

tomarily applied to the sets  $B + C$ ,  $B$  and  $C$ , respectively, derive their significance from this theorem.

A partial solution of the problem of the existence of linear subspaces of  $\mathfrak{S}$  invariant under  $T$  may now be formulated:

**THEOREM.** If  $(\lambda, \mu)$  is a closed interval to which the point  $\lambda = 0$  is exterior, and if  $\mathfrak{S}_{\lambda, \mu}$  is the closed linear subspace of  $\mathfrak{S}$  comprising all elements  $f$  such that  $E_{\lambda}f - E_{\mu}f = f$ , then  $T$  is defined throughout  $\mathfrak{S}_{\lambda, \mu}$  and transforms it in a one-to-one manner into itself. The space  $\mathfrak{S}_{\lambda, \mu}$  may contain the sole element 0, may be an  $n$ -dimensional unitary space, or may be a complex Hilbert space.

<sup>1</sup> Presented to the American Mathematical Society, October 27, 1928.

<sup>2</sup> *Proc. Nat. Acad. Sci.*, 15, p. 198, 1929.

<sup>3</sup> J. von Neumann, *Göttinger Nachrichten*, 1927, pp. 32-33. The appellation "resolution of the identity" seems to be an appropriate translation of his "Zerlegung der Einheit" and is descriptive of the properties of the family  $E_{\lambda}$ .

<sup>4</sup> Stieltjes, *Annales Toulouse*, 1, 8 (1894), pp. J68-J75; Montel, *Leçons sur les familles normales*, Paris, 1927, p. 30; Bray, *Ann. Math.*, 20 (1918-19), pp. 177-186; Fréchet, *Trans. Am. Math. Soc.*, 8 (1907), pp. 439-44; Carleman, *Equations intégrales singulières*, Uppsala, 1923, pp. 25-28, 52-55, 81-82.

<sup>5</sup> Hellinger, *J. Mathematik*, 136 (1909), pp. 210-271, employed the method of contour integration to discuss bounded operators.

<sup>6</sup> This relation has been proved recently by von Neumann in an unpublished paper, kindly brought to my attention by Professor Weyl since the preparation of my first note. His proof, also indirect, is entirely different from that sketched here. The other theorems I have given can be derived from this, once it has been demonstrated.

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## AGE CHANGES IN ALCOHOL TOLERANCE IN *DROSOPHILA MELANOGASTER*

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While certain orderly physiological changes with advancing age are known for some organisms, notably man, in general it is true that the stigmata of senescence which are best known are morphological. There has been relatively little work of a systematic character regarding senescence on any other organism than man.

It is the purpose of this paper to report in a preliminary way some of the results of a study of physiological changes with age in *Drosophila* upon which we have been engaged for some years past in this Institute. Later a more complete account of the investigation will be published in our series of *Experimental Studies on the Duration of Life*.

In Table 1 are shown, for the indicated ages in days, the average time in minutes required for *Drosophila* to become completely anaesthetized by the vapor of absolute alcohol under experimental conditions standard, constant, and identical for each age. Briefly, the technique was to introduce into a wide-mouth bottle of 120 cc. capacity five normal flies of the same age. On the under side of the cork of this bottle was pinned a circle of thick filter paper, on which were placed 12 drops of absolute al-

