

## SOME TEMPERATURE CHARACTERISTICS IN MAN

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### I

General diathermy (hyperpyrexia) treatments have been given by one of us (Perkins, 1931) to patients at the Worcester State Hospital suffering from dementia paralytica. The treatment consists of insulating the recumbent patient with wrappings and passing high frequency alternating currents through his body. In the course of 2 or 3 hours the patient's temperature may be elevated to  $106 \pm ^\circ\text{F}$ . After turning off the current, several hours are usually required for the temperature to return to normal. Clinical records of pulse and respiration have been kept on some 70 subjects. Each subject received approximately ten treatments. The observations of pulse and respiration as a function of temperature were taken every 10 or 15 minutes throughout the course of a typical 4 hour treatment.

Fig. 1 is a modified reproduction of a typical clinical chart showing the course of pulse frequency and respiration as a function of the rectal body temperature measured with a calibrated resistance thermometer. Three experiments with the same patient, performed on different days, are shown in this figure. The scale of respiratory frequencies is small and the precision of reading is rather low. The pulse frequency scale is larger and the data are more reliable than are those for respiration. The records of respiration, pulse, and temperature, in general, are fairly symmetrical for rising and falling temperatures. In Arrhenius equation plots, to be discussed presently, no consistent differences were found for the rising and falling values. The black rectangles of Fig. 1 indicate the duration of application of the current which elevates the patient's temperature.

Fig. 2 is a composite plot of data obtained from ten treatments of

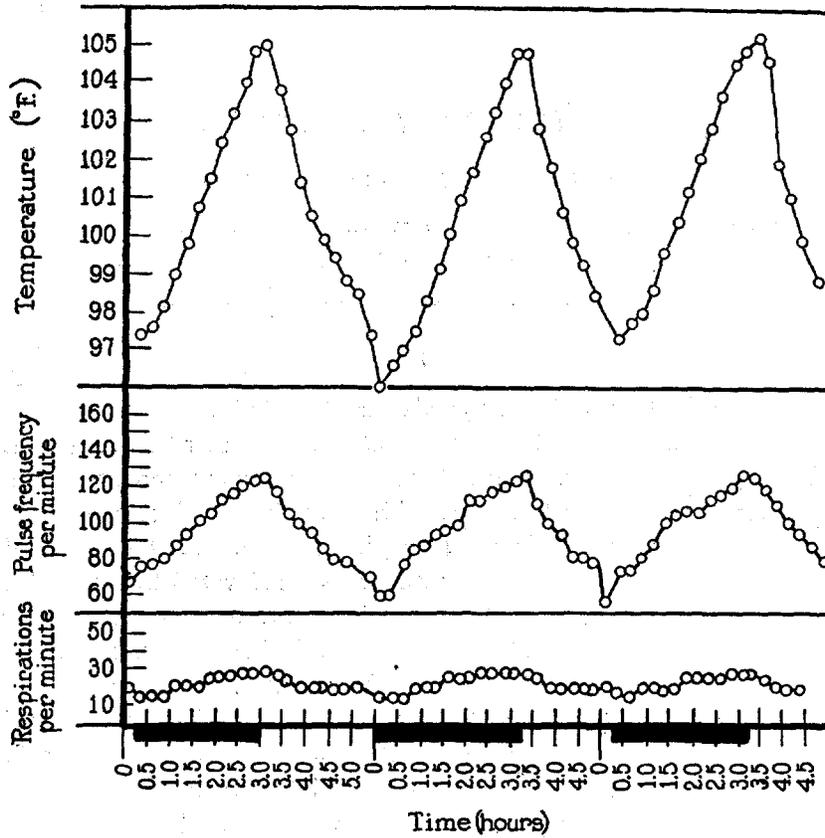


FIG. 1. Modified reproduction of a typical clinical data sheet showing three experiments on one individual, each of about 5 hours duration. Pulse and respiratory frequencies are recorded as a function of the internal body temperature. The solid rectangles indicate the duration of the passage of the alternating current used to elevate the body temperature.

the same patient administered on different days. The data are plotted according to the Arrhenius equation

$$\ln \frac{k_1}{k_2} = \mu/2 \left( \frac{1}{T_2} - \frac{1}{T_1} \right)$$

where  $k_1$  and  $k_2$  are the respective pulse frequencies at temperatures  $T_1$  and  $T_2$  and  $\mu$  is the temperature characteristic. The variation of distribution of points of Fig. 1 is large, but if it be assumed that the

Arrhenius equation holds and a straight line be drawn through the points, a value of  $\mu =$  about 29,000 calories is obtained.

