Population ageing A map showing median age figures for Population ageing is the increase in the number and proportion of older people in society. Population ageing has three possible causes: Ageing has a significant impact on society. Young people tend to have fewer legal privileges if they are below the age of majority , they are more likely to push for political and social change, to develop and adopt new technologies, and to need education. Older people have different requirements from society and government, and frequently have differing values as well, such as for property and pension rights. Consequently, fertility rates have continued to decline and life expectancy have risen. Life expectancy at birth is over 80 now in 33 countries. Ageing is a "global phenomenon," that is occurring fastest in developing countries, including those with large youth populations, and poses social and economic challenges to the work which can be overcome with "the right set of policies to equip individuals, families and societies to address these challenges and to reap its benefits. According to the United Nations , this process is taking place in nearly every country in the world. In the United States for instance, the Bureau of Labor Statistics estimates that one in four American workers will be 55 or older by  This poses challenges for governments with ageing populations to ensure investments in pension systems continues in order to provide economic independence and reduce poverty in old age. These challenges vary for developing and developed countries. UNFPA stated that, "Sustainability of these systems is of particular concern, particularly in developed countries, while social protection and old-age pension coverage remain a challenge for developing countries, where a large proportion of the labour force is found in the informal sector. In order to elevate this pressure "social protection floors must be implemented in order to guarantee income security and access to essential health and social services for all older persons and provide a safety net that contributes to the postponement of disability and prevention of impoverishment in old age. This has been considered as a negative phenomenon and effective strategies like labour productivity enhancement should be considered to deal with negative consequences of ageing.

## Chapter 2 : Biological Theories of Aging

*Biological Aging Theories. Theories of biological aging need to explain how aging relates to the evolution process. More specifically, if the evolution process has caused organisms to evolve myriad other ways to survive longer and reproduce more, why does aging still exist?*

Age-related deterioration is affecting an ever-growing number of people. There are many theories about the mechanisms of age related changes, and they are mutually exclusive, no one theory is sufficiently able to explain the process of ageing, and they often contradict one another. Modern biological theories of ageing in humans currently fall into two main categories: The programmed theories imply that ageing follows a biological timetable regulated by changes in gene expression that affect the systems responsible for maintenance, repair and defense responses , and the damage or error theories emphasise environmental assaults to living organisms that induce cumulative damage at various levels as the cause of ageing [2]. Modern programmed aging theories â€" There is an evolutionary cost associated with surviving beyond a species-specific age. Theories of Ageing In his review of the modern theories of ageing, Jin [2] highlights three sub-categories of the programmed theory, and four sub-categories of the damage or error theory, and also relates some to how these might be observed in ageing populations. The Programmed Theory 1 Programmed Longevity, which considers ageing to be the result of a sequential switching on and off of certain genes, with senescence being defined as the time when age-associated deficits are manifested. The Damage or Error Theory 1 Wear and tear theory, where vital parts in our cells and tissues wear out resulting in ageing. Further Theories Trindade et al [4] provide a different viewpoint again, stating that to understand the evolution of ageing, we have to understand the environment-dependent balance between the advantages and disadvantages of extended lifespan in the process of spreading genes. These researchers have developed a fitness-based framework in which they categorise existing theories into four basic types: Some of the more commonly discussed theories and their relation to ageing are summarised below: Withdrawal may be initiated by the ageing person or by society, and may be partial or total. It was observed that older people are less involved with life than they were as younger adults. In America there is evidence that society forces withdrawal on older people whether or not they want it. Some suggest that this theory does not consider the large number of older people who do not withdraw from society. This theory is recognised as the first formal theory that attempted to explain the process of growing older. Is another theory that describes the psychosocial ageing process. Activity theory emphasises the importance of ongoing social activity. To maintain a positive sense of self the person must substitute new roles for those that are lost because of age. And studies show that the type of activity does matter, just as it does with younger people. This system is a complicated network of biochemicals that govern the release of hormones which are altered by the walnut sized gland called the hypothalamus located in the brain. The hypothalamus controls various chain-reactions to instruct other organs and glands to release their hormones etc. The hypothalamus also responds to the body hormone levels as a guide to the overall hormonal activity. But as we grow older the hypothalamus loses it precision regulatory ability and the receptors which uptake individual hormones become less sensitive to them. Accordingly, as we age the secretion of many hormones declines and their effectiveness compared unit to unit is also reduced due to the receptors down-grading The Free Radical Theory [7] This now very famous theory of aging was developed [9] by Denham Harman MD at the University of Nebraska in  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. Because the free radical molecule has an extra electron it creates an extra negative charge. This unbalanced energy makes the free radical bind itself to another balanced molecule as it tries to steal electrons. In so doing, the balanced molecule becomes unbalanced and thus a free radical itself. It is known that diet, lifestyle, drugs e. As we grow older the cell membrane becomes less lipid less watery and more solid. This impedes its efficiency to conduct normal function and in particular there is a toxic accumulation The Mitochondrial Decline Theory [7] The mitochondria are the power producing organelles found in every cell of every organ. Enhancement and protection of the mitochondria is an essential part of preventing and slowing aging. In this

