The results of the study of the intensity of nuclear labeling showed that the proportion of intensively labeled nuclei falls significantly with age ($P < 0.05$ for all mitogens) whereas the number of weakly labeled nuclei rises correspondingly (for lymphocytes stimulated by PHA and con A $P < 0.01$, for lymphocytes stimulated by ATS $P < 0.05$), whether the indices of the proliferative response decrease with age or no significant differences in these indices are found. Since the incorporation of [^{3}H]thymidine is known to reflect DNA synthesis by the cell in the S phase of the cell cycle [2], the results described above can be interpreted as a decrease with age in the proportion of cells intensively synthesizing DNA under the influence of the mitogens on the third day of culture. Considering these findings, and also those of Barbaruk [1], who observed an earlier decrease with age in the number of mitoses than in the number of blast cells in cultures stimulated by PHA, and the reported shift of the maximum of the response to phytomitogens in cultures of PBL from old people compared with young from the third to the fifth day [6], it can be postulated that with age there is a reduction in the proportion of cells among the PBL that "react most quickly" to stimulation by mitogens. At the same time, the relative proportion of cells "reacting slowly" to mitogens increases. Under these circumstances qualitative changes in reactivity of the PBL to mitogens evidently precede the decrease in magnitude of the proliferative response.

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BIORHYTHMS OF HISTOPHYSIOLOGICAL INDICES OF THE THYROID GLAND AT DIFFERENT AGES

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Rhythmic changes in several histophysiological indices of the thyroid gland were studied in 144 A/He mice of three age groups: young (sexually immature), sexually mature, and aging. The rhythm of each index was found to be multicomponent in character, including a circadian component and also infradian and ultradian fluctuations. The leading role of the circadian component in the formation of biorhythms of the organ was established, whereas their adjustment during ontogeny is due mainly to a reduction in the power of the ultradian components.

KEY WORDS: histophysiological indices; biological rhythms; thyroid gland; age changes.

Numerous biochemical, radioisotopic and morphological investigation have demonstrated the cyclic character of thyroid gland activity. At the same time, there is indirect evidence of the multicomponent composition of biorhythms, as is shown in particular by the irregular shape of the curves and their several maxima [6, 9, 11], although the authors just cited did not mention this. No spectral analysis of the rhythms has been carried out. The writers have studied the spectral composition of rhythms of the structural elements of the thyroid

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Fig. 1

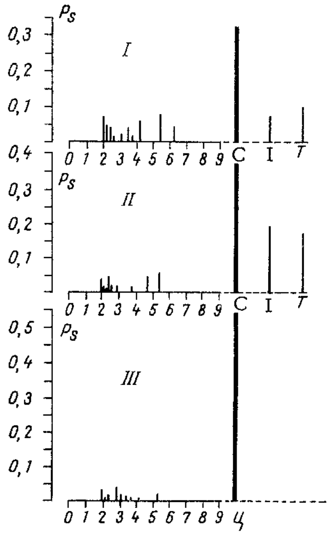

Fig. 2

Fig. 1. Curve of spectral density of rhythmic changes in relative volume of thyroid epithelium of mice of group 1. Three marked maxima can be clearly distinguished: one in the CR region and two in the region of UD components with periods of 4.24 and 2.24 h. The relative power of the individual components is plotted along the ordinate. infr.) Infradian, circ.) circadian.

Fig. 2. Spectral density (P_S) corresponding to different frequency components in three groups of mice. Abscissa, period of fluctuations, h; C) ciradian, I) infradian, T) trend. Roman numerals denote groups of animals.

gland and examined its age changes.

EXPERIMENTAL METHOD

Experiments were carried out on 144 male A/He mice of three age groups: 14-17 days (group 1), 55-60 days (group 2), and 160-170 days (group 3). Choice of age of the animals was made on the basis of a study of the histophysiology of the thyroid gland in mice of this strain at different stages of ontogeny [4]. For a period of 2 months the animals were adapted to artificial conditions of lighting, consisting of 12-h periods of light (from 8 a.m. to 8 p.m.) and darkness (from 8 p.m. to 8 a.m.), the intensity of illumination at the level of the cages containing the mice being about 500 lx.

