

electron microscope. Histological sections stained with E.E. have been used as control in order to evaluate the stage of the illness.

Results. The cell surface of the colon epithelial cells in normal individuals is formed by a glycoproteinous substance rather sharp and apparently cementing the adjacent cells (Figure 1a). Colitis makes the cell coat thinner and the epithelial cells appeared to break off in the sites where the effects of the pathological phenomena were more patent. In these sites, fibrillar bridges of polysaccharidic-like material appeared to be stretched from one membrane to the other among the same population of cells (Figure 1b). In cells completely detached, their 'glycocalix' appeared clearly discontinuous and the plasma membrane showed a characteristically irregular and fibrillar-like outline (Figure 1c).

On the contrary in normal conditions, the glycocalyx appeared as a continuous coat coating the surface of the microvilli regular in number and disposition (Figure 2a). In pathological conditions, the glycocalyx was not so clearly evident and seems to form an extremely loose, irregular net which left unsheltered the most part of the

microvilli. In these cases the microvilli were less numerous and showed a very irregular disposition (Figure 2b).

Discussion. The morphological alteration observed in the glycocalyx of the colon epithelium is probably due to the pathogenetic processes, and this, in turn, might be related to the action of lymphocytes. In fact, these lymphocytes, sensitized during the pathological process as antimucus-antibody-lymphocytes, might be responsible for the alteration of the glycocalyx, in all the above epithelial structures^{11,12}. But it is also possible that the action of specific virus might alter not only the genetical patrimony of the cell, but also the whole mechanism of proteinuous synthesis. Then, in this case, the virus might be able to modify the biochemical and histochemical composition of both the cellular coat and glycocalyx.

¹¹ M. SAMTER, *Immunological Diseases* (Little Brown and Co, Boston 1971), vol. 1 and 2.

¹² P. A. MIESCHER and H. J. MÜLLER EBERHARD, *Textbook of Immunopathology* (Grune and Stratton, New York, 1969), vol. 1 and 2.

Evidence of Diurnal Fluctuation of Sensitivity to Noradrenaline in the Rat - the Role of the Thyroid

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Summary. The capacity for heat production, under the influence of the same amount of noradrenaline, in the rat was significantly higher in the evening (20.00 h) than in the morning (07.00 h). Thyroidectomy produces not only a lower level of heat production, but also a complete disappearance of the differences between the morning and the evening experiments.

In mammals and birds the existence of diurnal fluctuations was demonstrated in the general metabolism, body temperature, adrenocortical function, catecholamines, sodium and potassium excretion, urine volume excretion as well as in some other functions^{2,3}. It was also found

that oxygen consumption in the rat adapted to 29°C was higher in the evening and during the night than in the morning. This difference disappeared completely after the thyroidectomy⁴. It is well established that noradrenaline produces an increase in the heat production in the rat and mouse adapted to cold or to thermoneutral zone⁵⁻¹⁰. However, until now no data have been available concerning the changes of the sensitivity to noradrenaline during the day and night.

Material and methods. Observation was made in 6 groups of albino male rats of Wistar strain, weighing 180–200 g each group consisting of 10 animals. Rats were adapted to room temperature (19–22°C) for about 4 weeks, with daily illumination, food and water ad libitum. Noradrenaline (Galenika) was injected i.p. in doses of

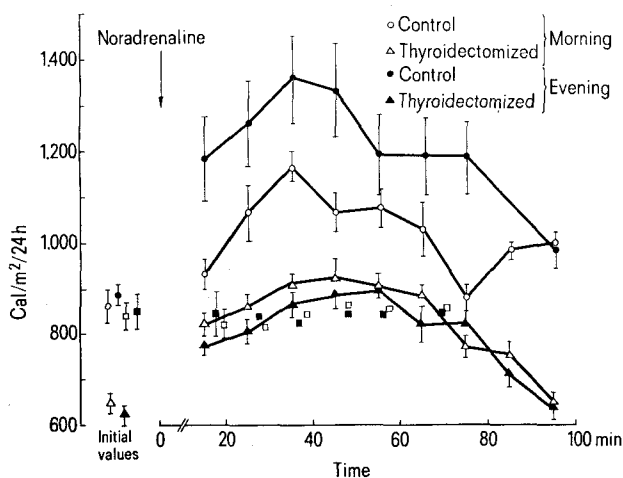


Fig. 1. The effect of noradrenaline (1.6 mg/kg) on the heat production in the rat adapted to 19–22°C and measured at 30°C.