theory it is the binding of glucose simple sugars to protein, a process that occurs under the presence of oxygen that causes various problems. Once this binding has occurred the protein becomes impaired and is unable to perform as efficiently. Living a longer life is going to lead to the increased possibility of oxygen meeting glucose and protein and known cross-linking disorders include senile cataract and the appearance of tough, leathery and yellow skin. Further information on video In addition to these explanations, you can see several presentations about the biological theories of ageing on YouTube: The Wear and Tear Theory: Pamela Enz provides two lectures on the theories of ageing: Theories of biological aging. Accessed 25 September  Modern biological theories of ageing. A novel classification system for evolutionary aging theories. Re-engaging the Disengagement Theory of Aging: Activity Theory of Aging. Neuroendocrine Theory of Aging: Chapter 2 Adaptive Homeostat Dysfunction. Accessed 25 September from https: The Membrane Hypothesis of Aging. On the role of cross-linking of cellular proteins in aging.

## Chapter 3 : Theories of Aging - Physiopedia

*Biological Aging Defined Aging is a complex biological process in which changes at molecular, cellular, and organ levels result in a progressive.*

Article Featured Sociological theories focus on the changing roles and relationships that accompany aging. In this blog, we will discuss the following sociological theories: Disengagement Theory The Disengagement Theory, one of the earliest and most controversial theories of aging, views aging as a process of gradual withdrawal between society and the older adult. This mutual withdrawal or disengagement is a natural, acceptable, and universal process that accompanies growing old. It is applicable to elders in all cultures, although there might be variations. According to this theory, disengagement benefits both the older population and the social system. Gradual withdrawal from society and relationships preserves social equilibrium and promotes self-reflection for elders who are freed from societal roles. It furnishes an orderly means for the transfer of knowledge, capital, and power from the older generation to the young. It makes it possible for society to continue functioning after valuable older members die. There is no base of evidence or research to support this theory. Additionally, many older people desire to remain occupied and involved with society. Imposed withdrawal from society may be harmful to elders and society alike. This theory has been largely discounted by gerontologists. Activity Theory The Activity Theory, developed by Havighurst and associates in , asserts that remaining active and engaged with society is pivotal to satisfaction in old age. This mentality is diametrically opposed to the Disengagement Theory. Successful aging equals active aging. Activity can be physical or intellectual in nature, but mainly refers to maintaining active roles in society. To maintain a positive self-image, the older person must develop new interests, hobbies, roles, and relationships to replace those that are diminished or lost in late life. This theory proposes that an older person should continue a middle-aged lifestyle, denying the limitations of old age as long as possible. Likewise, society should avoid the injustice of ageism by applying the same norms to old age as it does to middle age. Society should not demand declining involvement of its aging members. Activity is preferable to inactivity because it facilitates well-being on multiple levels. Because of improved general health and prosperity in the older population, remaining active is more feasible now than when this theory was first proposed by Havighurst nearly six decades ago. The activity theory is applicable for a stable, post-industrial society, which offers its older members many opportunities for meaningful participation. Some aging persons cannot maintain a middle-aged lifestyle, due to functional limitations, lack of income, or lack of a desire to do so. Many older adults lack the resources to maintain active roles in society. On the flip side, some elders may insist on continuing activities in late life that pose a danger to themselves and others, such as driving at night with low visual acuity or doing maintenance work to the house while climbing with severely arthritic knees. In doing so, they are denying their limitations and engaging in unsafe behaviors. Continuity Theory The Continuity Theory of aging relates that personality, values, morals, preferences, role activity, and basic patterns of behavior are consistent throughout the life span, regardless of the life changes one encounters. This theory builds upon and modifies the Activity Theory. Unlike the other two sociological theories, the Continuity Theory offers the backdrop of life perspective to describe normal aging. The latter part of life is simply a continuation of the earlier part of life, a component of the entire life cycle. For instance, a garrulous extrovert at 25 years of age will most likely be a social butterfly at 70 years of age; whereas a laconic, withdrawn young person will probably remain reclusive as he ages. In fact, personality traits often become more entrenched with age. Patterns developed over a lifetime determine behavior, traditions, and beliefs in old age. Past coping strategies recur as older adults adjust to the challenges of aging and facing death. Successful methods used throughout life for adjusting to situational and maturational stressors are repeated. Aging is a complex process, and the Continuity Theory explores these complexities to a greater extent than the other sociological theories, and within a holistic framework. Aspects of aging are studied in regards to their relation to other aspects of human life. It encourages young people to consider that their current behaviors are laying the foundation for their own future old age. What one becomes in late life is a product of a lifetime of personal choices. Within the

sociological theories of aging, variables of ethnicity, gender, lifestyle, and socioeconomic status are only minimally considered, if taken into account at all. None of the three theories can be supported with evidence-based data. Gerontological nursing 7th ed. Concepts and controversies 6th ed. Upper Saddle River, NJ:

