DETERMINATION OF SPECIES LENGTH OF LIFE

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The concept of species length of life (SLL), based on the idea that the periods of existence of organisms are genetically determined, has recently been widely used in the biology of aging [1, 2]. However, up to now the value for the SLL has not been precisely determined for any biological species. The basic difficulty when measuring SLL is the fact that the longevity of an organism depends not only on genotype, but also on conditions of life. Therefore, the question of the existence and measurement of the parameter characterizing only the SLL of a biological species has remained open until recently.

In this work a method is presented that permits for the first time the precise measurement of the species length of life of organisms. As species length of life we mean a value having the dimension of time that is not dependent on conditions of existence or sex of the animal and that is determined only by the biological species. It has been shown that this value actually does exist and can be calculated based on data concerning the age dynamics of organism mortality. Thus, for example, the SLL for man, rats, and *Drosophila* constitute 98 ± 5 years, 610 ± 50 days, and 57 ± 2 days, respectively.

The method for measuring SLL consists of two stages of analyzing statistical data concerning animal mortality.

1. First is the use of experimental data according to the age dynamics of mortality to determine the parameters R_0 and α in the equation of Gompertts and Meikkhem

$$R_t = A + R_0 \exp(\alpha t), \quad (1)$$

where R_t is the probability of death or the mortality of animals (the ratio of the number of animals that have died to their original number) at age t during a randomly assigned, but constant length of time A; R_0 and α are the parameters of the Gompertts—Meikkhem equation. Formula (1) is an overall principle for animal death. Its validity has been demonstrated for populations of humans [3, 4], horses [4, 5], Dall mountain sheep [5], rats [3, 4], mice [5, 6], house flies [3, 5], mosquitos [5, 7], and *Drosophila* [3, 4]. It must be noted that the Gompertts—Meikkhem equation has a theoretical basis and can be derived using the apparatus of reliability theory [3, 8, 9]. These facts provide the basis for wide utilization of this equation to analyze statistical data concerning animal mortality. In order to determine the values of the parameters R_0 and α in humans, we analyzed 285 abridged tables of mortality, which used United Nations data for all geographical regions of the world: Africa, America, Asia, Europe, the USSR, Australia, and Oceania. The method of calculating the coefficients R_0 and α in the Gompertts—Meikkhem equation was described in detail by us previously [3]. For populations of laboratory animals, the calculation of the coefficients R_0 and α is substantially simplified, since the value A, reflecting background mortality for reasons independent of age can usually be disregarded. Since in this case a linear dependency is observed in the coordinates of the logarithm of mortality (log R_t)—age (t), the coefficients R_0 and α can be easily calculated by the method of least squares. Results of such calculations for populations of *Drosophila* and rats are presented in Tables 1 and 2. It can be noted that the dependency of log R_t on t was actually very close to linear. In 88% of the *Drosophila* cases, these dependencies had a coefficient of correlation of $r \geq 0.98$ (Table 1). Slighly smaller values for r were observed in the rat populations, which is associated with low numbers (135-288 individuals) in these populations. Nevertheless, in 80% of the cases, a dependency of $r \geq 0.97$ was obtained (Table 2).

2. Calculation of species length of life was conducted based on the correlation existing between the coefficients R_0 and α:

$$\ln R_0 = M - B\alpha, \quad (2)$$

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TABLE 1. Values for the Parameters R_0, α, and the Coefficient of Correlation r for Populations of *Drosophila melanogaster**

$\alpha \cdot 10^2$, day^{-1}	$\ln(R_0 \cdot 10^4)$ for 6 days	r	Range of linearization, days	Number of points	Number of Drosophila in population	Source of data
			Males			
4,47	2,50	0,98	28–55	27	1000	[12]
6,35	2,19	0,98	25–55	6	1407	[13]
7,80	1,75	0,99	28–55	10	1200	[14]
9,31	1,50	0,99	28–55	10	2400	[14]
			Females			
3,90	2,65	0,99	28–55	27	1000	[12]
5,93	2,16	0,97	25–55	6	1415	[13]
9,32	1,35	0,99	28–55	10	1200	[14]
13,07	0,36	0,98	28–55	10	2400	[14]

*Calcualted by us based on published tables of survival [12-14]. The values R_0, α, and r were determined by the method of least squares in coordinates log R_t—t. A six-day interval was chosen to calculate mortality.

