

Humoral Theory Of Aging: A Narrative Review

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ABSTRACT

The phenotypic appearance of aging is easy to recognize, but the mechanism of aging is complex and ill-understood. Several attempts have been made to unravel the mystery of aging, but the search for a universally accepted general theory of aging is still ongoing. Aging is the inevitable, irreversible, continuous process that results in deterioration of organs, leads to functional impairment, decreases the ability to adapt to the environment, and responds to challenges to maintain homeostasis, ultimately causing death. In the elderly, phenotypic manifestation is the result of a sequence of changes that takes place at the cellular, molecular, tissue, and organ levels. According to the principle of Unani medicine, the entire universe, including the human body, is built of four basic constituents, fire, air, earth, and water, called arkān (elements). Each of the arkān has its specific qualities and properties. During the formation of a compound by intermixing of the basic constituents (ark ān), the mutual interaction among the four contrary primary qualities of arkān generates a specific quality in the compound, which is uniform throughout, called the temperament of that compound/ body. As the interaction of arkān in the compound is an incessant process, it causes refashioning in temperament throughout the ages. The temperament of adulthood is hārr raṭb (hot-moist), which is regarded as mu'tadil (equipoise or moderate); with advance in age, the body temperament shifts towards cold-dry. The temperament of the elderly is cold-dry, which causes structural deformity, decline in vigor, and intellectual power.

Keywords: Aging, Geriatrics, Gerontology, Humoral theory, Temperament.

1. INTRODUCTION

It is believed that geriatric medicine evolved in the twentieth century AD, However, description of the health of the elderly, interest in prolongation of the life span, and philosophy of death have been traced back to the Hippocratic corpus. In the Hippocratic era, medical scholars and philosophers attempted to describe the all-natural phenomenon, including birth, health, disease, aging, and death in a rational way, which was further contributed to by Greek, Roman, and Arab physicians.¹ Till the mid-nineteenth century, the art of medicine was solely based upon the Humoral theory of Hippocrates. Modern geriatricians assume that geriatric medicine was an invention of the twentieth century. But there is a little controversy about its establishment. Some American geriatricians assert that it was created by Ignatz Nascher in 1909, who coined the term geriatrics. While British geriatricians claim that it was founded in 1935 AD, in London, associated with the work of Marjory Warren.^{1,2,3,4} In 1976, Strehler postulated that aging is a universal, intrinsic, progressive, deleterious phenomenon.⁵ The American gerontologist defined aging as intrinsic, deleterious, progressive changes throughout the life span (must also occur in young individuals), a universal phenomenon that occurs in different degrees in all individuals of a species.⁶

Old age: Age is the measurement of time of the existence of a person or object and is estimated from the degree of anatomical development. For human beings, old age is the chronological age of 60 and above (from birth).⁷ Senescence is progressive structural and functional deterioration over time in normal human ageing. The concept of old age is multidimensional, which includes chronological, biological, psychological, and social age.^{8,9} In this study, the word elderly

is used for a person of old age.

Modern Theories of Aging: The signs and symptoms of ageing are as simple to recognize, but the process of ageing is as complex to understand. Live a long life and remain young till the last breath has always been the desire of human beings. Throughout history, medical scientists and philosophers have tried to unfold the mystery of ageing, prolongation of the lifespan, and the maintenance of good health in old age. Aging characteristics and lifespan vary enormously from species to species and within species, too.¹⁰ In the recent past, several attempts have been made to decode the process of aging, and a large number of theories have been postulated in this regard. In 1990, about 300 theories of aging were listed by Zhores Medvedev. Out of these many like, the rate of living theory proposed by Pearl, the preliminary version of the wear and tear theory, Rubner's theory, Mechnikov's theory, the poisoning theory, the entropy theory, etc, are outdated, hence, obsolete in the light of the contemporary knowledge of the biological basis for aging.¹¹ Many theories consider aging and death as a programmed event called programmed theories, while many others consider aging as a result of environmental distress to living organisms that induce progressive damage at several levels called the error theories, and many theories contain certain elements of both the mentioned category is categorized as a third separate category called Combined theories.^{5,12} But to date, none of the theories could explain aging satisfactorily. The search for a general theory that can explain the phenomenon is continued