## Chapter 4 : Ageing - Wikipedia

*The Cross-Linking Theory of Aging is also referred to as the Glycosylation Theory of Aging. In this theory it is the binding of glucose (simple sugars) to protein, (a process that occurs under the presence of oxygen) that causes various problems.*

Biological Aging Theories Theories of biological aging need to explain how aging relates to the evolution process. More specifically, if the evolution process has caused organisms to evolve myriad other ways to survive longer and reproduce more, why does aging still exist? Simple Deterioration Theories - Fundamental Limitations - "Wear and Tear" Many people believe that biological aging is simply the result of universal deteriorative processes such as oxidation, entropy, or wear and tear that cause aging in machinery, exterior paint, and other inanimate objects. These theories are superficially attractive if only human aging is considered but fail if life span characteristics of other species are also examined. Deterioration and death from aging clearly does not help humans to live longer and breed more so why do we age? Contemporaries actually wrote Darwin and asked this question! The obvious answer is that aging results from fundamental limitations such as laws of physics or chemistry that, by definition, cannot be overcome by the evolution process. There is no question but that many aspects of aging look like the accumulation of damage. Examples are oxidative damage, mutations, and the protein cross-linkages that cause our collagen to lose flexibility with age. But the essential mystery is why the body is able to avoid these problems for many decades, but then permits the damage to occur in old age. And why do some animals age so much more slowly than other, very similar animals? Why would universal laws of physics or chemistry affect biochemically very similar species so differently. These are reasons that aging requires a more complex explanation. Consequently few bioscientists still believe in simple deterioration or "accumulated damage" theories although deteriorative processes such as oxidation and other molecular damage are part of most aging theories. See longer description of wear and tear theories. He suggested that the evolutionary need to live longer decreases following the age at which an organism is first capable of reproducing and also depends on many other internal and external circumstances that are specific to a particular species such as gestation time, mating seasons, predation, and seasonal attrition. There would therefore be strong evolutionary force toward avoiding aging until the age at which an organism could complete a first reproduction. Medawar further suggested that there would be no evolutionary benefit from a species evolving ways to overcome internal causes of deterioration aging beyond the age at which essentially all of the individuals would have died from external causes. If a thousand mice were born today we could easily imagine that under wild conditions few would survive more than two years and therefore the internal ability to survive longer would not have any evolutionary value. This hypothesis was widely embraced by bioscientists because it provided a good explanation for the gross variation in life spans seen in different, but biochemically similar, species. Immortality or even just a somewhat longer lifespan would not help a population and therefore did not evolve. Multiple theorists including G. Wild animal studies confirmed this by showing that wild animal death rates increased with age, which presumably would not happen in an immortal population, or one in which aging caused no disadvantage. These theorists therefore concluded that aging must convey some compensating benefit to offset the declined but still non-zero disadvantage of aging. Some non-programmed theories contend that aging is an unavoidable adverse side-effect of some beneficial function. All such theories have to explain why the evolution process was unable to find a way to accomplish the beneficial effect without the adverse side-effect, a significant difficulty and one of the problems with non-programmed theories. Non-programmed theories compete with each other, have apparent logical flaws, and have difficulty in explaining many observations. The following articles contain descriptions of each of the main non-programmed non-adaptive, passive theories of mammal aging including discussion of their apparent logical flaws:

## Chapter 5 : Theories of Aging: An Ever-Evolving Field

*Programmed aging theories suggest non-aging species result from failures in their aging programs and consequently are likely to become extinct from loss of the long-term evolutionary benefit of a limited lifespan.*