Normal control: measurement made in the morning (07.00 h) ○—○; in the evening (20.00 h) ●—●. Thyroidectomized: measurement made in the morning (07.00 h) △—△; in the evening (20.00 h) ▲—▲. Physiological solution: measurement made in the morning □—□; in the evening ■—■. Mean ± SEM of 10 animals.

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² F. HALBERG, *A. Rev. Physiol.* 31, 657 (1969).

³ R. T. W. L. CONROY and J. N. MILLS, *Human Circadian Rhythms* (J. and A. Churchill, London 1970).

⁴ V. POPOVIĆ, P. POPOVIĆ and V. PETROVIĆ, *C. r. Soc. Biol., Paris* 150, 1249 (1956).

⁵ L. JANSKÝ, R. BARTUNKOVÁ and E. ZEISBERGER, *Physiologia bohemoslov.* 16, 336 (1967).

⁶ B. HOŠEK and L. NOVÁK, *Experientia* 24, 1214 (1968).

⁷ L. JANSKÝ, R. BARTUNKOVÁ, J. KOCKOVÁ, J. MEJSNAR and E. ZEISBERGER, *Fedn. Proc.* 28, 1053 (1969).

⁸ J. LEBLANC, *Am. J. Physiol.* 212, 530 (1967).

⁹ R. PORTET, R. BERTIN, M. C. LAURY and L. CHEVILLARD, *Non-shivering Thermogenesis*. Proc. of the Symposium (Swets and Zeitlinger N. V., Amsterdam, Academia, Prag 1970), p. 57.

¹⁰ V. M. PETROVIĆ and L. MARKOVIĆ-GIAJA, *Experientia* 29, 1295 (1973).

1.6 mg/kg of body wt. Control groups were injected only physiological solution. The oxygen consumption was measured individually in a gas analyzer, based on the closed circular airing system adapted to the small animals¹¹. The measurements were started at 30 min before the injection of noradrenaline and continued after the injection over the period of the duration of the effect. All the measurements were realized at 36°C, starting at 07.00 h or 20.00 h. Thyroidectomy was performed under ether anesthesia and oxygen consumption measurement was carried out on the 7th day following the operation.

Results and discussion. The results are expressed in calories per m²/24 h and presented in Figure 1. As is evident, the initial values of the heat production, prior to the injection of noradrenaline or of physiological solu-

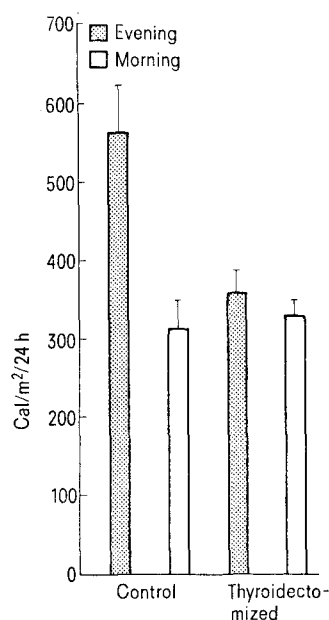


Fig. 2. Differences between the maximal level of the heat production under the influence of noradrenaline and the initial values obtained prior to the injection in the morning and in the evening experiments in normal control and thyroidectomized rats (Mean \pm SEM of 10 animals).

tion, were somewhat higher in the evening than in the morning experiments. These findings are similar to those reported by Popović et al.⁴. In the normal control rats, a significant increase in heat production was observed 25 min after the injection of noradrenaline in both the morning and the evening experiments, being 21% and 40% respectively. Maximum increase was reached at about 40 min after the injection of noradrenaline. The difference between the maximal calorogenic effect registered in the morning experiment and that obtained in the evening experiment, in the first period of the duration of the effect of noradrenaline (Figure 2), was statistically significant ($p < 0.01$).

