MITOTIC ACTIVITY OF THE CORNEAL EPITHELIUM IN ANIMALS KEPT AT DIFFERENT TEMPERATURES

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During recent years considerable attention has been paid to the study of the mechanisms regulating mitotic activity in the body. Little is known, however, of the role of energy metabolism and its effect on mitotic activity.

We have therefore compared the mitotic activity in animals differing from one another in the indices of their energy metabolism as a result of having been kept at different temperatures. It must be pointed out that the action of temperature on cell division has been examined by various workers [5, 6], but unfortunately their work has done little to elucidate the role of energy metabolism as a factor influencing cell reproduction.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats and mice. The level of their energy metabolism was judged by the volume of oxygen consumed per unit body weight of the animals. In order to stimulate the energy metabolism in rats and mice previously kept in warm conditions, they were placed in a cold room. The opposite effect was obtained by transferring animals kept in the cold to a warm room. While this was done, we recorded the gas exchange and, in some experiments, also the blood sugar concentration.

The intensity of the gas exchange was determined by N. I. Kalabukhov's method [1] and the blood sugar by the Hagedorn-Jensen method. The mitotic activity was determined in total preparations of the corneal epithelium, stained with Carazzi's hematoxylin. The mitotic index was taken to be the number of divisions present on the average in 100 fields of vision, corresponding to 1 mm^2 of the area of the cornea.

A series of experiments was carried out on fasting rats and mice, kept in different temperature conditions.

EXPERIMENTAL RESULTS

In the first series of experiments some of the rats and mice kept continuously at an atmospheric temperature of 25° were placed for 2 hr in gas-exchange chambers cooled to 10° and 4°, while others were left in the previous conditions.

TABLE 1. Mitotic Activity of the Corneal Epithelium and Gas Exchange in Mice and Rats in Different Temperature Conditions

Room temperature	Rats			Mice		
	No. of animals	Mitotic index	O_2 consumption per h per kg body wt. (in ml)	No. of animals	Mitotic index	O_2 consumption per h per kg body wt. (in ml)
25°	17	344	730	8	312	2 700
10°	8	118	1 750	—	—	—
4°	8	20	2 091	8	135	5 197
Significance of difference (P)	—	0,000	0,000	—	0,001	0,003

TABLE 2. Effect of Transferring Mice on Mitotic Activity and Blood Sugar Level

Group of mice	No. of mice	Mitotic index	Blood sugar (in mg%)
Control (room temperature 24°)	5	259	118
Mice transferred for 2 hr to another cage at the same temperature	5	227	115
Mice transferred for 2 hr to a cage cooled to 7°	5	89	86
P for the first and third groups*	–	0.011	0.017

*The differences between the first and second groups were not statistically significant.

TABLE 3. Mitotic Activity and Gas Exchange in Rats Transferred for 2 hr from a Cold (7-8°) to a Warm Room (25°)

Group of rats	No. of rats	Mitotic index	O_2 consumption (in ml/h/kg body weight)
Control (room temperature 7-8°)	8	274	3,765
Experimental	8	316	2,504
P	–	0.25	0.001

TABLE 4. Mitotic Activity, Blood Sugar, and Weight Loss in Rats after Fasting for 3 days in Different Temperature Conditions*

Room temperature	No. of mitoses			Blood sugar			Wt. loss (%)
	control	experiment	P	control	experiment	P	
20°	359	166	0,01	95	60	0,001	30
26°	342	292	0,843	87	84	0,981	16

*At 20° the control and experimental groups each contained 10 animals, and at 26°, 15 animals.

It will be clear from Table 1 that the oxygen consumption of the rats and mice kept in the cold rooms rose sharply, whereas their mitotic activity fell.

In the next series of experiments we studied the effect of transferring mice on their mitotic activity and blood sugar concentration. It will be seen from Table 2 that the lowering of the mitotic activity of the corneal epithelium and of the blood sugar level in mice transferred to a cold cell by comparison with control mice was significant. No change was observed in the mitotic activity and blood sugar of mice transferred to another cell at the same temperature.

In the next series of experiments, rats kept for a long time in a cold room were transferred to respiration chambers warmed to 25°. It is clear from Table 3 that by comparison with the controls, the gas exchange of the experimental rats was significantly changed. A slight, but not statistically significant, increase in mitotic activity was observed in the experimental animals.

These facts suggest that there is a connection between the degree of exhaustion of the energy resources of the starving animal and the level of its metabolic activity [4]. In order to verify this hypothesis, experiments were carried out in the course of which various changes in the energy balance of fasting animals were introduced.

It is seen from Table 4 that a three-day fast of rats (weight about 60 g) kept in a room at a temperature of 20° led to a significant decrease in weight, accompanied by an equally appreciable depression of mitotic activity. At the same time, a clear fall in the blood sugar concentration was observed.

Different results were obtained in the case of the experimental and control animals kept in a room with an atmospheric temperature of 26°. In these conditions fasting for 3 days was not accompanied by such a marked loss of weight as in the preceding experiments. The blood sugar level in the experimental animals showed practically no difference from the control level, and the decrease in mitotic activity was not statistically significant.

In earlier work [3] we found a marked fall in the number of divisions in the corneal epithelium of fasting mice at a room temperature of 20°.

We carried out experiments which showed that elevation of the environmental temperature from 20° to 27° leads to a marked decrease in the weight loss in fasting mice; the mitotic activity of these animals showed no change from that in the controls (Table 5).

These experiments indicate a connection between the energy expenditure of the animal, as determined by the environmental temperature, and the mitotic activity of its corneal epithelium. A sudden lowering of the temperature increases the energy metabolism and, at the same time, lowers the mitotic activity. Under these circumstances,

TABLE 5. Mitotic Activity and Weight Change in Mice Fasting for 2 Days at Different Environmental Temperatures

Group of mice	Room temperature	No. of mice	Mitotic index	Change in wt. (%)
Control	20°	5	360	+2
Experimental	20°	5	32	—27
Experimental	27°	5	375	—8

Note. P for the first and third groups 1.000; P for the first and second, and second and third groups 0.000.

as A. A. Manina and L. I. Chekulaeva [2] have shown, the intensity of protein synthesis is considerably diminished. In our opinion, this is associated with a disturbance of the plastic metabolism, due to the intensive heat production of the body.

It must be remembered, however, that in the cold period of the year, when a stable equilibrium is established in animals between heat production and heat output [1], no such depression of mitotic activity is observed. In these conditions it appears that a normal correlation is maintained between the levels of the plastic and energy metabolism, supported by food and by certain physical thermoregulatory mechanisms. For this reason, a decrease in the level of the energy metabolism in animals transferred to a higher environmental temperature does not cause any significant increase in the mitotic activity, which is maintained at an optimal level at a low temperature also. The decrease in the energy expenditure in fasting animals enables them to maintain their normal level of cell reproduction for a longer period of time.

SUMMARY

A study was made of the effect of different temperatures on the mitotic activity of the rat and mouse corneal epithelium. As established, additional energy expenditure of the organism connected with the heat production requirements when suddenly placing the animals in conditions of cold, caused a marked depression of the mitotic activity of the corneal epithelium, accompanied by intensified gaseous exchange and reduction of the blood sugar content. In starving rats and mice kept in optimal temperature conditions it was possible to prolong the normal mitotic activity of the corneal epithelium. The extent of body weight loss in these animals was decreased.

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