Cancer is to a great degree a disease of the elderly, and age is thus a very important factor in cancer development. However, individuals of any age, including very young children, can be stricken with the disease. In many developed countries cancer deaths inâ€¦ Biological theories of aging Aging has many facets. Hence, there are a number of theories, each of which may explain one or more aspects of aging. There is, however, no single theory that explains all of the phenomena of aging. This theory finds support in the fact that people with parents who have lived long lives are likely to live long themselves. Also, identical twins have life spans more similar in length than do non-twin siblings. Learn about differences in the aging process between human beings, naked mole rats, and the jellyfish Turritopsis dohrnii. The number of repeats in a telomere determines the maximum life span of a cell, since each time a cell divides, multiple repeats are lost. Once telomeres have been reduced to a certain size, the cell reaches a crisis point and is prevented from dividing further. As a consequence, the cell dies. In humans, variations in a gene known as TERC telomerase RNA [ribonucleic acid] component , which encodes an RNA segment of an enzyme known as telomerase, have been associated with reduced telomere length and an increased rate of biological aging. TERC also appears to influence the telomere length that individuals possess from the time of birth. Persons who carry TERC variations are believed to be several years older biologically compared with noncarriers of the same chronological age. This is precisely what happens in the instance of mutations in the TERC gene. Such mutations disrupt the normal function of the telomerase enzyme. As cells grow and divide, a small proportion of them undergo mutation. This change in the genetic code is then reproduced when the cells again divide. Actually, age changes are much more marked in the overall performance of an individual than in cellular processes that can be measured. The age decrement in the ability to perform muscular work is much greater than any changes that can be detected in the enzyme activities of the muscles that perform the work. It is possible that aging in an individual is actually due to a breakdown in the control mechanisms that are required in a complex performance. Aging could also be the result of an accumulation in cells of damaging reactive molecules produced as byproducts of day-to-day cellular activities, such as cellular respiration. Other nongenetic theories consider aging as a complex psychosociological process. Animals, however, unlike machines, have some ability to repair themselves, so that this theory does not fit the facts of a biological system. A corollary to the wear-and-tear theory is the presumption that waste products accumulate within cells and interfere with function. Cross-linking theory With increasing age, tendons , skin , and even blood vessels lose elasticity. This is due to the formation of cross-links between or within the molecules of collagen a fibrous protein that give elasticity to these tissues. These cross-links could alter the structure and shape of the enzyme molecules so that they are unable to carry out their functions in the cell. Glycation, in which simple sugars e. Such effects may be similar to the elevated glucose levels and shorter life spans observed in diabetic humans. Oxidative damage theory Reactions that take place within cells can result in the oxidation of proteins and other cellular molecules. Oxidation entails the loss of electrons from these molecules, causing them to become unstable and highly reactive and leading to their eventual reaction with and damage of cell components such as membranes. Such reactive molecules are known as free radicalsâ€”any atom or molecule that has a single unpaired electron in an outer shell. Oxidative damage oxidative stress accumulates with age, and this has given rise to the free radical theory of aging, which is concerned in particular with molecules known as reactive oxygen species ROS. This theory was first proposed in the s by American gerontologist Denham Harman and was supported in part by evidence that antioxidant proteins, which neutralize free radicals, are more abundant in aging cells, indicating a response to oxidative stress. The initial free radical theory of aging was later extended to include ROS derived from cellular organelles known as mitochondria , which are the primary sites of energy production in most eukaryotic organisms eukaryotic cells are cells with clearly defined nuclei. This in turn results in the accumulation of mutations in mitochondrial DNA and a