As in investigations of the effect of temperature on physiological processes in poikilothermic animals, variation of the data is found to be less for single experiments than for averages of many experiments. This is due in part to fluctuations in the position of the curve as determined by its intercept on the ordinate axis, quite aside

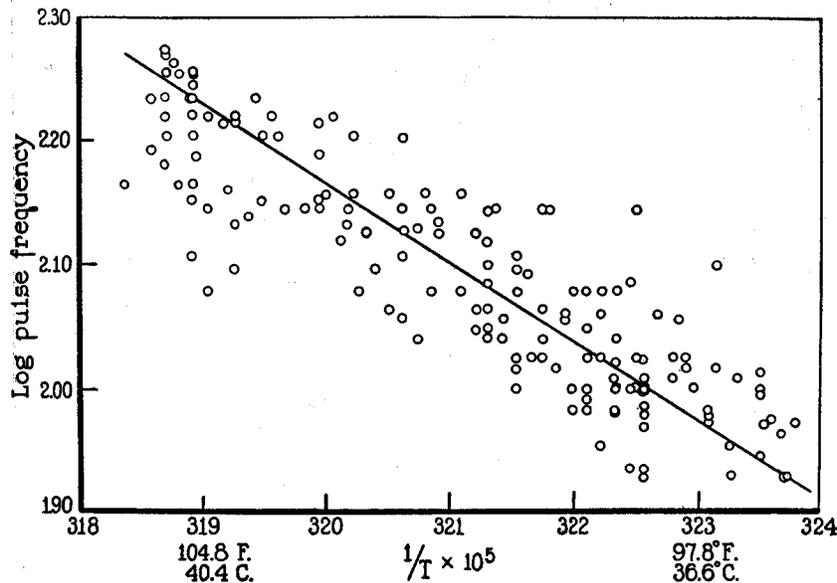


FIG. 2. Arrhenius equation plot of heart beat frequency (pulse) as a function of temperature, yielding a temperature characteristic of 29,000 calories. 164 observations from ten experiments on one individual are plotted. The value of  $\mu$  is the arithmetic mean obtained by determining the temperature characteristics of each of the ten experiments separately.

from fluctuations in the slope of the line, which determines the magnitude of  $\mu$ .

The temperature characteristic of 29,000 calories was obtained by plotting the data of each of the ten experiments separately, and averaging the value of  $\mu$  for each experiment. As may be seen in Figs. 3 and 5 the scatter of data for one experiment is not excessive. Fig. 3 shows the results of two experiments on two individuals in

which pulse *vs.* temperature is plotted according to the Arrhenius equation. The ordinate scale does not correspond to the absolute frequencies. The slopes of the lines are seen to be the same ( $\mu = 29,500$ ).