TABLE 2. Values for Parameters R_0, α, and the Coefficient of Correlation r for Populations of Wistar Rats*

Year	Males			Females		
	$\alpha \cdot 10^3$, day^{-1}	$\ln R_0 \cdot 10^3$ for 100 days	r	$\alpha \cdot 10^3$, day^{-1}	$\ln R_0 \cdot 10^3$ for 100 days	r
1956	4,62	1,23	0,96	5,00	0,90	0,97
1957	5,90	0,88	0,97	5,35	0,82	0,95
1958	6,75	0,58	0,92	3,28	1,19	0,81
1959	4,92	1,08	0,97	5,26	0,76	0,96
1960	7,44	0,37	0,99	6,10	0,54	0,99
1961	6,41	0,63	0,97	7,53	0,17	0,99
1962	4,48	1,14	0,97	7,23	0,22	0,98
1963	6,85	0,58	0,97	6,35	0,63	0,97
1964	6,76	0,61	0,98	8,31	0,10	0,99
1965	4,78	1,22	0,97	4,73	1,13	0,97

*Calculated on the basis of published tables of survival [11]. Values for parameters R_0, α, and r were determined by the method of least squares in coordinates log R_t—t. The age range of linearization constituted 300-750 days. Each dependency contained 10 points. A 100-day interval was chosen for calculating mortality (R_t).

where M and B are the parameters of equation (2) determined by the method of least squares. This dependency was first noted in 1960 when comparing the values for R_0 and α in human populations in countries with different levels of mortality [4]. However, a strict proof for Eq. (2) for humans was given only in 1978 [3]. This same principle was shown to be valid for rat and *Drosophila* populations (Table 3); consequently, there is a basis to propose that Eq. (2) is a general principle for animal death. It was shown by us previously [3] that the significance of Eq. (2) is as follows: For a given biological species all straight lines in the coordinates of logarithms of age mortality [log $(R_t - A)$] vs age (t) have one common point of intersection independently of the conditions of its existence (Fig. 1). The coordinates of this point of intersection correspond to the parameters M and B in Eq. (2). It can be noted that the value B has a dimension of time, it does not depend on conditions of existence (according to the very method of calculating it), it does not depend on age of an animal (Table 3), and consequently it characterizes only the biological species. Therefore, the parameter B incorporates all the properties of a species length of life (SLL), while the method we proposed to calculate the SLL permits the objective and precise measurement of this value in animals of very different classes.

The basic theoretical result of this work is the demonstration for the first time of the existence of a SLL. Actually, from the very fact of the existence of a SLL follows a number of important conclusions. First, the validity of ideas concerning the genetic determination

TABLE 3. Value for Species Length of Life for *Drosophila*, Rats, and Humans*

Biological species	Species length of life $B \pm \sigma$, days	Number of points (R_0 and α pairs)	Coefficient of correlation between ln R_0 and α
Drosophila			
males	50 ± 5	4	−0.992
females	57 ± 1	4	−0.9997
both sexes	57 ± 2	8	−0.995
Rats			
males	660 ± 40	10	−0.987
females	580 ± 50	10	−0.968
both sexes	610 ± 50	20	−0.941
Humans			
men	99 ± 6 years	82	−0.914
women	98 ± 5 years	82	−0.944
both sexes	98 ± 5 years	164	−0.945

*Calculated on the basis of data presented in Tables 1 and 2. Values for parameters R_0 and α for humans (164 pairs) are not presented here because of limited space.

