

**CLASSIFICATION, ANALYSIS, AND USE OF THE BIOLOGICAL AGE
PARAMETERS FOR PREDICTING LIFE EXPECTANCY**

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A classification of the biological age parameters is discussed relative to the level of their manifestation in the organism. This refers to the molecular, organic, neurohumoral, organosystemic, external manifestation, and integral indication levels. Some demands were formulated for the complex of parameters used for practical biological age assessment. A mathematical model is proposed for the biological age evaluation and life expectancy predicting.

Biological age is a complex synthetic notion characterizing the relations between the organism's real physiological and psychological state and a certain "standard" state inherent in the organism having a certain chronological age under given life conditions. Aging is presumed to be a natural process genetically determined and programmed [1] but modified by the environment to a certain extent [2].

It is natural to assume that there are some objective parameters or indicators of the body's state characterizing its biological age, changing with time and in principle measurable by sufficiently sensitive methods.

The first level of changes taking place in the organism is the level of separate molecules of proteins, lipids, DNA or DNA repairs [3-5]. The accumulation, and any damages to or modifications in the structure or chemical composition of these molecules lead to a gradual loss of properties inherent in them in accordance with their type and differentiation. It is believed in particular that the accumulation of such errors leads to irreversible changes in the cell membrane permeability. It is clear that these phenomena are sufficiently difficult to establish and therefore they are investigated mainly on bacterial yeast cells. However, their study is very important because it is the impairments of separate molecules that directly connect the organism with the destructive environmental factors.

The next level of age-related body alterations is that of intracellular structures such as mitochondria, lysosomes and others, which demonstrate some morphological changes (6 - 8) accompanying weakening of functional and proliferative cell capacities.

The neurohumoral age-related changes underlying a decrease in the adaptive capacity, the organism's resistance, and its ability to respond to stressors adequately and quite rapidly form a third level of changes, at which indication may be accomplished in various methodical variants [9-10].

The fourth level, at which age-related body changes can occur, is the level of the organism's separate organs and systems such as changes in size, shape, structure, and functional capacity of the lungs, liver, heart, a decrease in the blood vessel and skin elasticity, chronic changes in blood composition and blood pressure, reduced erythropoiesis, and changes in connective-tissue structure, especially in its extracellular elements [11 - 13].

The fifth level, that of the traditional indication of biological age, is the level of external signs inherent in man such as graying hair, baldness, wrinkled and flabby skin, characteristic and visible skeletal changes, "fading" iris, age-related pigmentation [14], and some psychological personality characteristics more or less obviously manifesting themselves in various age compartments.

At present, there are relatively few serious investigations dealing with at least qualitative, if not quantitative, evaluation of the interrelations between age-related changes at different levels, except the fourth and fifth levels, where they are more or less obvious or may be easily established by the traditional methods. In particular, certain relations between the fourth and fifth levels manifest themselves in intensified age-related pathological processes: vascular sclerosis with memory and perception impairment, obesity with metabolic disturbances, the increased blood sugar level with the attendant The sixth level of biological age indication goes beyond the separate physiological, anthropometric or psychological measurements and observations. At this level the biological age may be related to some general complex indicator, characterizing the organism's state in general, or to some medical indices used in demography based on the statistical data [13-15]. This makes it possible to apply the biological age assessment for the prediction of a given individual's life expectancy on the basis of his (her) current state and its comparison with the average population parameters. This approach with the application of the indices of statistical probability reflecting the state of the population as a whole makes it possible to avoid serious difficulties caused by the fact that prediction of life expectancy of a given individual requires not only the knowledge of his (her) current biological age but also the dynamics of its changes at least at the first derivative level, which needs sufficiently long monitoring.

Thus, we are dealing with a complex determined-stochastic model with the biological age index as its core, while the output is the supposed life expectancy for a given individual. Some variant of this model developed by the authors and presented below involves, as the initial data, a number of the biomedical parameters related to a certain individual. This basic set of data should meet the following three strict requirements: 1) the totality of these indices must reflect age-related changes in all the principal body systems; 2) these indices must have no direct functional relations or strongly correlate with each other; 3) they must be measured with sufficient accuracy and simplicity by known methods and facilities.

The authors propose the following set of indices meeting the above requirements: blood

vessel elasticity, systolic and diastolic blood pressure, vital lung capacity, blood sugar level, and the rate of response to a standard external stimulus. This set may be further supplemented and modified. It is used for the general assessment of an individual's current state according to the technique described below, which takes into account not only each of the measured parameters but also their weight coefficients determined by the acceptable limits of their deviations from the norm.

