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AGE-RELATED CHANGES OF THE CORNEAL ENDOTHELIUM: A MATHEMATICAL PRINCIPLE THAT DETERMINES TISSUE AGING AND BODY AGING

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Introduction. As shown by numerous clinical observations, the condition of the posterior epithelium (endothelial monolayer) of the cornea is a leading factor determining its functional qualities as a whole, which has found practical application. In this regard, when selecting a donor cornea for keratoplasty, ophthalmologists focus on the density of endothelial cells as the main indicator of the age-related wear-out of this tissue. It is also taken into account that corneal endothelial cells are not renewed throughout life, and their number only decreases from birth to death.

Nevertheless, for all its clinical value, these data did not previously attract attention in terms of elucidating the very cause of endothelial cell loss with age. This is due to the fact that aging of tissues as well as the organism as a whole is considered only from the perspective of cell aging. Therefore, by default, the loss of endothelial cells in a monolayer is associated with their aging. However, the mathematical model of aging of the tissue system, built on this principle, will contradict the existing model of aging of the body, which has long been tested in gerontology and has no significant alternative.

Aim. Based on the analysis of the number (density) of corneal endothelial cells, it was constructed a graph of aging (loss of viability) of this tissue and compare it with the well-known real mathematical model of aging proposed by B. Gompertz for the body as a whole.

Materials and methods. The density of endothelial cells (cell/ mm²) depending on age was analyzed from data obtained by endothelial microscopy on 495 corneas from 394 cadaveric donors.

Results and discussion. The cell density ($M \pm m$ cells /mm²) by age groups was distributed as follows (Table 1).

Table 1

Change in the density of corneal endothelial cells with age

Group number	Age range	Average age (M±m)	Cell density per 1 mm ² (M±m)	The number of corneas	Number of donors
1	20-29	26,8±2,3	3360±340	38	22
2	30-39	36,1±1,4	3250±190	41	29
3	40-49	46,1±2,7	3100±200	84	74
4	50-59	55,7±2,5	2950±210	190	149
5	60-69	64,5±2,2	2850±250	110	98
6	70-79	76,5±2,5	2760±220	32	22

Looking at the table, you can see that average density of endothelial cells during the main period of aging - from 20 to 80 years - decreases exponentially.

Using tabular data, you can find the coefficient of elimination (mortality) of cells with age. Also, as is customary in demographic statistics, it can be defined as the ratio of the number of dead (eliminated) cells over a certain period of time to the original number at a given time. So, calculating this mortality rate for the entire interval between the first and last age groups, we obtain the values from 0.03 to 0.05:

mortality in the age interval between group 1 and 2 - $3360-3250/3360=0,033$;

mortality in the age interval between group 2 and 3 - $3250-3100/3250=0,05$;

mortality in the age interval between group 3 and 4 - $3100-2950/3100=0,05$;

mortality in the age interval between group 4 and 5 - $2950-2850/2950=0,034$;

mortality in the age interval between group 5 and 6 - $2850-2760/2850=0,033$.

Herewith, the lowest rates are noted in the youngest and oldest age group, i.e. the probability of cell loss is random and does not depend on age. Thus, there is a coincidence of the mathematical model of aging of the tissue system, which is the endothelial monolayer, and the well-known mathematical model of aging of Gompertz.

In the Gompertz's model, the probability of death is determined by age-independent loss of vitality, the nature of which this model does not disclose. However, it shows that there must be elementary structures in the composition of the body that ensure its viability and are regularly lost throughout life. Age-related changes in the corneal endothelium, which determine the functional state of this tissue as a whole, indicate that tissue aging is associated with age-independent elimination of the cells that form it. After all, the loss of each cell is the loss of a part of vitality, which, according to the mathematical law, is also lost in proportion to itself.

So, on the segment of life, which covers the bulk of the age-related changes in the body (from 20 to 80 years), the probability of death (elimination) of corneal endothelial cells does not increase. Obviously, the loss of cells reduces the functionality of the cornea and, in particular, its ability to withstand the penetration of chamber liquor into the corneal stroma.

Thus, it can be argued that the aging of the tissue system occurred as a result of cell death unrelated to their aging. In other words, the loss of cells in the tissue occurs in the same way as the loss of viability according to the Gompertz law, i.e. not depending on age, but in proportion to their own numbers. At the same time, the mortality rate calculated from tabular data does not show an upward trend over the entire age period, i.e. saves the properties of a constant.

Thus, the analysis of age-related changes in the density (number) of cells in the corneal endothelium makes it possible to see a real model of aging of the body. This model exploits not the supposed aging of cells, allegedly leading to aging of the whole organism, but is based on a real fact: age-independent loss of cells in the tissue system. The stochastic nature of the elimination of cells from the tissue system contradicts the concept of cell aging as a cause of aging in general.

Certainly, there are many cells in the organism whose aging and death can be observed throughout the life of the body in which they are located. In particular, these are blood cells, cells of epithelial integument and some other tissues, renewed throughout life due to the reserve of stem cells. However, most of the organs and tissues are represented by the so-called post-mitotic cells. They are not replenished due to the cambial reserve, and therefore, as a result of their loss, part of the function of the tissue system and organ as a whole is irretrievably lost. The loss of these functions is the result of aging that we see. However, as age-related changes in the corneal endothelium show, this senile decline in the functions of tissues and organs is not a consequence of cell aging.

The mathematical model of age-related elimination of corneal endothelial cells is logically connected with the Gompertz law, and the aging can be represented as a decay of the tissue system, with an exponential characteristic similar to radioactive decay. Based on such an exponent, life expectancy, including the maximum, can be calculated. However, for this, it will be necessary to obtain the same data on the dynamics of cell numbers in tissue systems with which life-supporting functions are associated, how was it possible for corneal endothelium.

Conclusions. The density of endothelial cells of 495 corneas obtained from 394 cadaveric donors of different ages from 20 to 80 years was studied. The study of age-related changes in the corneal endothelium allows to see the relationship between the mathematical model and the morphological substrate. Thus, the loss of each cell is the loss of a part of vitality, which, according to the mathematical law, is also lost in proportion to itself. The coincidence of two mathematical models: the Gompertz model, which describes the aging of the body, and the model of aging of the tissue system, which use an example that are proposed by corneal endothelium, indicates that conditional loss of vitality is nothing but the loss of cells in the tissue system.