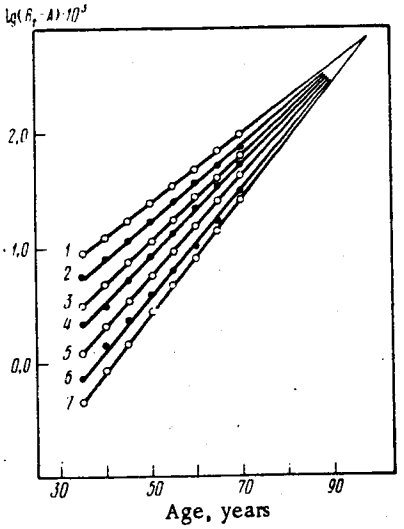

Fig. 1. Dependence of logarithm of age mortality $\log (R_t - A) \cdot 10^3$ on age of humans: 1) India, 1941-1950, men, $A = 7.87 \cdot 10^{-3}$; 2) Turkey, 1950-1951, men, $A = 3.16 \cdot 10^{-3}$; 3) Kenya, 1969, men, $A = 5.31 \cdot 10^{-3}$; 4) Northern Ireland, 1950-1952, men, $A = 0.43 \cdot 10^{-3}$; 5) Great Britain, 1930-1932, women, $A = 2.38 \cdot 10^{-3}$; 6) Austria, 1959-1961, women, $A = 0.68 \cdot 10^{-3}$; 7) Norway, 1956-1960, women, $A = 0.55 \cdot 10^{-3}$. Constructed on the basis of abridged tables of mortality published in United Nations yearbooks [10]. Values for R_t and A correspond to a one-year interval. The value for A was computed according to the formula:

$$A = \frac{1}{4} \sum_{t=45}^{50} (R_t - R_0 \exp(\alpha t))$$

of length of life is corroborated. Second, it turns out that rate of aging (or, more precisely, the rate of irreversible age changes that increase mortality) depends little on external conditions, i.e., a mechanism of biological time lies at the basis of aging. This conclusion follows from all mathematical theories of aging [3, 4, 9], which assume the existence of a SLL. Third, it turned out that the SLL in man, rats, and *Drosophila* was substantially lower than the so-called maximal length of life (MLL) of these animals. Therefore, it is impossible to use the MLL to estimate the SLL, as is now done [2]. In addition, for the MLL, as opposed to the SLL, it is impossible to determine confidence intervals or to exclude the influence of environment and sex of the animals. Finally, the value for the MLL, when other conditions are equal, must inevitably depend even on population numbers (and precisely, it increases with greater numbers). Consequently, the MLL can not be a characterization of a biological species just as the time for decay of the last atom is not a characterization of a radioactive element. The wide use of the MLL in experimental gerontology was based on the concept that species limits of life exist. However, as Feller [15] showed, this concept is theoretically groundless. Therefore, the MLL value, as opposed to the SLL, has neither practical nor theoretical importance. As far as the practical value of the SLL is concerned, it consists in the following for ecology and demography: knowledge of the value of the SLL permits forecasting of the age dynamics of mortality as a whole according to only one or two designated values of mortality.

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ANTIMUTAGENIC ACTIVITY OF THE ANTISPASMODIC PREPARATION HEXAMIDINE. EFFECT OF HEXAMIDINE ON LEVEL OF SPONTANEOUS MUTATION IN A NUMBER OF SUBJECTS

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The saturation of the human population with adverse mutations is rather high. In this regard, there is definite interest in identifying preparations with antimutagenic activity among drugs that are widely used in medicine and the use of which does not create a genetic hazard.

In this work the antimutagenic effect of the antispasmodic agent hexamidine is examined; it was recorded by us for the first time in operation on spontaneous mutation in mice, *Drosophila*, and the Welsh onion.

Hexamidine (Hexamidinum, Primidonum, Desocyphenobarbitone) is a derivative of barbituric acid, an antispasmodic agent, and a pure preparation produced by a Leningrad pharmaceutical plant. Male hybrid mice of generation I CBA × C57Bl/6, weighing 20-22 g, and two months old, were studied according to tests estimating mutations in somatic and germ cells. For this, a method of metaphase analysis of bone marrow cells [1] and the dominant-lethal test [1] were used. Hexamidine was injected intraperitoneally one time in a 1% starch suspension in doses of 400 mg/kg (~0.5 LD_{50} for mice), 100, and 25 mg/kg. During work with bone marrow, exposure was 12, 24, and 48 h. *Drosophila melanogaster* of the Berlin stock were investigated for frequency of occurrence of recessive, sex-linked, lethal mutations (Müller-5 method) [2]. The frequency for occurrence of partial and complete loss of sex chromosomes was studied in *Drosophila* males of stock $(R(1)2,yv/sc^{s}JB^{S}$. Imagoes were treated with hexamidine in concentrations of 6 and 12 mM. Preparations were dissolved in dimethyl sulfoxide

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