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Review Article

Ayurveda and the science of aging

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ABSTRACT

Since time immemorial, humanity has been concerned with developing and preserving youthful vigor, and extending longevity by stopping or delaying the aging process. By 2030, one in five of the world population will be over 65 years old. Longevity and old age are accompanied with a variety of health challenges and population studies indicate that the elderly will use between three to five times more healthcare services compared to the younger population. Modern medicine has made a great deal of progress in understanding the aging process and in controlling age-associated health issues including heart attacks, strokes, diabetes, cancer, senility, and arthritis. Thus, every individual is now looking forward to a youthful, productive lifespan of 100 or more years filled with unlimited health and opportunity. Research by aging experts is focused on ways to go against the natural order of the aging process in order to delay it. Interventions include among other things anti-aging pills, restricted food consumption and cloning body parts to stay young and delay biological aging. Ayurveda, one of the world's most authoritative mind-body-spirit medicinal systems, offers various concepts of the aging process. This system of medicine includes therapies for healthy aging so as to create an optimal health and lengthen an individual's healthspan by living in harmony with nature. This review will explore various aspects of aging and longevity by comparing the science of aging as defined by modern medicine with the Ayurvedic treatise of *Jara* and *Vriddhavastha*.

1. Introduction

Aging has been defined as the total sum of physiological changes that progressively leads to the death of the individual. It is also defined as the intrinsic, inevitable, and irreversible age-associated loss of viability that render us more susceptible to a number of diseases and death or a progressive functional decline of physiological function and a decrease in fecundity with age [1–4]. Undoubtedly, human aging is associated with a wide range of physiological and cellular changes that limit our normal functions and make us more susceptible to death. Aging has two main components, Chronological Aging which refers to the actual age of the person in terms of years, months, and days. This component of aging is unstoppable, unchangeable and irreversible. Physiological/Biological aging is the second component and refers to an individual's development and changes based on certain cellular or molecular parameters. This involves looking at the individuals as they are and as they function, and not when they are born [5,6]. Thus, biological aging is a set of processes that triggers deterioration of health and ultimately to death as a function of chronological age. Unlike chronological aging, biological aging can be reversed or delayed [5,6]. Other terms that constitute aging include:

Lifespan: It is the period of time during which we are alive. Lifespan also includes the years spent in poor health as there are several age-associated health conditions that lack proper treatment or cure [7,8].

Morbidity: The period of ill health during an individual's lifespan is referred to as morbidity. Although our lifespans have increased significantly due to better nutrition and modern medicine, middle-aged and elderly people suffer many years of ill health before they die. Age-associated diseases include heart disease, stroke, diabetes, osteoporosis, and other chronic problems resulting in the individual being in a state of morbid condition [7,8].

Healthspan: Health span is equal to the lifespan devoid of the amount of time an individual spends in ill health (Lifespan−morbidity). This is the period in an individual's life during

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which the person is generally healthy and free from serious or chronic illness. Thus, healthspan refers to how long an individual lives a disease-free healthy life [4,9,10].

Therefore, biological aging in terms of healthspan is a result of complex structural and functional changes across molecules, cells, tissues and whole body systems. Its manifestation is influenced by several factors including genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intra-and intercellular communication. Since aging is accompanied by impairment of normal physiological functioning of cells, tissue, organs and bodily systems that increases the risk of death, some in the aging field consider aging itself to be a deadly disease [11,12].

There is no one single cause or trigger of the aging phenomenon as there are many different and often conflicting theories of aging. At the cellular level, changes that contribute to aging include reduction in stem cell proliferation in a number of tissues, accumulation of toxic protein aggregates and free radicals, accumulation of senescent cells that trigger inflammation and impairment in mitochondrial function. At the genomic level, accumulation of mutations in DNA together with faulty DNA repair processes and telomere shortening are all associated with early signs of aging. Several researchers believe that a combination of several of these factors may contribute to overall aging [13–16]. Theories of aging include but are not limited to a) Genetic theory of aging, b) Damage or Error theory, c) Dilman's Neuroendocrine theory, d) DNA damage theory, e) Free radical damage theory, f) Gene mutations, g) Cell divisions/telomere shortening, h) Cellular senescence and i) Antagonistic Pleiotropy [12–16]. Some of these causes may appear non-specific with regard to suitable interventions, because it is unclear which among them is more amenable to pharmacological intervention in order to reverse the aging process.