TABLE 1  
TIME OF ANAESTHESIA OF *DROSOPHILA* AT DIFFERENT AGES

| AGE IN<br>DAYS                  | BOTH SEXES  |      | MALES       |    | FEMALES     |     |
|---------------------------------|-------------|------|-------------|----|-------------|-----|
|                                 | MINUTES     | N    | MINUTES     | N  | MINUTES     | N   |
| 1                               | 9.639±0.138 | 100  | 9.706±0.177 | 54 | 9.560±0.222 | 46  |
| 2                               | 5.873±0.071 | 100  | 6.140±0.103 | 53 | 5.572±0.091 | 47  |
| 3                               | 4.928±0.087 | 100  | 5.154±0.125 | 51 | 4.693±0.120 | 49  |
| 4                               | 6.913±0.121 | 50   | 6.898±0.149 | 32 | 6.939±0.228 | 18  |
| 5                               | 6.355±0.091 | 50   | 6.709±0.126 | 28 | 5.904±0.108 | 22  |
| 6                               | 5.808±0.075 | 100  | 5.751±0.097 | 60 | 5.893±0.120 | 40  |
| 7                               | 6.096±0.085 | 50   | 6.142±0.105 | 25 | 6.050±0.141 | 25  |
| 8                               | 6.590±0.136 | 50   | 6.842±0.167 | 36 | 5.943±0.214 | 14  |
| 9                               | 4.522±0.053 | 100  | 4.285±0.085 | 46 | 4.725±0.062 | 54  |
| 12                              | 4.576±0.081 | 50   | 4.736±0.129 | 27 | 4.389±0.092 | 23  |
| 15                              | 4.054±0.078 | 50   | 3.972±0.115 | 24 | 4.130±0.112 | 26  |
| 18                              | 4.968±0.083 | 50   | 5.017±0.117 | 33 | 4.872±0.104 | 17  |
| 21                              | 4.246±0.080 | 50   | 4.424±0.103 | 29 | 4.002±0.127 | 21  |
| 24                              | 3.957±0.047 | 50   | 3.858±0.066 | 27 | 4.073±0.067 | 23  |
| 27                              | 3.510±0.060 | 50   | 3.638±0.134 | 16 | 3.450±0.065 | 34  |
| 30                              | 3.512±0.057 | 50   | 3.616±0.080 | 25 | 3.408±0.084 | 25  |
| 33                              | 3.836±0.080 | 50   | 3.808±0.106 | 24 | 3.863±0.126 | 26  |
| 36                              | 3.943±0.055 | 50   | 4.145±0.167 | 9  | 3.899±0.060 | 41  |
| 39                              | 4.287±0.073 | 50   | 4.638±0.115 | 9  | 4.210±0.084 | 41  |
| 42                              | 4.386±0.096 | 50   | 4.576±0.207 | 17 | 4.289±0.106 | 33  |
| 45                              | 3.696±0.072 | 50   | 3.786±0.099 | 26 | 3.598±0.111 | 24  |
| 48                              | 4.050±0.100 | 50   | 4.047       | 7  | 4.050±0.105 | 43  |
| 51                              | 3.719±0.077 | 50   | 2.742       | 3  | 3.782±0.077 | 47  |
| 54                              | 4.116±0.060 | 50   | 3.922±0.120 | 13 | 4.185±0.070 | 37  |
| 57                              | 3.313±0.075 | 50   | 3.240       | 9  | 3.329±0.084 | 41  |
| 60                              | 4.142±0.103 | 50   | 3.949±0.134 | 25 | 4.336±0.160 | 25  |
| Total flies individually tested |             | 1550 |             |    | 708         | 842 |

cohol. Then with a stopwatch the time was recorded that it took each individual to reach a definite end stage of anaesthesia. All of the experiments were carried out at temperatures inside the bottle within  $\pm 1^\circ$  of  $25.5^\circ$  C. The flies used were from our Line 107 normal wild type, *Drosophila melanogaster*. The data here reported include ages up to 60 days only. It is more difficult, for obvious reasons, to get sta-

tistically adequate collections of data at more advanced ages, but in the final report on this work the curve will be extended to the extreme upper limit of fly life. At 60 days of age the life table for Line 107 flies<sup>1</sup> shows that 80 per cent of males are dead and 71.1 per cent of females.

From table 1 the following points are to be noted:

The total number of individuals for each of which the time of anaesthesia was measured is sufficiently large (1550) to give reasonable confidence in the results. At the early ages where the time of anaesthesia is changing rapidly per unit of time the observations were multiplied in number and more closely spaced in time. Owing to the fact that the flies for testing were taken from stock cultures at random except in respect of age, it results that there are more females than males in the series. This comes about because of the greater normal duration of life in females than in males. In a culture of *Drosophila* in which the flies are more than 40 days of age a random sample drawn from the culture will generally contain more females than males, because there are more females in the culture.

The general result which emerges from the data of table 1 is that as the fly grows older the length of time required for it to reach a definite stage of anesthesia under a constant dosage of alcohol vapor becomes shorter. Its alcohol tolerance becomes progressively lower. This change is very rapid at first and then slower with advancing age. Since we are concerned here only with adult flies (imagoes) in which there are no growth phenomena, any change in the characteristics of the organism which is progressive with advancing age may properly be regarded as a phenomenon of senescence. We then have, in these alcohol experiments, an index or measure of physiological senescence—of the rate of growing old, in short—quite distinct and apart from the phenomenon of death.

Study of the data suggested that the form of the curve of senescence for the physiological characteristic here studied was exponential. This is shown to be the fact, to a reasonable degree of approximation, in figure 1.

The smooth curve in figure 1 is the graph of the equation

$$y = 32.17e^{-1.525x^{1/4}} + 3. \quad (i)$$

In this equation  $y$  denotes time of complete anaesthesia;  $x$  is age in days and  $e$  is the Napierian base.