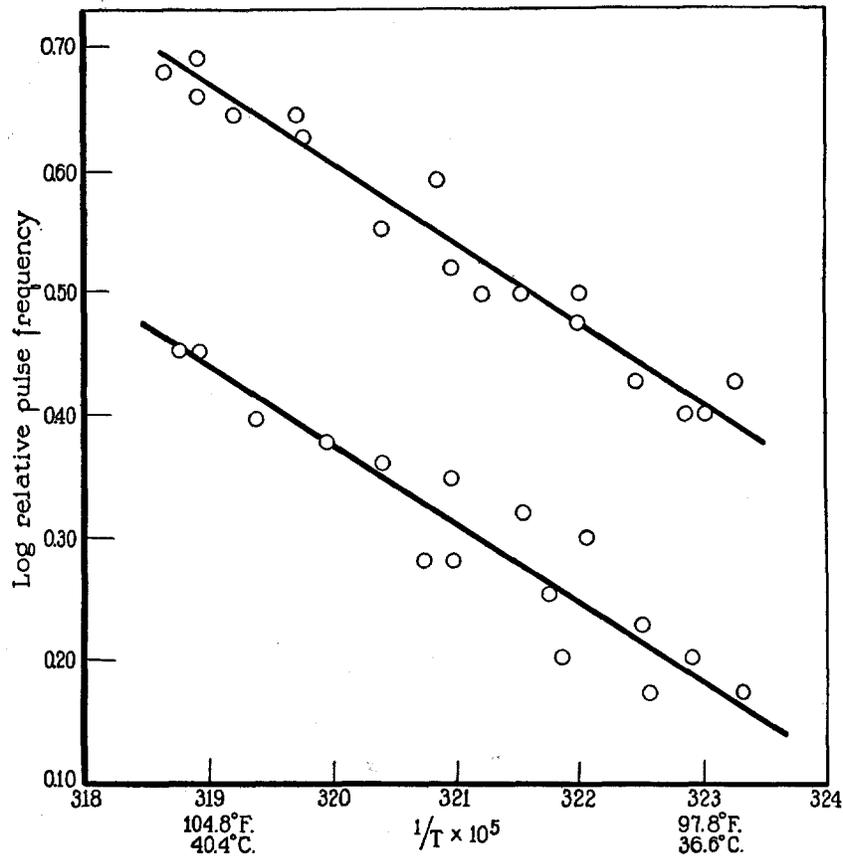


FIG. 3. Typical Arrhenius equation plots for two experiments on different individuals.

The considerable spread of data in Fig. 2 in a large measure results from the fact that, despite considerable constancy in the value of  $\mu$  (*cf.* Table I), differences in pulse rate were found to occur in the same individual on different days, thus resulting in somewhat different intercepts of the line with the ordinate axis from day to day. Von

Körösy, cited by Loeb (1916), found variations among resting individuals in pulse frequency of from 42 to 108 beats per minute. The constancy of  $\mu$  values illustrated in Table I is, therefore, especially interesting, suggesting a high degree of chemical specificity in the pace-making reaction despite differences in the absolute heart rates of individuals, and to a lesser degree in day-to-day fluctuations of the pulse for the same individual.

TABLE I  
*Temperature Characteristics for Human Hearts*

| Patient   | No. of observations | Experimental day | $\mu$  |
|-----------|---------------------|------------------|--------|
| A         | 124                 | 5 day mean       | 28,100 |
| B         | 202                 | 10 day mean      | 30,300 |
|           | 18                  | 2nd day          | 29,500 |
|           | 18                  | 6th day          | 29,300 |
| C         | 183                 | 10 day mean      | 29,900 |
|           | 18                  | 3rd day          | 30,000 |
|           | 18                  | 4th day          | 28,800 |
|           | 18                  | 10th day         | 30,400 |
| D         | 223                 | 10 day mean      | 29,900 |
| E         | 164                 | 10 day mean      | 29,000 |
| Mean..... |                     |                  | 29,400 |

Table I shows temperature characteristics obtained from five patients selected at random from the group of seventy. The mean  $\mu$  for 45 experiments involving 896 observations is 29,400 calories.

The value of the temperature characteristic agrees well with one of the smaller modal groups ( $\mu = 29,000$ ) obtained by Crozier (1925-26) from the analysis of many determinations of this constant for different physiological processes in poikilothermic organisms.

Fig. 4 shows the data of one typical experiment relating frequency of respiratory movements to temperature. The value of  $\mu$  from sixteen observations is roughly 41,000 calories. The respiratory data show, in general, a greater scatter than does the heart frequency data,

and the data are less reliable. The values of  $\mu$  obtained for respiratory movements are also much more variable, as is indicated by comparing Tables I and II.

