Explor Anim Med Res.
Vol. 14, Issue 1, 2024
DOI: 10.52635/eamr/14.1.1-5

ISSN 2277-470X (Print), ISSN 2319-247X (Online)
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Editorial

BIOLOGICAL AGE AND LIFESTYLE: KEY DECIDING FACTORS OF AGING AND DISEASE SUSCEPTIBILITY

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ABSTRACT: The biological age of an individual depends mainly on the genetic status and different epigenetic influences experienced by the individual and it has a direct relationship with aging and suffering from different diseases. It can be understood from the observable physiological parameters like the level of specific health indicators in the body, status of vision and hearing, condition of joints, immunity, nutritional status, presence of inflammatory markers and certain proteins in the blood, etc. Determining factors of biological age include the level of oxidative stress, glycation pattern of the DNA, protein, and lipid; different epigenetic factors, etc. The main genetic biomarkers of biological aging are the length of the telomeres, DNA methylation pattern, and the status of the epigenetic clock of an individual. The epigenetic and other related factors causing early aging and more susceptibility towards gene-related or unrelated diseases can be prevented and reversed by the exclusion of the detrimental practices from the lifestyle along with the inclusion of some positive factors. Lifestyle and nutrigenetics are the subjects engaged in the related study. The 'unique disease principle' describes diseases as an outcome of the disease reasons and environmental conditions (including health status) at the individual level. The microbiome profile and individual immunity status are given importance for the selection of ways to combat diseases in the Molecular Pathological Epidemiology (MPE). A specific diet plan, the DIP diet, is advocated along with following a designed lifestyle and getting assistance with some disease-specific physical measures for combating lifestyle diseases. The succulent parts of the effective medicinal plants are recommended for their direct therapeutic use in unaltered conditions in the form of bio-capsules prepared without the addition of any materials of synthetic origin along with following a designed lifestyle is another branch of research related to the topic.

Keywords: Aging biomarkers, DNA methylation, Length of telomeres, Epigenetic clock, Nutrigenetics, Microbiome, Molecular pathological epidemiology, DIP diet, Succulent biomedicine.

INTRODUCTION

The chronological age is calculated from the birth. It is considered everywhere as important, but not considered so important in the contemporary research of aging and disease susceptibility. For such effects, the biological age is only considered important. The biological age expresses the actual condition of the body at its cellular level and it does not depend completely on the genetics of the individuals. Many physiological, biological, and environmental factors work together from behind to determine the biological age of an individual. Genetic predispositions for the disease/s are also controlled by many such biological factors from behind before actual expression of these to any clinical disease [1, 2]. As per some recent research, the actual health status, aging, and susceptibility to various diseases are all dependent on biological age, environmental conditions along with past and present lifestyle of an individual - not only on the chronological age. The factors like intake of different components in the name of food, drink, healthcare assistance, cosmetics, etc., and their actual

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long-term cumulative effects, and other factors like physical exercise, stress, body clock maintenance, quality of breathing air and physical environment is not less important than the genotype of an individual [3,4].

BIOLOGICAL AGE AND AGING BIOMARKERS

Twelve influencing subjects of aging are listed by the Max Planck Institute for Biology of Ageing. These are genetic instability, degradation of the telomere, epigenetic changes, loss of proteostasis, impaired perception of nutrients, dysfunction of the mitochondria, cellular senescence, exhaustion of the stem cells, altered intercellular communication, deteriorated autophagy, chronic inflammation, and imbalance of the intestinal flora [www.age.mpg.de/how-do-we-age]. Along with chronological age, oxidative stress, glycation patterns of DNA, protein and lipids, and genetic status are also considered as the causative factors for aging by Cawthon (2016) [5]. The subject is analyzed differently by other authors.

A. Physiological biomarkers

It is noticed that even the homozygous twins who live in different environments and follow different lifestyles may have differences in aging parameters [6, 7]. The term biological age denotes the actual current status of the body. It is determined by analyzing some biomarkers in the present stage of research. These aging biomarkers are practically some characteristics that influence some predictions to determine the actual functional state of the body system. These include observable physical parameters like blood pressure, level of cholesterol, the status of vision and hearing, mobility stage of joints, nutritional status, immunity status, different inflammatory markers, and certain proteins in the blood, etc. - as all of these parameters generally show the overall deterioration of the systems along with the increase of age [2, 8, 9]. Two determining factors of such biomarkers are stated below.

i. Oxidative stress

During aerobic metabolism, single-atom oxygen develops, called free radicals, and has scavenging activities. These, if not managed by a supply of sufficient antioxidants, can damage different biomolecules of the body including DNA by acting as Reactive Oxygen Species [10].

ii. Glycation

Due to certain reasons, the glucose molecules bind with some DNA, protein, and lipid molecules of our body. Such binding can hamper the normal functioning of these molecules inside the body. Later, the concerned tissues fail to function properly, leading to early aging, more prone to various diseases and early death [5].

