KINETICS OF CELL POPULATIONS IN THE MATURING NONDIVIDING NEUTROPHIL COMPARTMENT OF RAT BONE MARROW

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The kinetics of passage of cells through the compartment of maturing nondividing neutrophils of Wistar rat bone marrow was studied by autoradiography with thymidine-^{3}H. Each cell subcompartment was shown to contain transit and reserve populations of neutrophils. The transit time of the maturing nondividing cells and the mean renewal time of the subcompartments of metamyelocytes, band cells, and segmented neutrophils were determined, making allowance for the reserve cell population.

KEY WORDS: *Maturing nondividing neutrophils; renewal time.*

The characteristics of the compartment of maturing nondividing granulocytes of bone marrow are at present limited basically to a description of the size of the granulocyte reserve and its response to various stimuli [3-6]. However, in order to assess granulocytopoiesis it is essential to know the temporal parameters of maturation and the character and rate of renewal of the maturing nondividing granulocytes in bone-marrow tissue.

The object of this investigation was to obtain such information.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200 g (aged 3-3.5 months) were used as the experimental animals. The number of neutrophils in the total volume of bone marrow and peripheral blood of the rats was determined by the method described by the writers previously [1]. Temporal parameters of maturation of nondividing forms of neutrophils were studied by an autoradiographic method with thymidine-^{3}H. The isotope was injected intravenously in a dose of 0.6 μCi/g body weight. The animals were killed at known time intervals in the course of 90 h (three rats at each time) and squash preparations were made from the femoral marrow. The method of preparation of the bone marrow autoradiographs was described previously [1]. In preparations from each rat 1000 metamyelocytes, band cells, and segmented neutrophils were counted separately, and the percentage of labeled cells was determined. The dynamics of entry of the neutrophils into the peripheral blood was determined on the basis of counting blood autoradiographs of 10 rats prepared at intervals of 12-24 h during the 10 days after injection of thymidine-^{3}H.

EXPERIMENTAL RESULTS

The number of cells in the compartment of maturing nondividing granulocytes in the bone marrow of the rats was as follows (all figures must be multiplied by 10^6): total number of myelokaryocytes 2000±70, number of granulocytes 802±80, maturing nondividing granulocytes 532±90, including 166±30 metamyelocytes and 366±60 band cells and segmented neutrophils, neutrophils 24.3±2.2.

Analysis of the curves reflecting the dynamics of progression of thymidine-^{3}H-labeled cells in the bone marrow and blood revealed a marked discrepancy between the influx of la-

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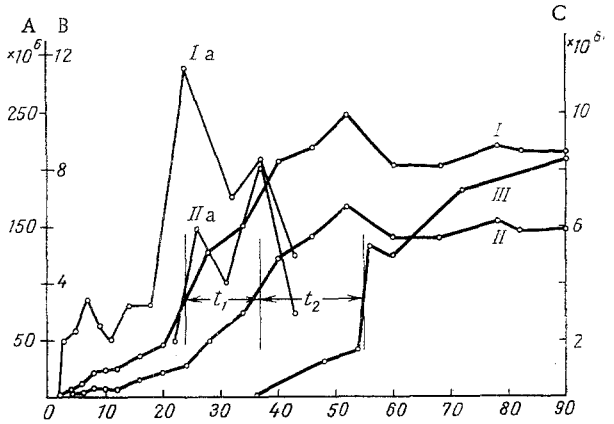

Fig. 1

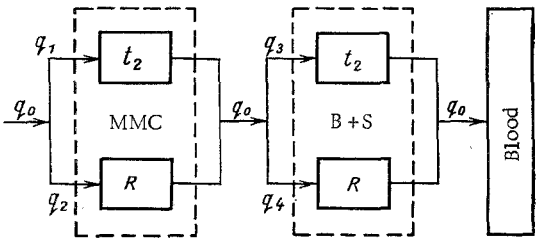

Fig. 2

Fig. 1. Kinetics of labeled nondividing neutrophils in bone marrow and peripheral blood. Ordinate: A) number of labeled cells in bone marrow · 10^6, B) rate of their influx per hour × 10^6, C) number of labeled cells in peripheral blood × 10^6; abscissa, time after injection of thymidine-^{3}H (in h). I) Total number of labeled metamyelocytes, band cells, and segmented neutrophils in bone marrow, Ia) rate of their influx per hour; II) number of labeled band cells and segmented neutrophils in bone marrow, IIa) rate of their influx per hour; III) number of labeled neutrophils in peripheral blood.