2. Factors that promote biological aging

While aging in itself is inevitable, there are ways to reduce or delay the pathological effects of aging. This involves looking at strategies to combat aging both at the cellular and/or genomic level and to see if any of the above mentioned triggers of aging are amenable to suitable drug interventions. Researchers propose at least seven highly intertwined processes that promote aging, thus providing a format for the identification of program mediators and therapeutic candidates. Deciphering these factors that are also responsible for age-associated diseases will be helpful in drug discovery efforts to decelerate aging [4,9]. Among these factors, one that has inspired a lot of excitement is metabolism, and researchers have been trying to understand why caloric restriction extends the life span in mice and other animals [17–21]. Metabolizing fewer calories could result in reduced oxidative damage or alternatively, absence of nutrients may trigger certain defense mechanisms that protect the body from decaying. Researchers have managed to identify several molecular pathways that govern metabolism. Modification of these pathways or their specific products through proper drug-based interventions, could one day mimic the life expanding effects of caloric restriction in humans without compromising on the food intake [16,19–23].

Another factor that is being thoroughly explored is the fallout from long term chronic inflammation. While several age-associated diseases involve the inflammatory process, long lived healthy individuals including centenarians are generally free from age-associated inflammatory diseases [24–26]. Interventions targeted to reduce chronic inflammation are being examined closely for their life enhancing effects [27–29]. Inflammation cannot be completely shut down as our bodies need the short term adaptive inflammatory process to fight infections and ward off short term stress [30–32]. Thus, we need to better understand the inflammatory process at a molecular level to see if drugs can be developed that specifically target the aberrant pathways.

In addition, extension of lifespan in humans could also be achieved by lowering the rate of free radical induced-oxidative damage to tissues, replacement and/or rejuvenation of damaged tissues and cells, reversal of harmful epigenetic changes, or enhancing the telomerase activity [33–35]. Several experts are also developing strategies to combat multiple age-associated diseases at the same time [23,36].

Aging is a major risk factor for most chronic diseases and researchers agree that if we can address the issue of aging itself, we could potentially delay and diminish age-associated diseases all at once [11,12]. Researchers are looking at slowing down aging with the premise that a drug targeting the aging process will not only slow down aging but will also delay age-associated pathologies and diseases [37,38]. This approach is very attractive as researchers do not need to discover drugs to combat specific age-associated conditions like cancer, diabetes or dementia, but instead treat the aging process itself [4,9,37,38].

3. Therapies for a successful healthspan

1) The free-radical theory of aging suggests that antioxidant supplements, such as vitamin C, vitamin E, Q10, lipoic acid, carnosine, and N-acetylcysteine, might extend human life. However, despite several studies, it is not clear if β-carotene supplements and high doses of vitamin E extend life span or increase mortality rates [28,39,40].
2) Resveratrol is a sirtuin stimulant that has been shown to extend life in animal models, but the effect of resveratrol on lifespan in humans is unclear [41–44].
3) The anti-diabetes drug metformin has shown to extend the life of animals and the US-FDA has permitted a clinical trial to see if the life-extending benefits replicate in humans. If metformin turns out to be successful in delaying the aging process, a person taking metformin would be young at 90 [44–46].
4) Drugs like acarbose (a common drug prescribed for Type 2 diabetes), and anti-inflammatory drugs such as masoprocol and basic aspirin extend lifespan in mice, but these drugs can have multiple effects, and their mechanism of action is not clear. The fact that they tackle chronic inflammation could just be one piece of the puzzle, not the whole solution [47–49].
5) The most promising drug to combat aging has been rapamycin, an immunosuppressant often used in organ transplants. In addition to life span extension, rapamycin has an unbelievably wide range of effects in mice ranging from preventing Alzheimer's and cardiovascular disease to reducing cancer [44,50,51].
6) Non-drug therapies that extend lifespan include calorie restriction (CR). CR also retards age-related chronic diseases in a variety of species, including rats, mice, fish, flies, worms, and yeast. The mechanism through which this occurs is unclear [17–21].
7) Therapeutic cloning, body part replacement and stem cell research could one day provide a way to generate cells, body parts, or even entire bodies that do not decay [52–54]. Researchers have succeeded in growing artificial body parts in the lab, including nose, ears, tear ducts, bladders and blood vessels from human stem cells. The use of human stem cells for the purpose of cultivating organs, that can be transplanted into people, is another attractive approach to combat age-associated organ decay [55–58].

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