The interesting thing about this curve is that, with two slight changes, unimportant from the standpoint of theory, it is Gompertz's original equation for the force of mortality,

$$\mu_x = Bc^x, \quad (ii)$$

where  $\mu_x$  is the force of mortality at any age  $x$ , and  $B$  and  $c$  are constants for any given mortality table. The only respects in which (ii) differs from (i) are, first, that we have added an asymptote, because observation demonstrates that even with flies up to 99 days of age and in the particular apparatus used the time required for complete anaesthesia never falls below a mean value of about 3 minutes; and, second, that the more rapid change in the rate of senescence in the fly in early life requires the employment of

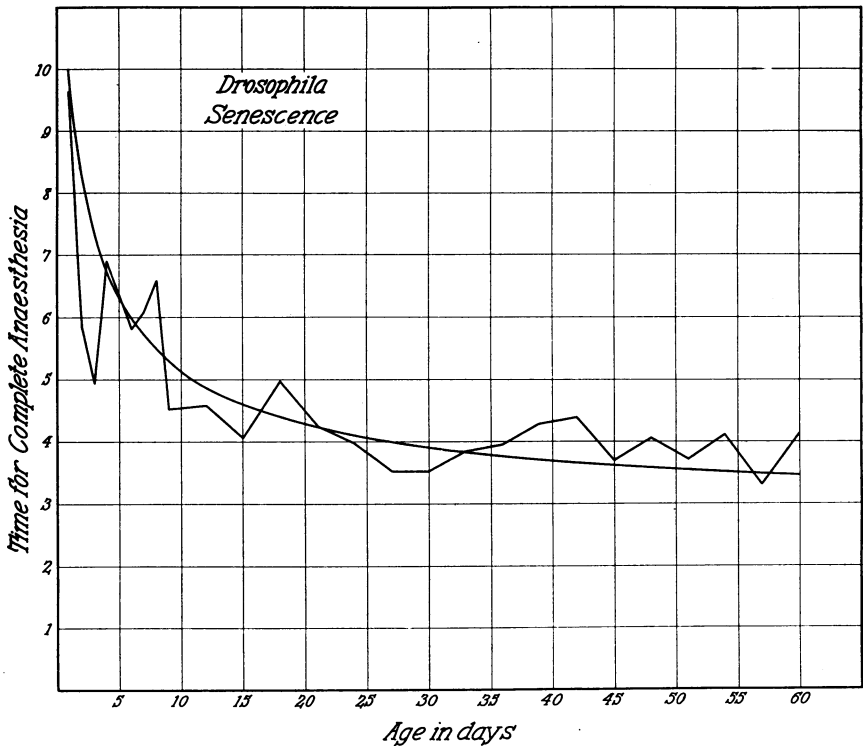


FIGURE 1

The change in the time required for complete anaesthetization of *Drosophila* by a standard dose of alcohol vapor, with advancing age. Both sexes combined.

the fourth root of age, rather than the age itself, which suffices to a rough approximation for man. The present data appear to demonstrate, for one particular organism, the essential truth of Benjamin Gompertz's assumption, a century ago, that the physiological process of senescence follows a geometrical progression. For the basis of Gompertz's physiological thinking on this matter was senescence, "a deterioration, or an increased in-

ability to withstand destruction," not mortality. Adequate systematic data regarding senescence were lacking. Hence the Gompertz "law" has been tested only on deaths.

The next point of interest in connection with the data arises out of the circumstance that du Noüy<sup>2</sup> has shown that the surface tension of colloid solutions (e. g., blood serum) decreases with time according to the equation

$$y = y_0 e^{-kx^{1/2}}. \quad (\text{iii})$$

which is again our equation (i), without the asymptote, and with the exponent  $1/2$  on time rather than our  $1/4$ . This decrease in surface tension is held to be due to the adsorption in the surface layer, in function of time, of the molecules in suspension. The bearing of all this, which suggests itself in the present connection, is that since we are dealing here with anaesthesia, and since the work of Meyer, Overton, Lillie, Osterhout and others has shown that the action of narcotics is somehow primarily on the boundary membranes of cells, it is possibly something more than a mere coincidence that decreased tolerance to alcohol with age and decreased surface tension of colloid solutions follow the same type of curve relative to time.

The final point to which attention may be called is that, in general, the time required for complete anaesthesia tends to be lower in the females than in the males, according to the data of table 1, at least up to age 45. After that age the males are too meagerly represented in the samples to give very trustworthy results. *Drosophila* females are longer lived, by a substantial amount, than males. An interesting correlation is suggested here, with the possibility of another and different line of experimental attack upon the problem of duration of life than any hitherto discussed.

A more detailed account of these investigations will later be published elsewhere.

<sup>1</sup> Pearl, R., and Parker, S. L. "Experimental Studies on the Duration of Life. IX. New Life Tables for *Drosophila*." *Amer. Nat.*, Vol. 58, pp. 71-82 (1924).

<sup>2</sup> du Noüy, P. L. "Surface Tension of Colloidal Solutions and Dimensions of Certain Organic Molecules." In *Colloid Chemistry, Theoretical and Applied*. Edited by Jerome Alexander. Vol. I, pp. 267-275. New York (Chem. Cat. Co.), 1926.