7. G. A. Ryazhkin, V. G. Vladimirov, A. D. Smirnov, et al., Voen.-Med. Zh., No. 9, 43 (1978).
8. A. B. Shekhter and G. N. Berchenko, in: Current Problems in Clinical Morphology [in Russian], Moscow (1982), p. 58.
9. V. M. Shipilov, K. K. Zaitseva, G. A. Kashkov, et al., Transactions of the Leningrad Society of Morbid Anatomists [in Russian], Vol. 23, Leningrad (1982), p. 280.
10. E. E. Peacock and W. van Wincle, Wound Repair, Philadelphia (1976).

ACTIVATION OF CELL DIVISION AND NUCLEIC ACID SYNTHESIS IN THE CORNEAL EPITHELIUM OF ALBINO RATS BY REPEATED STRESS

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Adaptation to unfavorable factors is accompanied by activation of nucleic acid and protein synthesis in systems responsible for adaptation [5].

In this investigation the possibility of similar changes taking place in structures not actively participating in adaptation was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 112 male albino rats weighing 160-190 g. Stress was induced by exposure for 1.5 h to sublethal (up to 41.5°C) hyperthermia, exposure of animals in a pressure chamber to an "altitude" of 9000 m for 4 h, and fixation of the animals in the supine position for 1 h, all these procedures being applied once or five times. The techniques of hyperthermia and hypoxia were described previously in greater detail [1, 7]. The animals were killed and the corneas removed for investigation within 1 h after the end of exposure to stress. The rate of RNA synthesis was judged from the mean number of grains of silver above 100 labeled cells. The corneas were preincubated with [^{3}H]uridine (10 μ Ci/ml, specific radioactivity 1.5 mCi/ml, 28 Ci/mmole) for 1.5 h. The mitotic index (MI), the index of [^{3}H]thymidine-labeled nuclei (ILN), and the intensity of thymidine labeling (LI) were determined by methods described previously [8].

EXPERIMENTAL RESULTS

The results indicate that after a single exposure to hypoxia, hyperthermia, and immobilization, MI in the corneal epithelium decreased (Table 1). DNA synthesis under these circumstances remained stable. These data are in harmony with views on reactive inhibition of mitosis during stress [9, 10]. A reduction of 2.2 times in the intensity of thymidine labeling in the corneal epithelium after single sublethal hyperthermia was evidently the result of the direct action of the high temperature [12]. A single exposure to immobilization caused a significant decrease in the intensity of [^{3}H]uridine labeling, whereas hyperthermia led to no significant changes in this parameter.

A different picture was found after repeated exposure to stress. After immobilization five times reactive inhibition of mitosis was absent, whereas after hyperthermia and hypoxia MI increased by 1.7 times. Another significant difference from the results obtained with a single exposure to stress was activation of DNA synthesis. This was shown by an increase in ILN by 2.1 times after five exposures to immobilization and hyperthermia and by 1.7 times

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TABLE 1. Changes in Efficiency of Nucleic Acid Synthesis and Activity of Corneal Epithelial Cell Division in Rats Exposed Once and Repeatedly to Stress (M ± m)

Exptl. conditions	DNA			RNA
	MI, %	ILN, %	LI	LI
Single immobilization	2,26±0,98*	10,32±0,52	46,0±5,91	11,02±0,5*
Control	9,64±0,58	9,96±0,28	42,38±0,64	16,12±0,71
Immobilization five times	10,01±0,9	11,7±0,56*	52,2±3,59*	14,8±1,46*
Control	8,43±0,73	5,49±0,22	19,9±1,04	11,18±0,48
Single hyperthermia	1,2±0,4*	6,6±0,38	13,08±0,56	7,47±0,42
Control	9,29±0,9	5,34±0,35	29,3±1,08	8,01±0,52
Hyperthermia five times	11,38±1,17*	11,2±1,18*	16,10±1,38*	13,4±0,91*
Control	6,5±0,46	5,5±0,7	12,54±0,63	7,34±0,32
Single hypoxia	3,85±0,94*	6,42±0,93	23,16±4,24	—
Control	8,43±0,73	5,49±0,22	19,9±1,04	
Hypoxia five times	16,6±1,93*	9,59±1,19*	35,2±1,48*	14,27±0,83*
Control	9,64±1,56	5,49±0,22	19,9±1,04	5,8±0,36

Legend. *P < 0.05 compared with control.

after five exposures to hypoxia. The increase in number of DNA-synthesizing nuclei was accompanied by acceleration of DNA synthesis, confirmed by an increase in LI after five exposures to stress: by 2.7 times after immobilization, 1.2 times after hyperthermia, and 1.7 times after hypoxia. Similar changes were found in parameters for the rate of RNA synthesis. The intensity of [^{3}H]uridine labeling increased by 1.2 times after five exposures to immobilization and by 1.8 and 2.4 times after hyperthermia and hypoxia respectively. When assessing the increase in the intensity of [^{3}H]uridine incorporation into the epithelial cells after repeated stress, it must be recalled that activation of proliferation is accompanied by intensification of synthesis of different classes of RNA [3, 4, 11].

The same poststress activation of nucleic acid synthesis was thus observed in the corneal epithelium, i.e., in an organ not specifically participating in adaptation processes, as in the heart and brain and immunocompetent and hematopoietic organs responsible for adaptation [2, 6]. Similar changes also were observed in other epithelial tissues (tongue, esophagus).

The mechanism of poststress activation of nucleic acid synthesis and formation of the structural trace of the stress syndrome is not yet clear. It has been suggested that various hormones may participate in this process [6]. In our view, tissue processes also play an essential role in the stimulation of cell division and nucleic acid synthesis in the epithelium. Cell death, accompanying stress, is a powerful activator of nucleic acid synthesis and of cell division, and ultimately leads to restoration of tissue homeostasis.

LITERATURE CITED

1. S. V. Vdovenko and S. S. Timoshin, Byull. Éksp. Biol. Med., No. 8, 86 (1983).
2. P. D. Gorizontov, O. I. Belousova, and M. I. Fedotov, Stress and the Blood System [in Russian], Moscow (1983).
3. O. I. Epifanova, Tsitologiya, 21, 1378 (1979).
4. O. I. Epifanova, Resting Cells [in Russian], Moscow (1983).
5. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981).
6. F. Z. Meerson et al., Patol. Fiziol., No. 5, 4 (1982).
7. M. I. Radivoz, S. S. Timoshin, and A. P. Baranov, Byull. Éksp. Biol. Med., No. 4, 98 (1982).
8. N. B. Simon, S. S. Timoshin, and N. B. Murzina, Byull. Éksp. Biol. Med., No. 7, 87 (1979).
9. G. S. Strelin and V. V. Kozlov, Arkh. Anat., No. 2, 3 (1959).
10. S. S. Timoshin, Arkh. Anat., No. 4, 83 (1983).
11. W. Fitschen and I. Parker, S. Afr. Cancer Bull., 24, No. 2, 61 (1980).
12. R. S. L. Wong and W. C. Dewey, Natl. Cancer Inst. Monogr., 61, 41 (1982).