B. Epigenetics and genetic biomarkers

The subject 'epigenetics' deals with the environmental influences on the genes for its expression and proper working. The negative effects of epigenetic changes are generally reversible and generally do not cause any change in the DNA sequence, though the reading of the DNA sequences in the body system can be influenced by such changes. DNA methylation, modification pattern of the DNA wrapping protein histones, and control of the activities of non-coding RNA to decide the synthesis of the proteins in the cells are the three main parts of epigenetics [www.cdc.gov/genomics/disease/epigenetics.htm].

It is observed that the genetic factors behind the risk of developing disease and aging are much more active in the younger age and the non-genetic factors play a very strong role in the latter stage of life. The late-age expressible genes have a higher chance of synthesis of abnormal or defective proteins than the early-age expressible genes [11, www.age.mpg.de/211116/what-is-biological-age].

Among the genetic biomarkers of biological aging, the length of the telomeres, DNA methylation pattern, and epigenetic clock are considered the most important.

i. Length of the telomeres

The chromosomes are made up of nucleotides. At the tail portion of the chromosomes, a long set of nucleotides are set. These nucleotides do not take an active part during the cell division. A portion of them are deleted during every phase of cell division, so the chromosomes become shorter every time. These extra nucleotides are termed as telomeres. The presence of the number of telomere nucleotides is controlled by the enzymatic activities of the cell. It is assumed that the reduction rate of the telomere nucleotide and the consequent rate of reduction of the size of the chromosomes are also influenced by many other non-genetic factors (such as lifestyle). A very high or abnormal shortening of telomere size can induce improper activities of the chromosome (short telomere syndrome - STS) leading to mutations and then the creation of many dangerous diseases.

Due to shortened telomere, the cells may die early and invite many diseases of infectious or non-infectious origin leading to early aging and early death of the

individual. Shortened telomere may cause many other important diseases other than early aging, like different neuro-degenerative disorders, etc. [4, 12]. In such an extreme condition, if the cells are compelled to synthesize more and more telomerase enzymes to increase the number of telomere nucleotides in the chromosome and prevent telomeres from becoming shorter, different cancers develop. These include cancers of the bone, pancreas, lung, prostate, kidney, bladder, neck head, etc. [5, https://dralexisshields.com/biological-age].

ii. DNA methylation pattern

Among the estimated 30000 genes of humans, instructions to carry out individual activities properly may not be performed each time by every one of them. The body has different control procedures over the entire system. But during working continuously, as a normal happening, methylation of the DNA molecules happens. However, the pattern of DNA methylation varies among individuals as per their lifestyle and other factors, like rusting in the iron kept in different environments. DNA methylation can control the expression of genes in many cases.

Examination of DNA methylation pattern is a part of the epigenetic study - the study of the expression of genes based on the lifestyle and the surrounding environment. As the DNA methylation pattern varies among people with different lifestyles, it may be an indicator of the influence of lifestyle on the biological age of an individual. Increased methylation of DNA can disrupt the normal functioning of the organ or body as they can fail to perform the work efficiently for which they are engaged [https://dralexisshields.com/biological-age].

iii. Epigenetic clock

The epigenetic clock is a hypothetical clock to measure the biological age of an individual, determined by analyzing the results of some specific biochemical tests. The tests are used mainly to know the level of DNA methylation of the individuals and calculate the methyl groups accumulated in the DNA molecules [13, https://dralexisshields.com/biological-age].

BIOLOGICAL AGE AND DISEASE

Disease susceptibility is influenced by the biological age. Early aging always brings more susceptibility to different diseases. Many diseases have the root of the genetic predisposition of an individual towards the disease. However, this is not a complete concept, as various epigenetic factors also work in this process. The genetic predisposition generally cannot cause the disease unless they are triggered. The triggering factors include following of wrong lifestyle and negative effects on the inner (inside the body) and surrounding outer environment of the individuals. There is a requirement to switch on one or a few triggering factors for the initiation of a disease. But the list of the triggering factors behind the diseases, particularly behind the so-called lifestyle diseases, may be very large in number and there may be cumulative activity of such factors behind such diseases. Our contemporary knowledge cannot supply us with any clear picture of such different switches diseases specifically, but such factors definitely work behind the stimulation of predisposing genetic conditions, or even maybe for non predisposing diseases in the way of expression as a disease. The wrong diet, lack of physical exercise, low production of Vitamin D by sunlight exposure, etc. added by habits like tobacco, alcohol, or narcotic drug intake, etc. can be the driving force for the expression of such diseases. Type 2 diabetes and other metabolic diseases, different cardiovascular diseases, lung diseases (from chronic bronchitis to pulmonary fibrosis), cancers, dementia, Alzheimer's disease, etc. may be considered as some examples [12, 14].