All the indices involved in the model are related to the fourth level of age-related changes, and their relative non-dimensional values are used to obtain the non-dimensional general index of the organism's current state.

Depending on the real possibilities, the indices of any other level may be used provided they (although correlating with each other to some degree) are not directly involved in a cause-and-effect relationship; otherwise repeated information enters the general index, devaluating its significance.

The formula for the general index (I) assessment is as follows:

$$I = g \sum_{i=1}^n a_i \frac{P_{it} - P_{iot}}{P_{iot}} - g \sum_{j=1}^m a_j \frac{P_{jt} - P_{jot}}{P_{jot}}.$$

where $n + m$ is the total number of involved biomedical parameters; n is the number of biomedical parameters whose values increase with age, on average; m is the number of biomedical parameters whose values decrease with age, on average; P_{iot} and P_{jot} are the mean values of i and j , respectively, in a t age compartment; P_{it} and P_{jt} are the mean values of i -th and j -th parameters in a given individual; a_i and a_j are the weight (significance) coefficients for i -th and j -th parameters; g is the normalizing factor determined from the equation:

$$g \sum_{i=1}^n a_i + g \sum_{j=1}^m a_j = 1.$$

The weight coefficients are determined by the formula:

$$a_i = \frac{P_{iot}}{P_{ib} - P_{iH}}; \quad a_j = \frac{P_{jot}}{P_{jb} - P_{jH}}.$$

where P_{ib} and P_{jb} are the upper limits (maximally allowable in terms of viability) for the values of i -th and j -th parameters; P_{iH} and P_{jH} the lower (minimally allowable) limits for the values of i -th and j -th parameters.

When $I = 0$ the state of an individual corresponds to the mean value for the t calendar age (the biological and calendar ages are equal). When $I < 0$, the biological age is under the calendar age; when $I > 0$, the biological age is over the calendar age for a given individual.

The obtained general index is transformed into the biological age by:

$$T = t + ql,$$

where T is the biological age, t is the calendar age, q is the dimensional factor.

As the initial demographic index the model involves the mortality rate [16], the index depending on life expectancy in the following way: it has high values on the first year of life, exponentially decreasing to some minimal level during the next 10-12 years, then increases (gradually before 35 and intensively after 35), stabilizing at a certain high level approximately by 75 - 80 years. This dependence may be analytically expressed in an equation containing the exponential polynomial in its right part:

$$\lambda(t) = \lambda_0 - K(1 - e^{-at}) + g(1 - e^{-bt}),$$

where $\lambda(t)$ is the mortality rate at the t age compartment; ng symptoms of diabetes, and so on λ_0 is the mortality rate in the first year of life; K, g, a, b are the constants typical of a given population, $b \geq a$.

Proceeding from this analytical expression the equation and the survival curve (the probability of reaching current age) may be obtained:

$$P(T) = \exp\left(-\int_0^T \lambda(t) dt\right),$$

where $P(T)$ is the probability of reaching the biological age T .

Then the distribution density of population life expectancy may be obtained by the differentiation of this equation:

$$f(t) = -P'(t),$$

$$f(t) = (K - \lambda_0 - Ke^{-at} + ge^{-bt} - g)P(t).$$

As applied to a given individual of a certain biological age, this distribution density is truncated on the left side, which needs correction of the equation to a certain degree [2]. Integration of this corrected distribution density, multiplied by t , between the limits from the current biological age to infinity gives the life expectancy of a given individual.

The density $S(t)$ of the new, truncated distribution at every point t within the interval from T to infinity is proportional to the density of the initial $f(t)$ at the same point:

$$S(t) = Cf(t)$$

where C is the proportionality factor.

For the new distribution:

$$\int_T^{\infty} S(t)dt = 1,$$

from where it follows:

$$C = \frac{1}{P(t)}$$

Therefore the new distribution density is:

$$S(T, t) = \frac{1}{P(t)} f(t)$$

Life expectancy of an individual having T biological age is now determined from the expression:

$$t_T = \int_T^{\infty} tS(T, t)dt.$$

Assuming that $T=0$ and $C=1$, life expectancy may be determined for newborns in a given population under current life conditions.

The above approach can be used to assess the effects of the environmental factors, including global changes and special prophylactic measures, on the biological age and life expectancy.

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