bioenergetic impairment, characterized by the failure of mitochondria to produce sufficient energy for cells to carry out their daily activities, which leads to tissue dysfunction and degeneration. Another consideration is the molecular inflammatory theory of aging, whereby the activation of redox- oxidation-reduction - sensitive transcription factors molecules that control gene activity by age-related oxidative stress causes increased expression of proinflammatory genes, leading to inflammation in various tissues. This inflammatory cascade is exaggerated during aging and has been linked to many age-associated pathologies, including cancer , cardiovascular disease , arthritis , and several neurodegenerative diseases. A year-old man with advanced rheumatoid arthritis. Such effects of calorie restriction have been attributed to its ability to lower the steady state of oxidative stress, slow the accumulation of age-associated oxidative damage, and increase metabolic efficiency. A common phenomenon in all of the aforementioned theories is that ROS serve as a contributing factor to many age-associated diseases. As people grow older, their behaviour changes, their social interactions change, and the activities in which they engage change. The psychosociological theory of aging can be divided roughly into four component theories: Disengagement theory is based on hampered relationships between a person and other members of society. Life-course theory is based on the developmental stages proposed by German-born American psychoanalyst Erik H. Continuity theory states that older adults try to preserve and maintain internal and external characteristics e. The distinction between semelparous and iteroparous modes of reproduction is important for an understanding of biological aging. Semelparous organisms reproduce by a single reproductive act. Annual and biennial plants are semelparous, as are many insects and a few vertebrates, notably salmon and eels. Iteroparous organisms, on the other hand, reproduce recurrently over a reproductive span that usually covers a major part of the total life span. In plants the senescent phase is usually an integral part of the reproductive process and essential for its completion. The dispersal of seeds, for example, is accomplished by processesâ€”including ripening and falling abscission of fruits and drying of seed podsâ€”that are inseparable from the overall senescence process. Moreover, the onset of plant senescence is invariably initiated by the changing levels of hormones , which are under systemic or environmental control. If, for example, the hormone auxin is prevented, by experimental means, from influencing the plant, the plant lives longer than normal and undergoes an atypical prolonged pattern of senescent change. Useful inferences can be drawn from the study of the aging processes of insects that display two distinct kinds of adaptive coloration: The two adaptation patterns have different optimal species-survival strategies: Both adaptations are found in the family of saturniid moths , and it has been shown that the duration of their post-reproductive survival is governed by an enzyme system that controls the fraction of time spent in flight: For example, tiger moths have aposematic, or warning, coloration, which is associated with prolonged post-reproductive survival, increasing their opportunity to condition predators to their warning strategy. Bruce Marlin These examples indicate that in semelparous forms, in which full vigour and function are required until virtually the end of life, senescence has an onset closely coupled with the completion of the reproductive process and is governed by relatively simple enzymatic mechanisms that can be modified by natural selection. Such specific, genetically controlled senescence processes are instances of programmed life termination. The iteroparous forms include most vertebrates, most of the longer-lived insects, crustaceans and spiders , cephalopod and gastropod mollusks, and perennial plants. In contrast to semelparous forms, iteroparous organisms need not survive to the end of their reproductive phase in order to reproduce successfully, and the average fraction of the reproductive span survived varies widely between groups: In iteroparous forms the onset of senescence is gradual, with no evidence of specific systemic or environmental initiating mechanisms. Senescence manifests itself early as a decline in reproductive performance. In species that grow to a fixed body size, decline of reproductive capacity begins quite early and accelerates with increasing age. In large egg-laying reptiles , which attain sexual maturity while relatively small in size and continue to grow during a long reproductive span, the number of eggs laid per year increases with age and body size but eventually levels off and declines. The reproductive span in such cases is shorter than the life span. These comparisons illustrate the influence exerted by factors of population dynamics on the evolution of reproductive and bodily somatic senescence. The proportional contribution of an individual to the rate of increase of the iteroparous population obviously diminishes as the number of its living progeny increases. These facts imply that there is

an optimum number of litters per lifetime. Whether or not these influences of population dynamics lead to the evolution of adaptive senescence patterns has long been debated by gerontologists but has not yet been investigated definitively. There is some evidence that calorie restriction delays reproductive senescence, which can be at least partially explained by the beneficial effects on the hypothalamus and pituitary gland to enhance the secretion of luteinizing hormone , which helps regulate the activity of the gonads, or sex glands. Species differences in longevity and aging There are large differences in life span between some species of animals. The taxonomic stratification of longevity can be seen among the mammals. Primates , generally, are the longest-lived group, although some small prosimians and New World monkeys have relatively short life spans. The murid mouselike rodents are short-lived; the sciurid squirrel-like rodents, however, can reach ages two to three times longer than the murids. In rodents, for example, sciurids such as squirrels may live two to three times longer than murids mouselike rodents. The dependence of life span on these traits can be expressed in the form of an equation: Mammalian life span L in months relates to brain weight E and body weight S in grams and to metabolic rate M in calories per gram per hour. The positive exponent for E 0. The negative coefficient for metabolic rate implies that life span decreases as the rate of living increases, if brain and body weight are held constant. The negative partial coefficient for body weight indicates that the tendency for large animals to be longer-lived results not from body size but rather from the high positive correlation of body weight with brain weight and its negative correlation with metabolic rate. The same kind of relation of L to E, S, and M holds for birds , but there is a tendency for birds to be longer-lived than mammals of comparable brain and body size despite their higher body temperatures and metabolic rates. The larger reptiles have life spans exceeding those of mammals of comparable size, but their rates of metabolism are about 10 times lower, so that their total lifetime energy expenditures are lower than those for mammals. The more highly cephalized animals i. The total lifetime energy output per gram of tissue is about 1,, calories for humans and , calories for domestic animals such as cats and dogs. The above relations hold for the homeothermic mammals, those with nearly constant body temperature. The heterothermic mammals, which are able to enter daily torpor , or seasonal hibernation , thereby reduce their metabolic rates more than fold. The insectivorous bats of temperate latitudes are the most dramatic example: The longevities of arthropod species extend from a few days to several decades. The extremely short-lived insects have a brief single reproductive phase; the longer-lived spiders and crustaceans are iteroparous, with annual reproductive cycles. The inheritance of longevity The inheritance of longevity in animal populations such as fruit flies and mice is determined by comparing the life tables of numerous inbred populations and some of their hybrids. The longevity of sample populations has been measured for more than 40 inbred strains of mice. Two experiments concur in finding that about 30 percent of longevity variation in female mice is genetically determined, whereas the heritability in male mice is about 20 percent. These values are comparable to the heritabilities of some physiological performances in domestic animals, such as lifetime egg or milk production. The slope of the Gompertz function line indicates the rate of actuarial aging. The differences in longevity between species are the result primarily of differences in the rate of aging and are therefore expressed in differences in the slope of the Gompertz function. Comparison of life tables between mouse strains of a single species indicates that the strain differences result primarily from differences in age-independent hardiness factors.