Programmed theories (Adaptive/Active): These theories argue that ageing is programmed by genes and beneficial for the species and group. It suggests that, like apoptosis in a multicellular organism, programmed death happened.¹³ A German biologist, Agust Weismann (1834-1914) explained ageing on evolutionary arguments, and articulated the idea that aging is a programmed trait that is beneficial for the species.^{14,15} These theories favor natural selection for the fittest; according to this, post-reproductive individuals are purposefully eliminated to avoid overpopulation for the benefit of young animals and speed up evolution. Hence, ageing is teleological and altruistic.^{11,13,16} Therefore, death is not a primary necessity; rather, it is a secondary acquired adaptation to eliminate the less valuable or harmful individuals from a given population.¹¹ Programmed theories did not specify and predict the mechanisms of death.¹³ Weismann attempted to explain the evolution of aging.¹⁷

Non-programmed /Stochastic theories (Error theories): Many researchers believe that ageing is the continuation of developmental growth.¹³ These processes are neither adaptive nor altruistic, and not even genetically programmed. It is a passive and non-programmed, irreversible, progressive, gradual accumulation of random molecular and cellular damage that is non-adaptive at the levels of natural selection.^{11,18} It is non-altruistic and not genetically programmed. According to this view, aging is a multi-causative accumulation of random molecular damage that can't be directly controlled, hence, difficult to eliminate by some sophisticated or therapeutic methods.¹⁹

Quasi-programmed theories: The arguments of these theories are different from both programmed and error theories. A quasi program is a developmental program that is not switched off on its completion; rather, it continues without purpose. According to these theories, aging is a manifestation of the developmental process, which finally leads to death.^{20,21} Growth and development are strictly programmed events; when they finish, cellular normal functions become hyperfunctions that lead to disease. Development is precise because of programming, ageing is not; therefore, age-related diseases occur at different ages.²¹ Aging in Pacific salmon and menopause in women are the manifestations of the aging process, which are quasi-programmed. The mechanism of aging is predicted by the mechanism of growth, differentiation, and development. The developmental growth and the onset of reproduction are genetic programs; after completion of these programs, it becomes quasi-programs. According to this, genes that are useful and crucial for growth, development, and survival in early life become harmful in later life, leading to senescence. Growth and development are purposefully programmed, and ageing is an aimless continuation of this program that was not switched off upon its completion.¹³ The above explanations contradict the programmed theory of natural selection.

Table.1

Comparison between three models of aging							
Model of aging	Programmed?	Altruistic?	Relation with disease	Menopause is...?	Extra calories are..?	Purposeful?	Beneficial for the organism?
Programmed	yes	Yes	Non-specified	Programmed and beneficial	unspecified	Yes	Yes

Non-programmed	No	No	vulnerability to diseases	beneficial	Beneficial for Health and delay ageing	No	No
Quasi-programmed	Never	No	manifested by diseases	not beneficial	accelerate aging via mTOR	No	No

Humoral theory of aging: Hippocrates and his fellow described the entire phenomenon of health and disease based upon humoral theory, which reflects the philosophical idea that everything is made up of four elements, namely earth, water, air, and fire.²² Later, his legacy flourishes much more and fully develops in later Western Greek and Latin medicine, and then in medieval and European thought, which remained the mainstream medical tradition for more than 2500 years and to date is in practice.²³ According to Unani medicine, human life is broadly categorized into four stages, which are as follows-

Growing age (Sinn-i-Numū): This is the nearest to birth, hence the amount of innate moisture is maximum at this stage of life, which is gradually utilized in growth and development as well as in the maintenance of life.²⁴