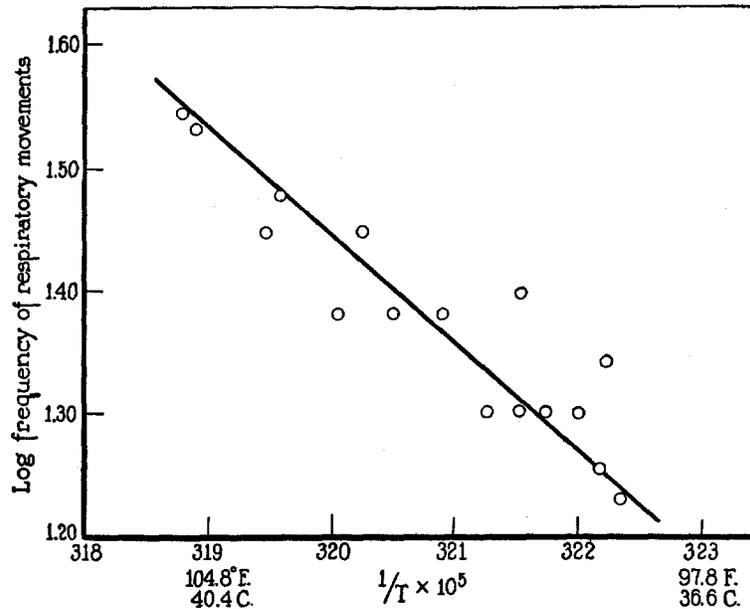


FIG. 4. Typical Arrhenius equation plot of respiratory movements as a function of temperature, yielding a temperature characteristic of 41,000 calories.

TABLE II

*Temperature Characteristics for Frequencies of Respiratory Movements of Five Patients Selected at Random*

| Patient | No. of observations | $\mu$  |
|---------|---------------------|--------|
| B       | 17                  | 44,300 |
| F       | 17                  | 34,700 |
| G       | 16                  | 41,200 |
| H       | 22                  | 38,400 |
| I       | 88                  | 43,800 |

From Fig. 4 and Table II it is clear that not much may be said concerning the value of  $\mu$  for respiratory movements, other than that it is consistently greater than that for the heart rate. Values of  $\mu$  of

the order of 40,000 calories are seldom encountered in poikilothermic organisms. During a treatment a patient may lose as much as 5 to 6 pounds of water through the skin and respiratory passages. The lack of precision of the respiratory data makes it impossible to be certain that the Arrhenius equation fits, although no systematic failure of the equation was detectable. The marked accelerations of respiration with increasing temperatures are probably the resultant of the control of the respiratory center by homeostatic neurological mechanisms involved in temperature regulation by elimination of water. This effect probably masks the normal pace-making mechanism of the respiratory center. It is, therefore, doubtful if the value of  $\mu = 40,000 \pm$  calories is at all comparable to values of temperature characteristics obtained from respiratory movements of poikilothermic animals.

## II

Recent studies of electrical potentials from the central nervous system have indicated that units in the central nervous system may be spontaneously active discharging impulses over efferent fibers at frequencies directly proportional to the rates of chemical changes going on in the centers. Spontaneous fluctuations of potentials have been recorded by Adrian and Buytendijk (1931) from the isolated brain stem of the goldfish at frequencies corresponding to normal opercular breathing rhythms. Similar spontaneous discharges from the respiratory center have been found from isolated ganglia of the beetle, *Dytiscus marginalis* (Adrian, 1931). Spontaneous activity in the central nervous system, not involving the respiratory center, has been recorded by other workers (Fischer, 1932; Bishop and Bartley, 1933*a*, 1933*b*; Bartley, 1933; Gerard, Marshall, and Saul, 1934; Prosser, 1934).

Investigations of the effect of temperature on the frequency of rhythms of activity of central nervous origin in poikilothermic animals have been made by Crozier and others (*cf.* especially Crozier, 1924-25). Such diverse phenomena as the frequency of chirping of crickets, the frequency of flashing of fireflies, the speed of creeping of insects, follow the Arrhenius equation and yield specific temperature characteristics. These studies have antedated observations of spon-

taneous central nervous activity obtained by the electrical recording methods and are consistent with the notion of continuous chemical mechanisms in the central nervous system releasing motor discharges at frequencies directly proportional to the velocities of the mechanisms. It is interesting that Crozier and Stier (1924-25), for example, found a critical increment of  $\mu = 16,500$  calories for the frequency of opercular breathing of goldfish before Adrian and Buytendijk recorded the spontaneous electrical effect from the brain stem.