The evidence that the same amount of noradrenaline produced markedly higher calorogenic effect if applied in the evening than in the morning suggests the existence of the diurnal fluctuation of the sensitivity to this hormone in the rat. As the circadian rhythm of thyroidal iodine release was found¹², and the disappearance of the circadian rhythm of oxygen consumption after the thyroidectomy was registered⁴, we suspected that the thyroid might be involved in the control of the diurnal fluctuation of the sensitivity to the applied noradrenaline in the rat. To investigate this possibility, a preliminary study was undertaken to examine the effect of noradrenaline in the thyroidectomized rats. As shown in Figure 1, in thyroidectomized animals the initial values of heat production prior to the injection of noradrenaline was significantly lower than in the controls ($p < 0.01$). Noradrenaline still produced a significant increase in heat production in both groups, i.e. in animals examined in the morning as well as in those examined in the evening ($p < 0.01$). It should be pointed out that the level of the heat production under the influence of the same dose of noradrenaline (1.6 mg/kg of body weight) was significantly lower in thyroidectomized animals than in the controls ($p < 0.01$). In addition to this no difference in the calorogenic effect of the injected noradrenaline was found between groups examined in the morning and in the evening. Therefore, diurnal fluctuation in the calorogenic effect of the applied noradrenaline seems to be dependent on the thyroid.

¹¹ J. GIAJA, *Biologie méd.* 42, 545 (1953).

¹² Y. C. PATEL, H. W. G. BAKER, H. G. BURGER, M. W. JOHNS and J. E. LEDINEK, *J. Endocr.* 62, 421 (1974).

Destruction of Afferent Nerve Terminals in the Inner Ear of Frog by Aminooxyacetic Acid

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Summary. The drug aminooxyacetic acid, which inhibits GABA-transaminase, destroys the afferent nerve endings in the inner ear of the frog. The efferent nerve endings and the sensory cells are not affected.

Sensory cells in the *acustico-lateralis* system of vertebrates are innervated by afferent and efferent nerve fibres^{1,2} (Figure 1). The synaptic connections between the sensory cells and the nerve fibres on structural and functional grounds appear to be chemically mediated^{3,4}. The synaptic transmitter at the efferent contacts is probably cholinergic^{5,6} but the transmitter is unknown at the afferent synapse, although catecholamine-like compounds⁷⁻⁹, glutamate¹⁰, and γ -aminobutyric acid¹¹ (GABA) are possible candidates.

Injection of drugs that interfere with catecholamine metabolism have previously been shown to affect the

¹ H. ENGSTRÖM, *Acta oto-lar.* 49, 109 (1958).

² K. HAMA, *J. Cell Biol.* 24, 193 (1965).

³ T. FURUKAWA and Y. ISHII, *J. Neurophysiol.* 30, 1377 (1967).

⁴ Å. FLOCK and I. RUSSELL, *Nature New Biol.* 243, 89 (1973).

⁵ I. RUSSELL, *J. exp. Biol.* 54, 643 (1971).

⁶ S. IURATO, L. LUCIANO, E. PANNESSE and E. REALE, *Acta oto-lar.*, suppl. 279 (1) (1971).

⁷ P. MONAGHAN, *Cell Tiss. Res.* 163, 239 (1975).

⁸ M. P. OSBORNE and R. A. THORNHILL, *Z. Zellforsch.* 127, 347 (1972).

⁹ R. A. THORNHILL, *Comp. gen. Pharmac.* 3, 89 (1972).

¹⁰ A. B. STEINBACH and M. V. L. BENNETT, *J. gen. Physiol.* 53, 580 (1971).

¹¹ Å. FLOCK and D. M. K. LAM, *Nature* 249, 142 (1974).