Adulthood (Sinn-i-Shabāb): The temperament of adulthood is hot and dry; it is near to the motadil (equipoise) but drier than the growing age and moister than the age of decline and superannuation.⁹

Age of decline (Sinn-i Kuhulāt): The temperament of this age is cold-dry, in this stage, the best vigor has passed, and the intellectual power begins to decline. Temperament is cold-dry but less in acuity than that of the elderly.^{25,26}

Age of superannuation/ Senility (Sinn-i-Shaiykhūkhat): In this stage, the vigor and intellectual power both obviously decline.²⁵ The philosophy of innate heat provides the earliest explanation of the phenomenon of aging and death. According to this philosophy, an organism gets moisture at the time of conception called innate moisture, which is essential for the maintenance of life, because it feeds the spirit and innate heat.⁹ The synonyms of innate moisture are Ruṭūbat-e-gharīziyya; Humidum radical/primigenium; Primitive moisture/humor, and synonyms of innate heat are Ḥarārat-e-gharīziyya; Calidum innatum; Calor innatus/nativus/vitalis; and vital heat.^{27,28} During fetal formation, the body gets a special quality called innate temperament (Mizāj ulā) from the parent through the seed of conception, which provides a unique property to the body.²⁹ The temperament is individual specific, and the duration of life depends on this innate temperament; hence, it accountable for the different durations of each one's life.⁹ Innate heat is not elemental heat it is different from temperament. It is inherited from the parent at the time of conception through the seed in the innate moisture.³⁰ In the human body, the innate heat spreads from the heart through the arteries to the whole body to operate the vital functions and is cooled down by the inspired air in the lungs.^{31,32} It is the tool for the vegetative soul to achieve the physiological functions of life and generation.²⁷ A fixed amount of innate moisture received at birth from the parent, refreshed by food, provides fuel to the innate heat, hence undergoes a slow consumption and dissolution, which reflects in aging, ultimately leading to extinction and the death of the organism.^{24,28} The intensity of innate heat and quantity of innate moisture also determine their respective temperament. There are three different opinions about the intensity of innate heat at different stages of life. One group of scholars believes that innate moisture is maximum and moderate in heat during the growing age because it is nearest to birth. Another group of scholars believes that the innate heat of adulthood is far greater than that of growing age, because of their hotter temperament, more energetic movement, better digestion, and plenty of thicker blood. But Galen's teaching is opposed to both of the above groups. As per his opinion, heat is the same in each age group. As he says—"let us imagine first a single measure of 'heat,' or a subtle body of unit heat, penetrating an abundance of moist substance—as it might be, water. Then imagine a unit of heat penetration through a small bulk of stone. The heat in the water would then be more in quantity but less in quality, whereas the heat in the stone would be less in amount but of great intensity. This is analogous to the state of affairs regarding the heat of juvenility and youth".^{9,30} Innate moisture is the material cause of growth, and innate heat (instrumental cause) utilizes it for growth and other vital functions. Life itself depends upon the innate heat, and growth depends on innate moisture. Indeed, the innate heat is present in and nourished by innate moisture. At the initial stages of life, the innate moisture is adequate for the maintenance of innate heat and growth. The innate moisture is being steadily used up by innate heat for growth and development, as well as in the accomplishment of all vital and organic functions, resulting in its lessening both in quantity and quality. Environmental factors and pathological conditions also contribute to drying up this moisture.²⁶ Innate heat protects the body from unhealthy physical conditions, and during disease conditions, nature tries to bring these pathological irregularities to a normal state, apparently by the action of innate heat, which leads to the premature dissolution of innate moisture. Premature consumption or corruption and dissolution due to faulty diet, regimen, physical factors, and disease of the innate moisture may lead to early aging and premature death.⁹ With the advancement in age, the degree of innate moisture is declining both in quantity and quality; ultimately, the moisture is in too small a proportion, which becomes

insufficient to maintain the innate heat. After the prime of life, the innate heat of the body begins to fail. This is the mechanism by which the innate heat remains at a constant level up to senescence. During these periods, there is no corresponding growth.^{29,33,34}