## Chapter 6 : Senescence - Wikipedia

*theories of biological aging The complexity of the aging process diminishes the probability that any one theory would satisfactorily explain aging. The concept that some age-related changes may be programmed, whereas others are stochastic and unpredictable, is now generally accepted.*

The concept that some age-related changes may be programmed, whereas others are stochastic and unpredictable, is now generally accepted. However, some theories include both kinds of changes and are impossible to classify as one or the other. In fact, experts probably would not even agree on a common list of aging theories, so the following list should not be regarded as definitive or exhaustive. A further complication is the need to distinguish between the aging process itself and the effects due to phenomena such as diseases. A detailed discussion of various theories can be found in Modern Biological Theories of Aging Warner et al. Random damage theories The most prominent random damage theoryof aging was proposed by Denham Harman in  This theory postulates that free radical reactions, primarily oxygen- free radicals , cause slowly accumulating damage to nucleic acids, proteins, and lipids that eventually leads to loss of their specific functions in the cell. This damage is caused primarily by the production of oxygen- free radicals as a by-product of normal metabolism in the mitochondria. Thus, while this damage may be slow, it is continuous, and the well-accepted assumption is that the individual cells are unable to neutralize all of the free radicals generated by the mitochondria or to completely repair the damage that occurs. A small amount of free radicals may also be generated in nonmitochondrial biochemical reactions, and by external insults such as radiation. This general phenomenon is also referred to as oxidative stress, and the theory predicts either that the generation of free radicals increases with age, or that antioxidant defense systems decrease with age, or both. Many scientific reports have attempted to prove this theory of aging. They document increased levels of oxidative damage with increasing age in a variety of animal model systems, but rarely has it been possible to implicate this increased damage as a cause of aging. Nevertheless, there is strong evidence that oxidative stress is a major factor in the damage occurring following a stroke or heart attack , two major age-related events leading to loss of organ function or death. It is also thought that oxidative stress is a factor in the age-related loss of neurons that accompanies a variety of neurodegenerative pathologies. Thus, any comprehensive theory of aging must include oxidative stress as a likely factor in the loss of biological function through human aging. The free radical , or oxidative stress, theory of aging is a prototype for other, similar theories that suggest random damage occurs and that much, but not all, of it can be repaired. Complete repair is thought to be impossible, so damage slowly accumulates and eventually leads to dysfunction and overt pathology. These related theories include error catastrophe theory and DNA damage theory. The glycation theory of aging proposes that the nonenzymatic condensation of glucose with amino groups in proteins leads to dysfunction of those proteins, a process that is accelerated in diabetics because of their increased level of circulating glucose. This is well documented in hemoglobin, and for proteins in the eye lens, leading to premature cataract formation. Glycation also leads to protein cross-linking, which not only alters both the structure and function of these proteins, but also prevents their normal degradation. This may generally be true for mammalian species, but birds live much longer than might be predicted by their high metabolic rates and high circulating glucose levels. The wear and tear theory of aging is a similar version of this class of theories. Programmed aging theories The other major group of theories postulates that genetically programmed changes that occur with increasing age are responsible for the deleterious changes that accompany aging. It is well known that development is genetically programmed, so logic dictates that aging changes might also be programmed. The principal systems implicated in this group of theories are the endocrine and immune systems. It has been easy to demonstrate that the immune system changes with age. The major function of the immune system is to recognize foreign biological entities antigens and destroy or inactivate them either by tagging them with very specific antibodies or by directly killing them. To do this, mammals produce circulating cells called lymphocytes in either the thymus T-lymphocytes or the bone marrow B-lymphocytes. However, the thymus gradually disappears and is essentially gone by young adulthood. Thus, further