Fig. 2. Scheme of kinetics of cell populations in compartment of maturing nondividing neutrophils. MMC) metamyelocytes; B+S) band and segmented neutrophils; R) reserve population; q_0) influx into compartment of maturing nondividing neutrophils and into blood stream per hour; q_1) outflow from metamyelocyte subcompartment in transit per hour; q_2) outflow from reserve part of metamyelocytes per hour; q_3) outflow of cells moving in transit into peripheral blood per hour; q_4) outflow of cells stored in subcompartment of band and segmented neutrophils into peripheral blood per hour.

beled cells into the compartment of maturing nondividing neutrophils and the number entering the blood stream (Fig. 1). During unit time the number of cells entering the blood from the bone marrow was only one-sixth of the number entering the compartment of maturing nondividing neutrophils from the proliferative compartment. This discrepancy, in the writers' view, may be due to differences in the rate of progression of the nonproliferating cells through the bone marrow. Besides cells moving in transit into the blood stream, some of the labeled cells were stored in the compartment of maturing nondividing neutrophils. Meanwhile, an equal number of unlabeled cells retained previously in that compartment entered the blood stream. On the basis of these facts the following scheme can be proposed for the kinetics of cell populations in the compartment of maturing nondividing neutrophils (Fig. 2).

The value $q_0=q_1+q_2=q_3+q_4$ was found from the greatest influx of labeled cells per unit time into the compartment of maturing nondividing neutrophils, on the assumption that this value will be as close as possible to the number of cells passing during the same period of time from the compartment of dividing maturing cells into the postproliferative compartment. The maximal influx of labeled cells was recorded 24 h after injection of thymidine-^{3}H. The value of q_0 was $11.8\cdot10^6$ cells/100 g body weight/h. The greatest influx of labeled cells into the compartment of band and segmented neutrophils was observed 37 h after injection of thymidine-^{3}H, when it was 70% of the value of q_0. Hence it follows that q_1 was $8.2\cdot10^6$ cells/100 g/h and q_2 was $3.6\cdot10^6$/100 g/h. The maximal influx of labeled cells, which was observed 55 h after injection of thymidine-^{3}H, was $1.85\cdot10^6$ cells/100 g/h (q_3), or only 16% of the number of cells entering the subcompartment of band and segmented neutrophils in 1 h. Consequently $9.95\cdot10^6$ cells/100 g/h (q_4) were put into reserve, with the liberation of an equal number of unlabeled cells into the blood stream.

The transit time of the nondividing neutrophils of different levels of maturity was determined from the time interval between the maxima of the influx of labeled cells into the corresponding subcompartments. The transit time of metamyelocytes was 13 h and transit through the subcompartment of band and segmented cells was 18 h. These values agree satis-

factorily with the corresponding values for nondividing neutrophils in rats of another strain [2]. The mean renewal time of the subcompartments of metamyelocytes and band and segmented neutrophils, allowing for the reserve population, was 14.1 and 31 h respectively. Hence it follows that the mean total transit time through the compartment of nondividing neutrophils in rats is 45.1 h.

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CYTOLOGICAL ANALYSIS OF THE INTACT AND REGENERATING LIVER OF VARIOUS STRAINS OF RATS

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A comparative cytological study was made of the control and regenerating liver in two strains of rats: August and cotton-tail. Two-thirds of the liver was removed from both groups of experimental animals and the intact organ served as the control. The animals were killed five or six at a time 30 h and 3, 8, 42, and 120 days after partial hepatectomy. The number of binuclear cells, the dimensions of the mononuclear hepatocytes and of their nuclei, and the mitotic activity and ploidy of the cells were studied. With the exception of mitotic activity, the regenerating and intact liver of the August rats differed from the regenerating and intact liver of the cotton-tail rats in all the above-mentioned cytological parameters. It is concluded that differences in the cytological parameters between the two different strains are due to the genotype of the particular strain.

KEY WORDS: *Hepatocytes; regenerating liver; August rats; cotton-tail rats.*

There is little information in the literature on the dependence of the cytological features of regenerating mammalian internal organs on genotype. For instance, in inbred mice considerable differences have been found in the number of nucleoli in the lymphocytes and liver cells [4]; polymorphism of certain proteins in different strains has been discovered [1]; significant differences in the number of ovulations and in the pre- and postimplantation mortality of embryos have been demonstrated in female mice of different strains [5]; differences in the cell composition of the liver have been established [3] and differences in mitotic activity, associated with different rates of regeneration of the liver after resection have been found in mice of different strains [2].

The object of this investigation was to compare the cytological features of the intact and regenerating liver of rats belonging to different strains.

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