SPONTANEOUS FLUCTUATIONS IN THE TOTAL SERUM PROTEIN CONCENTRATION IN HEALTHY RABBITS

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Regular estimation of the total blood serum protein concentration in healthy rabbits for 53 days revealed spontaneous periodic changes in this parameter. Fluctuations in the total serum protein level of the healthy rabbits has a period of 21.6 ± 1.2 days and an amplitude of 0.41 ± 0.10 g%, with a statistical mean level of 6.45 ± 0.03 g%. The periodic process thus revealed is expressed mathematically.

In clinical practice determination of the total protein concentration and protein fractions in the blood serum is used as a valuable diagnostic and prognostic test in many diseases. As a rule the pathological picture of the serum proteins is compared with a normal established by each investigator individually. The reason is that normal values determined by different workers vary considerably despite the use of identical biochemical methods [1-9]. The reason for this phenomenon has not yet been adequately clarified and it is interpreted differently [7, 10]. Recently, in connection with the study of "biological clocks" investigations have been undertaken to determine the role of periodic changes in metabolism under normal and pathological conditions [11, 12, 14].

The object of this investigation was to study the character of fluctuations in the total serum protein concentration in healthy rabbits.

EXPERIMENTAL METHOD AND RESULTS

Experiments lasting for 53 days (from August 19 to October 10) were carried out on 10 male chinchilla rabbits weighing initially 3.3 kg. The animals were kept under enclosed conditions at a temperature of 18-20°C and a humidity of 60-70% on a standard diet. Every 3-4 days between 9 and 10 A.M., blood was taken from the auricular vein of the unfed rabbits. The total serum protein concentration was determined refractometrically.

During the 53 days of the experiment two periods of fluctuations in the total serum protein concentration were found for each rabbit, and the phase of the fluctuations frequently differed from one animal to another. When the changes in the mean-protein concentration on successive days were plotted, a curve consisting of a wave with unequal rises and falls was obtained (Fig. 1). It was difficult to describe this waveform process quantitatively because the fluctuations in the total serum protein concentration of the individual rabbits were not synchronized. The curves obtained for different rabbits were therefore superposed after deliberate displacement of the maxima and minima. This gave a wave-like line (Fig. 2) on which the required quantitative characteristics of the periodic process could be detected: the statistical mean total serum protein concentration was 6.45 ± 0.03 g% (M ± 2m). This figure is the mean of all determinations in 10 rabbits for 53 days. The mean period of fluctuation was 21.6 ± 1.2 days, and the amplitude of the waves for consecutive maxima was 0.44 ± 0.24 and 0.37 ± 0.12 g%, and for consecutive minima 0.48 ± 0.02, 0.50 ± 0.09, and 0.19 ± 0.05 g%.

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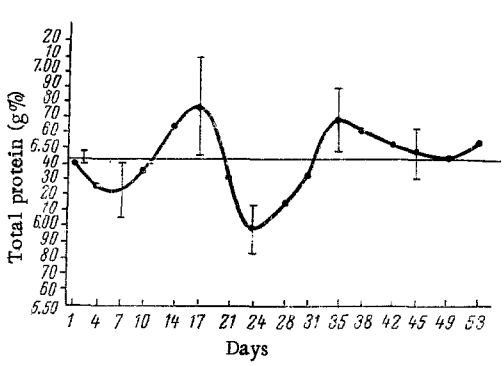

Fig. 1

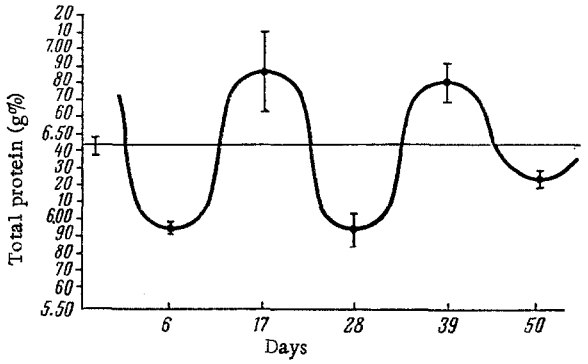

Fig. 2

Fig. 1. Dynamics of total serum protein concentration (M ± 2m) of rabbits in the course of the experiment.

Fig. 2. Dynamics of total serum protein concentration (M ± 2m) of rabbits after synchronization of periods of fluctuation of this index in individual animals.

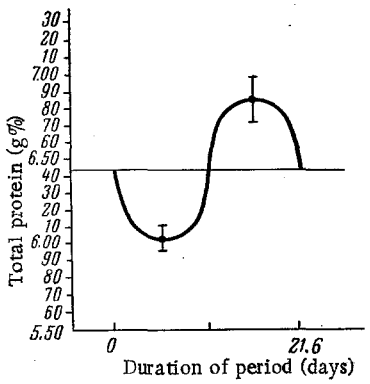

Fig. 3. Graphic representation of the periodic process.

As the results given in Fig. 2 show, the amplitude of the fluctuations in the total serum protein concentration measured for the duration of the experiment was definitely unstable in its value.

According to the theory of automatic control [13], a well-regulated system (in this case, the body of a healthy rabbit) must give out uniform waves of output indices (in this experiment the total serum protein concentration) with amplitudes of equal value. Disturbance of the normal amplitudes and, even more, of the normal periods is evidence of the considerable dependence of the regulatory systems on the action of external factors.

The change in amplitude in the present case undoubtedly means that the concept of "stability" of laboratory conditions is purely relative, and that alternation of the seasons of the year (summer–autumn), changes in atmospheric pressure, and very slight changes in the method of keeping the animals, almost imperceptible at first glance, do in fact exert a marked influence on the rabbits.

To determine the true amplitude of the fluctuation in the total protein concentration on either side of its mean value in the rabbits' serum the mean value was determined from all individual maximal and minimal amplitudes. As a result, true values of amplitudes allowing for all the factors to which laboratory animals are usually exposed in animal houses, were obtained: for the maxima 0.41 ± 0.13 g% and for the minima 0.41 ± 0.07 g% (M ± 2m). By substituting the values for the periods and amplitudes of the spontaneous fluctuations in total serum protein concentration of the rabbits thus obtained in the graph, a general picture of the periodic process was obtained (Fig. 3). This curve approximates to the law of change in this index in healthy chinchilla rabbits weighing 3.3 kg during the summer–autumn period when kept in the laboratory animal house. Mathematically, this law is described by the sinusoid:

$$A_t = 6.45 + 0.41 \cdot \sin \frac{\pi \cdot t}{10.8},$$

where A_t is the protein concentration on the given day (in g%), 6.45 is the statistical mean-total protein concentration (in g%), 0.41 is the amplitude of the waves (in g%), to the number of days from the beginning of the period, and 10.8 the half-period of the waves (in days).

This equation is general in character, but to apply it to animals of different species and sexes, and also to man, the precise values of all the coefficients must be obtained.

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