REVERSION OF THE BIOLOGICAL AGE

i. Lifestyle modification

The epigenetic and other factors switching various diseases and inviting early aging can be controlled. In many cases, the ugly condition of the health can be revised. The early the initiatives taken the better will be the achievement. Control of the surrounding environment is not always under the control of an individual, but the lifestyle is always under control. A detailed list of the common harmful practices in the lifestyle and their possible modification for better health is discussed in some articles. Grossly, exclusion of all processed foods, chemical or chemical-added food, and drinks, chemical-added healthcare materials, etc., and inclusion of naturally available food (in the form of vegetable salad, seed, and nut salad, fruit salad, etc. as well as eating of food prepared by nature-derived ingredients only following simple procedures of cooking), nature-derived drinks (green coconut to lemon water), nature gifted healthcare materials, etc. at unaltered state, imposing restrictions in the lifestyle like maintenance of body clock, the addition of natural forces like regular sunlight exposure to the skin, loan walking, etc. and practicing mental

refresher techniques like meditation, etc. in the lifestyle is advocated in these articles [3, 4]. Efforts are made to uncover mechanisms behind positive effects on health due to such modification of the lifestyle-related factors attempted in some other articles [14, 15, https://dralexisshields.com/biological-age].

ii. Nutrigenetics-the gene-nutrient interaction theory

According to this theory, the expression of the genetic predisposition is dependent on the availability or non-availability of proper nutrients inside the body system. Apart from the main nutrients like carbohydrates, protein, and fats, different micronutrients as well as different anti-oxidants of the diet are required in the body's system to keep it healthy. Personalized nutrients based on individual genetics are proposed in this system. The association and interaction of genes and nutrients have been already identified in many lifestyle-associated diseases and that creates the base of that theory [16].

Studies suggest that maintaining or adopting a healthy lifestyle can reverse the effect of short telomere syndrome and associated complexities [4] and also can cause reversion of the negative effects of unhealthy DNA methylation patterns [12, 13].

CHIEF HEALTHCARE CONSIDERATIONS IDENTIFIED

Many types of research are going on for the identification of different aspects of healthcare depending upon the genotype, lifestyle, and the surrounding environment of an individual. Among them, three major aspects can be short-listed.

i. Molecular pathological epidemiology (MPE)

It is a proposed system of considering the outcome of a clinical disease as the final result of different molecular alterations within the cells as well as their microenvironment, influenced by various exogenous and endogenous factors. It considers heterogeneity among different individuals in pathology and pathophysiology at the molecular level. Based on "the unique disease principle", a disease incidence and/ or mortality is thought to be an outcome of the interaction between the disease subtypes and the specific environmental exposure at the individual level. So, there should be accurate medicine/ preventive procedures for the prevention and treatment of any disease as per the personalized status of an individual. The immunity status and the microbiome profile of the host are given importance in this system for the selection of procedures to combat a disease.

Research directed with several interdisciplinary areas (such as pharmaco-MPE, Microbial-MPE, Immuno-MPE, etc.) has already started to identify the actual etiologic mechanisms behind a clinical disease at the individual level. That approach can calculate disease-specific risk estimates leading to genome-wise disease possibility pattern studies on public health [17, 18, 19].

ii. Following the disciplined and intelligent people diet (D.I.P diet) plan

This diet plan includes mainly plant-based ingredients. Some specific protocols are there for their dietary use at different times of the day. Fruits, nuts, etc. are advocated for dietary use in their raw form, not in any processed form. As per that branch of health research, diseases like high blood pressure, thyroid problems, diabetes, arthritis, kidney problems, cancers, liver diseases, obesity, etc. can be prevented and even reversed by following a reversion of lifestyle towards a specific direction, taking help of some disease-specific physical measures and following that particular diet plan [20, 21].

iii. Use of succulent biomedicine capsules for combating diseases

Along with following a designed lifestyle, parts of the effective medicinal plants in their unaltered state can directly be used in healthcare. These can be used as general immune-modulators or disease-specific preventive as well as curative biomedicines. The succulent parts of effective medicinal plants can be encapsulated following some specific procedures and then preserved and transported globally for different healthcare purposes. The addition of any synthetic chemicals or materials in any name or form is not permitted for use in the preparation of these biomedicines and some specific cold chain transportation is advocated with some specifically designed systems [3, 22, 23].

CONCLUSION

Aging and disease susceptibility depends on the biological age of an individual. The genetic predisposition of an individual is triggered by epigenetic factors like wrong lifestyle habits to cause diseases. Many biomarkers are identified to understand the biological age of the individuals. Prevention and reversion of aging speed and disease condition are

studied under umbrellas like nutrigenetics, Molecular pathological epidemiology, DIP diet plan, and therapeutic use of Succulent biomedicine capsules. In all these branches of study, modification of lifestyle is considered a precondition. Further thorough study is needed for efficient application of these proposed systems, singly or together.

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Cite this article as: Pattanayak S. Biological age and lifestyle: key deciding factors of aging and disease susceptibility. Explor Anim Med Res. 2024; 14(1), DOI: 10.52635/eamr/14.1.1-5.