The androstenedione concentration in the blood of immature and adult male baboons is at approximately the same level, namely about 2 ng/ml. It has been shown [8] that most androstenedione in adult male baboons is synthesized in the adrenals. Probably the high blood level of androstenedione in the monkeys is the result of activation of adrenocortical function by pituitary ACTH; the sensitivity of the adrenals, moreover, is much higher in immature than in adult animals [6].

To conclude, even a single injection of metopirone into immature primates causes marked and persistent disturbances of the steroid hormonal balance, which can be observed for 3 days or more.

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REGENERATION OF HEMATOPOIESIS DURING LOCAL IRRADIATION

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During local irradiation of part of the body lymphocytosis develops in the depopulated bone marrow [2], mainly as a result of accumulation of lymphocytes of thymic origin [11]. T cells stimulated postirradiation regeneration of erythropoiesis [3]. The development of lymphocytosis preceded an increase in the number of hematopoietic stem cells, capable of forming colonies in the spleens of lethally irradiated recipients, in the bone marrow [1, 3].

The object of this investigation was to study the effect of T lymphocytes on proliferative activity of hematopoietic stem cells during local irradiation.

EXPERIMENTAL METHOD

Experiments were carried out on 600 BALB/c mice weighing 18-20 g. Local irradiation of the right hind limb of the mice was given in a dose of 7.0 Gy on the RUM-17 x-ray apparatus (dose rate 0.65 Gy/min). Thymectomy or mock thymectomy was performed on some mice 1 month before irradiation. On the 5th-8th day after irradiation the mice were killed by destruction of the cervical spinal cord. The total number of myelokaryocytes was determined in the bone marrow of the irradiated femora. The myelogram was studied in bone marrow films. The population of hematopoietic stem cells (CFU-C) in the bone marrow was studied by the exogenous cloning method [9] in lethally irradiated (7.5 Gy) syngeneic recipients. Colonies were counted

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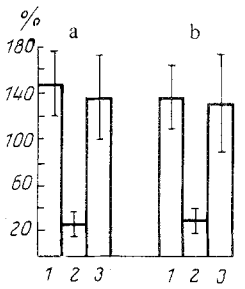

Fig. 1. Number of lymphocytes in locally irradiated mouse bone marrow on 5th day of experiment: a) animals not undergoing operation: 1) without serum, 2) receiving ATS, 3) receiving control serum; b) animals undergoing: 1) mock thymectomy, 2) thymectomy, 3) thymectomy + injection of thymocytes. Ordinate, number of cells (in % of control). Confidence limits at P = 0.05 level.

TABLE 1. Dynamics of Number of CFU-C per Spleen in Locally Irradiated Mouse Bone Marrow during Regeneration of Hematopoiesis (M ± m)

Time after irradiation, days	Mice not undergoing operation	Mice not undergoing operation but receiving ATS	Mice not undergoing operation but receiving control serum	Mice undergoing mock thymectomy	Thymectomized mice	Thymectomized mice receiving thymocytes
Control (before irradiation)	14,7±0,8	14,7±0,8	14,7±0,8	14,5±1,25	14,0±1,2	14,0±1,2
5	10,0±1,3	8,5±2,0	9,8±1,1	8,1±1,8	9,1±1,9	11,0±2,2
6	16,4±1,6	10,0±1,5	15,6±1,3	14,9±1,0	10,6±1,3	17,3±1,8
7	21,4±2,1	14,4±1,6	19,5±1,9	20,2±1,9	13,1±1,7	22,5±2,3
8	19,1±2,2	—	—	—	14,0±1,5	—

TABLE 2. State of Proliferative Activity of CFU-C in Locally Irradiated Mice during Regeneration of Hematopoiesis

Time after irradiation, days	Number of cells "killed" by thymidine		
	mice not undergoing operation	thymectomized mice	thymectomized mice receiving viable thymocytes
Control (before irradiation)	11	9	9
5	40,5	46	43,5
6	54	49,5	55
7	57	54	54,5
8	25	23	—

in the recipients' spleens on the 8th day after transplantation of a standard number of cells (0.5×10^5). Proliferative activity of the CFU-C was studied by the "thymidine suicide" method [8]. Suspensions of bone marrow cells were incubated at 37°C for 20-23 min (specific activity of the added [^{3}H]thymidine was 925 GBq/mmole). In some cases 4×10^7 thymocytes from intact donors were transplanted intravenously into each thymectomized mouse 4.5 days after irradiation. The recipients were given an intraperitoneal injection of 40-50 IU heparin 15-20 min before injection of the cells to prevent the animals from developing shock during transplantation of the large number of thymocytes. In special experiments, on the 3rd-5th day af-

ter irradiation, mice not undergoing the operation received an intraperitoneal injection of 0.2 ml of antithymocytic serum (ATS) [5] or of serum from unimmunized rabbits (ATS titer 1:256).

EXPERIMENTAL RESULTS

On the 5th day of the experiment lymphocytosis developed (Fig. 1) in the irradiated hematopoietic tissue of mice not undergoing operation and receiving or not receiving the control serum, and in animals undergoing mock and genuine thymectomy (with transplantation of thymocytes). Accumulation of lymphocytes in the bone marrow during local irradiation was due to migration of T cells from lymphoid tissue not damaged by irradiation [1, 2]. In the thymectomized animals and in mice receiving ATS, the yield of exocolonies on the 6th-8th day of the experiments was significantly lower than in mice not undergoing operation. Meanwhile injection of thymic cells into athymic mice restored the colony-forming activity of the irradiated bone marrow (Table 1). The ATS which was used, when injected intraperitoneally 3 times into intact normal mice, had no effect on the yield of CFU-C of bone marrow (13.6 ± 1.5).

In the light of these results it seemed logical to explain the difference revealed in the dynamics of CFU-C by the stimulating effect of T cells on proliferation of hematopoietic precursor cells capable of producing colonies in the spleens. However, experiments to study the proliferative activity of the CFU-C did not confirm this suggestion (Table 2). The percentage of cells "killed" by thymidine in animals of the different groups at corresponding times of observation were about equal. The increased yield of exocolonies from irradiated bone marrow in mice not undergoing operation compared with that in the thymectomized animals was due to a decrease in migration of hematopoietic stem cells in the latter into the locally irradiated bone marrow. Migration of stem cells into the spleen from an area of bone marrow screened during irradiation has been shown to be much reduced in thymectomized mice. Transplantation of syngeneic thymus or lymph node cells into such mice restores normal stem cell migration [7]. Thymectomy leads to a decrease in the number of CFU-C in the peripheral blood [6]. The difference in the number of CFU-C in animals of the different groups during local irradiation found in these experiments was probably due to these mechanisms.

During local irradiation T cells, which accumulate in the depopulated hematopoietic tissue, thus have no effect on proliferation of hematopoietic precursor cells forming colonies in the spleens of lethally irradiated recipients, nor do they affect the morphological type of the colonies which they form [1]. Meanwhile thymus-derived lymphocytes, under these conditions, selectively accelerate postradiation regeneration of erythropoiesis [3], stimulating proliferation of erythroid cells [4].

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