Granulocytopoietins stimulate proliferation of stem cells in the spleen of lethally irradiated mice and their differentiation into granulocytes. The mechanism of action of granulocytopoietins on the stem cell requires special study.

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RESPONSE OF ANTERIOR PITUITARY CELLS AFTER ACUTE COOLING IN RATS

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The anterior lobe of the pituitary (ALP) of rats exposed to general cooling to −10°C for 6 min was investigated by histological and autoradiographic methods. The diurnal cycle of changes in the functional state of the glandular cells of ALP, the number of mitoses, and the number of labeled cells synthesizing DNA was examined 3, 6, 12, 18, and 24 h after cooling. Marked activation of thyrotrophs and doubling of the number of mitoses were observed 12 h after cooling, with no change in the index of labeled cells in the course of 24 h. The results showed that the stressor response to cold in rats is characterized by potentiation of the thyrotrophic function and by acceleration of mitosis in the cells of ALP.

KEY WORDS: cold stress; thyrotrophs; DNA synthesis; mitosis.

The stressor response consists of a basic essential nonspecific component, in the form of activation of corticotrophs, to which a selective and marked increase in thyrotroph function may be added depending on the type of stressor. During a study of the ultrastructure of the anterior lobe of the pituitary (ALP) in rats exposed to acute cooling, marked activation and an increase in the number of thyrotrophs in the gland were observed by the present writers during the first 24 h [2]. In the investigation described below the effect of acute cold stress on DNA synthesis and reproduction of the cells of ALP was studied in rats and the diurnal cycle of changes in the state of the thyrotrophs was examined. Changes in these functions were judged on the basis of previous information [1] on the diurnal rhythm of DNA synthesis, reproductive activity, and the functional morphology of the glandular cells of ALP in intact rats. There are indications in the literature of an increase in the corticosterone concentration in the blood of rats after short-term general cooling [3] and also of an increase in the thyrotrophin concentration under these conditions [4, 5].

EXPERIMENTAL METHOD

Fifteen male rats weighing 100-120 g were exposed to acute cooling in a chamber at −10°C for 6 min. The pituitary was removed 3, 6, 12, 18, and 24 h after cooling from 3 animals at each time. Meanwhile the pituitary gland of 15 control rats was investigated. DNA synthesis in the glandular cells was investigated by an autoradiographic method with [^{3}H]thymidine with a specific activity of 5.6 Ci/mmole and in a dose of 1 μCi/g body weight. [^{3}H]Thymidine was injected intraperitoneally 1 h before sacrifice. The pituitary glands

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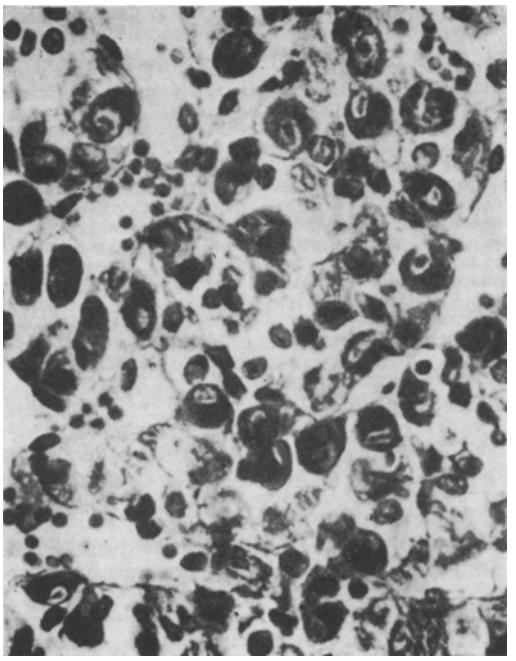

Fig. 1. Strongly activated thyrotrophs, increased in volume and number, lie adjacent to walls of sinusoids. Marked disorganization of complexes of ALP cells. Stained with aldehyde–fuchsin, 400×.