These matters, together with the finding that the "spontaneous" frequency of the repetitive discharge of nerve impulses from the peripherally unstimulated neuromasts of fish obeys the Arrhenius equation, led one of us (Hoagland, 1933) to consider that the estimation of durations of time by man might depend upon the rate of continuous underlying chemical events in the nervous system. If this were true, the frequency of counting seconds should follow the Arrhenius equation and might yield a significant critical increment. Naive subjects whose body temperature was altered by diathermy, as well as those whose temperature varied as a result of fever, were asked to count to 60 at a rate of what they believed to be 1 per second. The counting was found to be faster the higher the temperature, in accordance with the Arrhenius equation, yielding a  $\mu$  of 24,000 calories. The fact that the value of  $\mu$  coincides with one of the modal peaks found for temperature characteristics of poikilothermic animals (Crozier, 1925-26) suggests that the pace-making reaction, upon which judgments of duration are based, may be of the nature of an irreversible chemical reaction and may be catalyzed in a specific way corresponding to  $\mu = 24,000$  calories—a value which has been found associated with certain cellular oxidation processes.

The lower curve of Fig. 5 shows a plot of the effect of temperature on judgments of duration for six subjects (*cf.* Hoagland, 1933). On the same figure are typical plots showing the effect of temperature on the pulse frequency for two other subjects. The plot was made by eliminating absolute differences in the speed of counting, by telescoping the ordinates so as to bring the data for the estimation of duration for all of the subjects together on the graph, thus showing the uniformity of the slope of the line which determines the value of  $\mu$ .

A similar procedure was used for eliminating absolute differences in heart rates of the two patients at the same temperatures.

The values of  $\mu$  for the pulse and for the speed of counting are distinctly different. Whatever may be the chemical pace maker mechanism for judgments of short durations, it is clearly not the

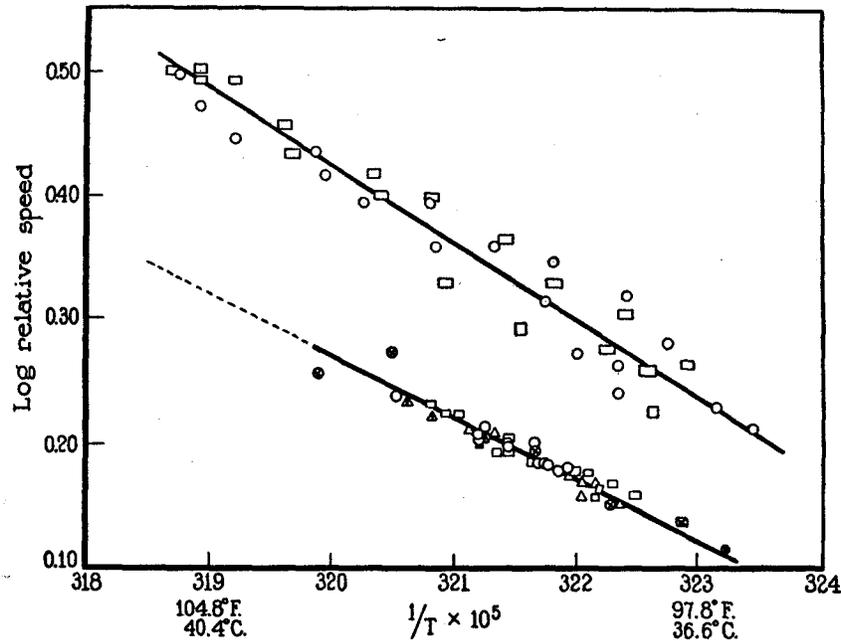


FIG. 5. Arrhenius equation plots of pulse data from two patients (upper curve) and for the effect of temperature on estimations of duration (lower curve), six subjects.

The positions of the sets of data with respect to the ordinate axis are arbitrary. The curves are arranged to show the differences in the slopes of the lines for the two functions.

same as the chemical determinant for the heart beat. The suggestion, often made, that the pulse may serve as a sort of master clock determining one's sense of duration is evidently not tenable.

#### SUMMARY

The value of  $\mu = 29,400$  has been found for the human heart beat over the temperature range of approximately  $4.7^\circ\text{C}$ . This value is

different from that of 24,000 calories which has been obtained for the effect of temperature on judgments of short durations.

The evidence indicates that the estimation of short time intervals is controlled by a chemical master reaction which is independent of the pulse rhythm.

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