production of T-lymphocytes depends upon cell proliferation and expansion of the existing pool of T-lymphocytes. The lymphocyte pool always consists of naive T-lymphocytes, which are not yet responsive to a specific antigen, and memory T-lymphocytes, which are programmed to respond to a particular antigen. As age increases, memory T-lymphocytes comprise an increasing percent of the T-lymphocyte pool, and the remaining T-lymphocytes are less able to respond to an immunologic challenge such as a bacterial infection. The immune system is also able to distinguish between foreign antigens and nonforeign antigens. In fact, a number of age-related diseases are thought to be due to these inappropriate autoimmune responses; thus these apparently programmed changes could be important factors in aging. It is also known that the levels of circulating hormones may change with age. This is particularly true for growth hormones, dehydroepiandrosterone DHEA , and melatonin. It is not known whether the decreases observed are developmentally programmed to benefit the organism in some way, or whether they are simply another example of dysregulation with increasing age. A much clearer example is provided by estrogen. Estrogen declines rapidly after menopause in women, and menopause is programmed to occur at about age fifty. Besides the loss of reproductive capability, this decline in estrogen production greatly increases the risk of age-related diseases such as osteoporosis and cardiovascular disease. Thus, late-life programmed changes may produce a variety of effects, many of which are not beneficial. Usually one or more organ or system is more compromised than the others, so failure of that system is identified as the cause of death. Two examples are heart failure and stroke. Whereas the immediate cause of death in both cases is a blood clot that obstructs blood supply to critical cells heart muscle cells or neurons, respectively , the aging-related cause is the gradual obstruction of arteries by protein and lipid deposits. Both genetic and environmental factors may contribute to this deposition, but it can hardly be considered programmed. A continuing controversy is whether there is such a thing as aging without such disease, or whether aging is simply the accumulated effects of wear and tear from disease and the various other life stresses. Are there genes for aging? While it is clear that longevity is genetically determined, it is widely believed that specific age-related changes cannot have evolved by natural selection , because most aspects of aging manifest themselves well after reproduction has ceased in humans. This does not mean that aging cannot be altered by genetic intervention. Work begun in the s, and continued with great success in the s, demonstrated clearly that life span in diverse invertebrate organisms can be dramatically extended by mutations in, or overexpression of, specific genes e. These genes also code for a wide variety of proteins involved in processes such as signal transduction, hormone production, protein synthesis, and metabolic regulation. It has also been possible to isolate a long-lived strain of fruit flies by selecting for female flies that reproduce late in life, suggesting that certain gene combinations may be particularly beneficial in slowing aging. However, although it is clear that genes do control longevity and the rate of aging, this does not mean that aging is precisely genetically programmed in most organisms. Warner See also Accelerated Aging: Disposable Soma; Theories of Biological Aging: Error Catastrophe; Theories of Biological Aging: Modern Biological Theories of Aging. Cite this article Pick a style below, and copy the text for your bibliography.

## Chapter 7 : Theories of Biological Aging | www.nxgvision.com

*Aging: Aging, progressive physiological changes in an organism that lead to senescence, or a decline of biological functions and of the organism's ability to adapt to metabolic stress.*

A heavily lined face is common in human senescence. Organismal senescence is the aging of whole organisms. The Gompertzâ€"Makeham law of mortality says that that the age-dependent component of the mortality rate increases exponentially with age. In , a group of scientists defined nine hallmarks of aging that are common between organisms with emphasis on mammals: Aging has been defined as "a progressive deterioration of physiological function, an intrinsic age-related process of loss of viability and increase in vulnerability. Cloning from somatic cells rather than germ cells may begin life with a higher initial load of damage. Dolly the sheep died young from a contagious lung disease, but data on an entire population of cloned individuals would be necessary to measure mortality rates and quantify aging. The evolutionary theorist George Williams wrote, "It is remarkable that after a seemingly miraculous feat of morphogenesis , a complex metazoan should be unable to perform the much simpler task of merely maintaining what is already formed. For example, a mouse is elderly at 3 years while a human is elderly at 80 years. Planarian flatworms have "apparently limitless telomere regenerative capacity fueled by a population of highly proliferative adult stem cells. The onset of this neurological disease is on average at age 45 and is invariably fatal within 10â€"20 years. Haldane assumed that, in human prehistory, few survived until age  Since few were alive at older ages and their contribution to the next generation was therefore small relative to the large cohorts of younger age groups, the force of selection against such late-acting deleterious mutations was correspondingly small. Therefore, a genetic load of late-acting deleterious mutations could be substantial at mutation-selection balance. This concept came to be known as the selection shadow. If a genetic disaster Antagonistic pleiotropy[ edit ] Another evolutionary theory of aging was proposed by George C. Williams [11] and involves antagonistic pleiotropy. A single gene may affect multiple traits. Some traits that increase fitness early in life may also have negative effects later in life. But, because many more individuals are alive at young ages than at old ages, even small positive effects early can be strongly selected for, and large negative effects later may be very weakly selected against. Williams suggested the following example: Perhaps a gene codes for calcium deposition in bones, which promotes juvenile survival and will therefore be favored by natural selection; however, this same gene promotes calcium deposition in the arteries, causing negative atherosclerotic effects in old age. Thus, harmful biological changes in old age may result from selection for pleiotropic genes that are beneficial early in life but harmful later on. An example of antagonistic pleiotropy may be the trade-off between investing resources in reproduction, rather than maintenance of the body â€" the "Disposable Soma" theory. The reproductive-cell cycle theory suggests that aging is regulated by changes in hormonal signaling over the lifespan. Cellular senescence Cellular senescence upper Primary mouse embryonic fibroblast cells MEFs before senescence. Cells accumulate damage over time, but this may be counterbalanced by natural selection to remove damaged cells. In particular DNA damage , e. This can prevent highly mutated cells from becoming cancerous. In culture, fibroblasts can reach a maximum of 50 cell divisions; this maximum is known as the Hayflick limit. Cells can also be induced to senesce via DNA damage in response to elevated reactive oxygen species ROS , activation of oncogenes and cell- cell fusion , independent of telomere length. The cellular senescence theory of aging posits that organismal aging is a consequence of the accumulation of less physiological useful senescent cells. In agreement with this, the experimental elimination of senescent cells from transgenic progeroid mice [17] and non-progeroid, naturally-aged mice [18] [19] [20] led to greater resistance against aging-associated diseases. Ectopic expression of the embryonic transcription factor, NANOG, is shown to reverse senescence and restore the proliferation and differentiation potential of senescent stem cells. The cellular debris that cells accumulate is not evenly divided between the new cells when they divide. Instead more of the damage is passed to one of the cells, leaving the other cell rejuvenated. Cancer cells avoid replicative senescence to become immortal. This leads to an inescapable dilemma between two possibilities - the accumulation of physiologically useless senescent cells, and cancer - both of which lead