2. DISCUSSION:

According to humoral theory, the maximum life span is fixed and coded in innate temperament (mizāj ulā), which is individual-specific.²⁴ Every individual gets a fixed amount of innate moisture from their parent at the time of conception, which undergoes slow consumption in growth, development, and maintenance of life, ultimately becoming insufficient to sustain life, resulting in death.³⁴ As a result of metabolism, the gradually increasing production and accumulation of alien moisture causes hindrance in the nourishment of organs, leads to dryness of the primitive fluid (rutūbate asliyya), and causes damage to organs.^{26,30} The effect of six essential factors for life (Asbāb sitta darūriyya) and non-essential factors influences the rate of consumption of innate moisture.^{35,36} Every organism has a unique temperament. The temperament of the child is hot-moist, which gradually shifts towards cold-dry, and death is the ultimate consequence of a cold-dry temperament.^{24,29} Hence, Maximum lifespan is programmed, but ageing is a multi-factorial meta-phenomenon that leads to progressive intrinsic deterioration of the homeodynamic capabilities of the body, resulting in progressive structural and functional deprivation of organs, making the body vulnerable to disease and eventually death of the organism. Here, the term multi-factorial collectively stands for innate temperament, decreasing amount of innate moisture, decreasing intensity of innate heat, cold-dry temperament, increasing amount of alien moisture, and exogenous environmental factors. In this definition, the term meta-phenomenon collectively stands for interdependent structural and functional deprivation in organs, which reflects as a phenotypic sign of ageing. We can interpret the concept of humoral theory as the maximum life span of an individual is planned and programmed as per their innate temperament (mizāj ulā), but it can be achieved only under the influence of favorable environmental conditions.²⁴ A similar concept has been postulated in gene /biological clock theory, i.e., aging is programmed and coded in the genes of a cell or organism.³⁷ As the organism gets a limited amount of innate moisture at the beginning of life, which is gradually utilized to perform the function of life, leading to a lessening in its amount, it ultimately becomes insufficient to continue life.³⁴ The Telomere shortening theory describes that in somatic cells, a small amount of DNA is lost at each chromosome end at every cell division, resulting in ever-shorter telomeres, which results in terminally arrested cell division. It means cells have a limited replicative capacity up to a critically short length (Hayflick limit), then die out.³⁸ Other than innate temperament and moisture, certain other endogenous and exogenous factors also contribute to aging. As a result of metabolism, alien moisture is produced and accumulates in organs. This alien moisture adversely affects the nourishment of organs and imparts its toxic effect, which leads to senescence and death. A similar explanation has been made in error theories, like in DNA damage, mitochondrial dysfunction, and free radical theories, that, as a result of cellular metabolism, the toxic oxygen-free radicals are generated, which, if not eliminated, lead to accumulation and cause cell damage.⁶ A strong argument of humoral theory is that the temperament of an individual shifts from the hot-moist (of the child) towards the cold-dry with the advancement of age.³⁰ The cold-dry (of the elderly) is the worst temperament for life.³⁹ Coldness of temperament defects the nourishment of organs; enhances the production of alien moisture and causes weakness in faculties, which leads to senescence. Dryness of temperament dries up the essence (A‘dā’ asliyya ka jawhar) of the simple organ. Because of increasing dryness, growth and differentiation cease, the rigidity and fixity increase, which ultimately leads to death.²⁶

3. CONCLUSION:

It is concluded that aging is a programmed phenomenon that results from the extinction of innate moisture and cold -dry temperament. The human being is mortal, and the maximum life span is coded in their innate temperament, which is individualistic. Aging imparts its effect on every organ.

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