Material was collected by the dynamic observation method [7] over the period of 2 days at intervals of 1 h. The glands were fixed in formalin–alcohol–acetic acid fluid by Lillie's method and embedded in paraffin wax. Sections, 5 μ in thickness, were stained with hematoxylin and eosin. All stages of histological treatment were strictly standardized. The relative volumes of the follicular and interfollicular epithelium, colloid, and stroma were determined in the sections and the ratio between the volumes of epithelium and colloid and follicular and interfollicular epithelium, the stereological index of resorption, and the mean height of the follicular epithelium were calculated. Details of the methods were described previously [3, 12]. To determine the spectral composition of the biorhythms, the data were analyzed on the Minsk-32 computer by the NBKAT program, based on determination of the power of the individual components of the rhythms obtained by calculation of the autocorrelation function [2, 8]. The results of the morphometric investigation were analyzed by computer in the Laboratory of Processing of Medico-Biological Information, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, (Head, Dr. Med. Sci. N. I. Moiseeva) by V. V. Matseev and V. M. Dorinicheva.

EXPERIMENTAL RESULTS

Changes in all the histophysiological indices studied were found to be rhythmic in character. Spectral analysis showed the multicomponent character of the cyclic changes. Virtually no histophysiological index could be found whose rhythm could be described by only one frequency component. By determination of the spectral density, the composition of the rhythm of each index could be described and the relative power of the individual rhythmic components could be estimated (Fig. 1).

A circadian rhythm (CR) with a period of 20-28 h, ultradian (UD) components with a period of under 20 h, and infradian (ID) components with a period of 28 h to 2.5 days were detected [14, 15]. For a certain proportion of the UD waves, with a period of 20 min to 2-4 h, the name "circahoralian" has regrettably been adopted [1], but not all of the UD components identified in these experiments belonged to this group (Fig. 2). A component with a period equal to infinity also was detected, and this must be regarded as a constant shift of the process (its trend). Since the object of the investigation was to study the CR and UD components, the periods of the experiment were limited to 48 h and, for that reason, no detailed analysis could be made of the ID components, and only their presence and their total power will be indicated.

In each age group spectra of the rhythmic waves of the indices, each had their own characteristic features. For most indices of the animals of group 3 (aging) the power of CR was much greater than that of the UD components. Conversely, in the animals of group 1 (young, sexually immature mice) the UD components of many indices were comparable in power with CR or were more powerful. The dynamics of the indices of the animals of group 2 (adult, sexually mature) occupied an intermediate position in this respect. The difference in the power of the spectral components in the three age groups is demonstrated by Fig. 2, which reflects the mean power of all the indices for the animals of this group, belonging to each frequency component. Clearly, despite the well-marked CR in all groups, with age there was a clear decrease in the relative power of the UD components.

A UD rhythm has been described after a study of the accumulation of radioactive iodine by the thyroid gland in ducks [13], but the authors in question regarded it as the sole manifestation of cyclic activity of the organ. In the present investigation UD components with period of 2 to 5.5 h were only one of the components of a multicomponent rhythm.

The nature of the UD rhythms has not been finally established. They are evidently a direct reflection of fluctuations of activity in metabolic chains [5]. In connection with the considerable changes in intensity of the UD waves in the course of adaptation of the animals, their special significance in adaptive processes has been postulated [10]. These observations are supported by the results of the present investigation; in the youngest animals, in which processes of adaptation were evidently most active, the UD rhythms obtained maximal expression.

It can thus be concluded from these results that the circadian component plays the leading role in the formation of biorhythms of the thyroid gland, whereas their adjustment during ontogeny is due mainly to a reduction in the power of the UD components.

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