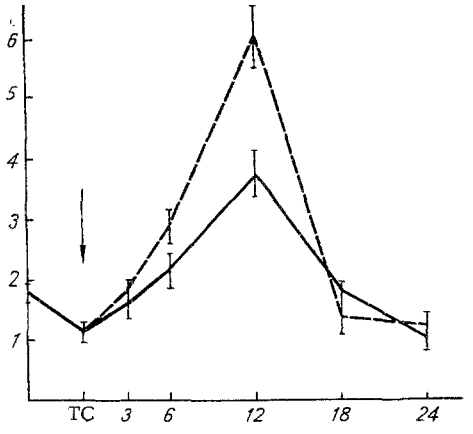

Fig. 2

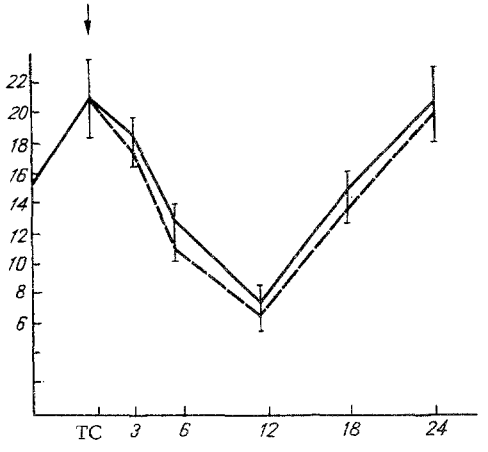

Fig. 3

Fig. 2. Diurnal cycle of changes in mitotic index in control and after cooling. Continuous line, control; broken line, experiment. Ordinate, number of mitoses per 1000 cells; abscissa, time after cooling, in h. TC) Time of cooling.

Fig. 3. Diurnal cycle of changes in index of labeled cells in control and after cooling. Legend as in Fig. 2. Ordinate, number of labeled cells per 1000.

were fixed in Carnoy's fluid and in 10% neutral formalin. Horizontal sections were cut to a thickness of 5 μ. Type R emulsion was used. The autoradiographs were stained with Mayer's hemalum and counterstained with eosin; for histological investigation they were additionally stained by the trichrome–PAS and aldehyde–fuchsin methods. The mitotic index and index of labeled nuclei were calculated per 1000 cells by examination of 9000 cells from each animal. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The histological investigation showed that 3-6 h after cooling nearly all the glandular cells were differentiated and in an active functional state, whereas only solitary transitional and principal cells were present. The nuclei of the glandular cells were large and pale, with a small quantity of chromatin close to the nuclear membrane and with one or two distinct nucleoli. Most of the functionally active cells located chiefly along the capillaries, and producing secretion, were oxyphils. Large and vacuolated thyrotrophs, revealed by staining with aldehyde–fuchsin, mingled with them. Twelve hours after cooling nearly the whole of the perivascular zone was occupied by activated thyrotrophs. Their cytoplasm was capacious and rich in granules and merged with the capillary wall. The phase of active hormone liberation by the thyrotrophs continued. The oxyphils, at this time in the stage of accumulation of secretion, were located more centrally in the band of cells and had a large, pale nucleus and a few granules in their cytoplasm. In the center of the glandular bands degranulated thyrotrophs, intermediate forms of other functional types, and also single principal cells were found (Fig. 1). It can be concluded from comparison with electron micrographs [2] that the few cells with strongly translucent cytoplasm and with a small nucleus, found mainly close to the vessels, were activated corticotrophs.

The functional activity of the gland 18 h after cooling was somewhat lower than at the previous time. Fewer thyrotrophs were found close to the vessels and their cytoplasm was indistinct and vacuolated in parts. In the oxyphils close to the vessels the cytoplasm was filled by numerous granules. In the center of the glandular bands activated forms of oxyphils mingled with intermediate forms of both types of chromophils and with solitary principal cells.

Most glandular cells 24 h after cooling were oxyphils. All the chromophilic cells had a somewhat bulky cytoplasm and a pale nucleus of considerable size. Mainly oxyphils lay close to the capillary walls, i.e., the structure of the gland was close to normal.

In intact rats in the course of the 24-h period changes were observed in the number of mitoses and labeled cells with a regular reciprocal relationship between the mitotic index and the index of labeled cells. After cooling this ratio was still preserved, but the index of labeled cells increased very slightly, whereas the mitotic index 6 h after cooling was significantly higher than normal, and 12 h after cooling was almost doubled. At other times of the 24-h period it was close to normal (Figs. 2 and 3).

The results indicate that immediately after cooling mobilization of thyrotrophs with emergency liberation of secretion takes place in the ALP of rats, and this is accompanied by a simultaneous increase in the function of the corticotrophs and other cell forms. This acute intensification of the activity of the gland caused by cooling terminates toward the end of the 24-h period. The marked increase in the mitotic index in the absence of any increase in DNA synthesis suggests that acute stress accelerates mitosis in cells which are in the premitotic phase at the time of exposure. A characteristic feature of the response to general cooling is thus seen to be a temporary but marked increase in the activity of the thyrotrophs, accompanied by acceleration of the mitotic process in ALP cells prepared for division.

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