to increasing rates of mortality with age. Curtis in One of the earliest aging theories was the Rate of Living Hypothesis described by Raymond Pearl in [32] based on earlier work by Max Rubner , which states that fast basal metabolic rate corresponds to short maximum life span. While there may be some validity to the idea that for various types of specific damage detailed below that are by-products of metabolism, all other things being equal, a fast metabolism may reduce lifespan, in general this theory does not adequately explain the differences in lifespan either within, or between, species. Calorically restricted animals process as much, or more, calories per gram of body mass, as their ad libitum fed counterparts, yet exhibit substantially longer lifespans. The damage can include breakage of biopolymer chains, cross-linking of biopolymers, or chemical attachment of unnatural substituents haptens to biopolymers. Certain metal ions found in the body, such as copper and iron , may participate in the process. These processes termed oxidative stress are linked to the potential benefits of dietary polyphenol antioxidants , for example in coffee, [36] red wine and tea. These adducts can further rearrange to form reactive species, which can then cross-link the structural proteins or DNA to similar biopolymers or other biomolecules such as non-structural proteins. People with diabetes , who have elevated blood sugar , develop senescence-associated disorders much earlier than the general population, but can delay such disorders by rigorous control of their blood sugar levels. There is evidence that sugar damage is linked to oxidant damage in a process termed glycoxidation. Free radicals can damage proteins, lipids or DNA. Glycation mainly damages proteins. Damaged proteins and lipids accumulate in lysosomes as lipofuscin. Chemical damage to structural proteins can lead to loss of function; for example, damage to collagen of blood vessel walls can lead to vessel-wall stiffness and, thus, hypertension , and vessel wall thickening and reactive tissue formation atherosclerosis ; similar processes in the kidney can lead to renal failure. Damage to enzymes reduces cellular functionality. Lipid peroxidation of the inner mitochondrial membrane reduces the electric potential and the ability to generate energy. It is probably no accident that nearly all of the so-called " accelerated aging diseases " are due to defective DNA repair enzymes. Biomarkers of aging If different individuals age at different rates, then fecundity, mortality, and functional capacity might be better predicted by biomarkers than by chronological age. Biogerontologists have continued efforts to find and validate biomarkers of aging, but success thus far has been limited. Levels of CD4 and CD8 memory T cells and naive T cells have been used to give good predictions of the expected lifespan of middle-aged mice. Genetics of aging A number of genetic components of aging have been identified using model organisms, ranging from the simple budding yeast Saccharomyces cerevisiae to worms such as Caenorhabditis elegans and fruit flies Drosophila melanogaster. Study of these organisms has revealed the presence of at least two conserved aging pathways. Gene expression is imperfectly controlled, and it is possible that random fluctuations in the expression levels of many genes contribute to the aging process as suggested by a study of such genes in yeast. A set of rare hereditary genetic disorders, each called progeria , has been known for some time. Sufferers exhibit symptoms resembling accelerated aging , including wrinkled skin. The cause of Hutchinsonâ€"Gilford progeria syndrome was reported in the journal Nature in May

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*Programmed Theories assert that the human body is designed to age and there is a certain biological timeline that our bodies follow. Programmed Longevity: Aging is caused by certain genes switching on and off over time.*

## Chapter 9 : Theories of Aging | Nurse Key

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