# Effect of Low-Dose Radiation on the Main Organs of Erythro- and Lymphocytopoiesis in the Human Fetus

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The liver, thymus, and blood of 31 human fetuses of 6-32 weeks of gestation obtained from parents who are permanent residents in radionuclide-contaminated regions are studied by histological methods. The pathological effect of environmental factors on fetal liver and thymus development are shown. Both the liver hemopoiesis and thymic lymphocytopoiesis are inhibited. In the thymus an increased secretion in the stromal epithelium is associated with the formation of specific microtubules.

**Key Words:** *organs of the human fetus; radiation*

Earlier it was established that one of the most important pathophysiological factors of radiation is damage to the immune system of the organism [3], a process which involves not only the blood, but also the central organs of hemopoiesis [5]. In particular, irradiation of laboratory animals leads to changes in the liver and thymus, and to the appearance of atrophic alterations [7].

The histophysiology of the central hemopoietic organs of the fetus is determined by the status of the maternal organism, which provides specific ecological conditions for their normal development. At the beginning of the first trimester all hemopoietic function of the human fetus is concentrated in the liver, whereas later it moves to the red marrow [2] and the thymus, a special central organ of lymphocytopoiesis [6]. As gestation proceeds, these two organs govern the development of the blood [2] and of the immune system as a whole [4].

The Chernobyl nuclear accident not only stimulated the study of immune system organs in children and adults, but also prompted analogous investigations in fetuses conceived of parents living in radionuclide-contaminated regions. The goal of the present study was to investigate the structure of the liver, thymus, and blood of the human fetus at different stages of development but especially in the early period of embryogenesis, when the processes of hemo- and lymphocytopoiesis are only just forming.

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## MATERIALS AND METHODS

Material was obtained in the towns Klintsy and Novozybkov in Bryansk Region, which suffered fall-out after the accident at Chernobyl. The objects studied were the liver and thymus from fetuses of 6-32-weeks gestation obtained after medical abortions. Only one 32-week fetus was obtained as a result of spontaneous abortion by an essentially healthy mother. Fetal age was determined according to the supposed date of ovulation, and the length of body and foot. The material was fixed with 10% Formalin and embedded in paraffin. Sections were stained with hematoxylin-eosin and Schiff reagent. For electron microscopy, the material was fixed with 2.5% glutaraldehyde and embedded in Epon-Araldite. Semithin sections were prepared on an LKB ultratome and stained with

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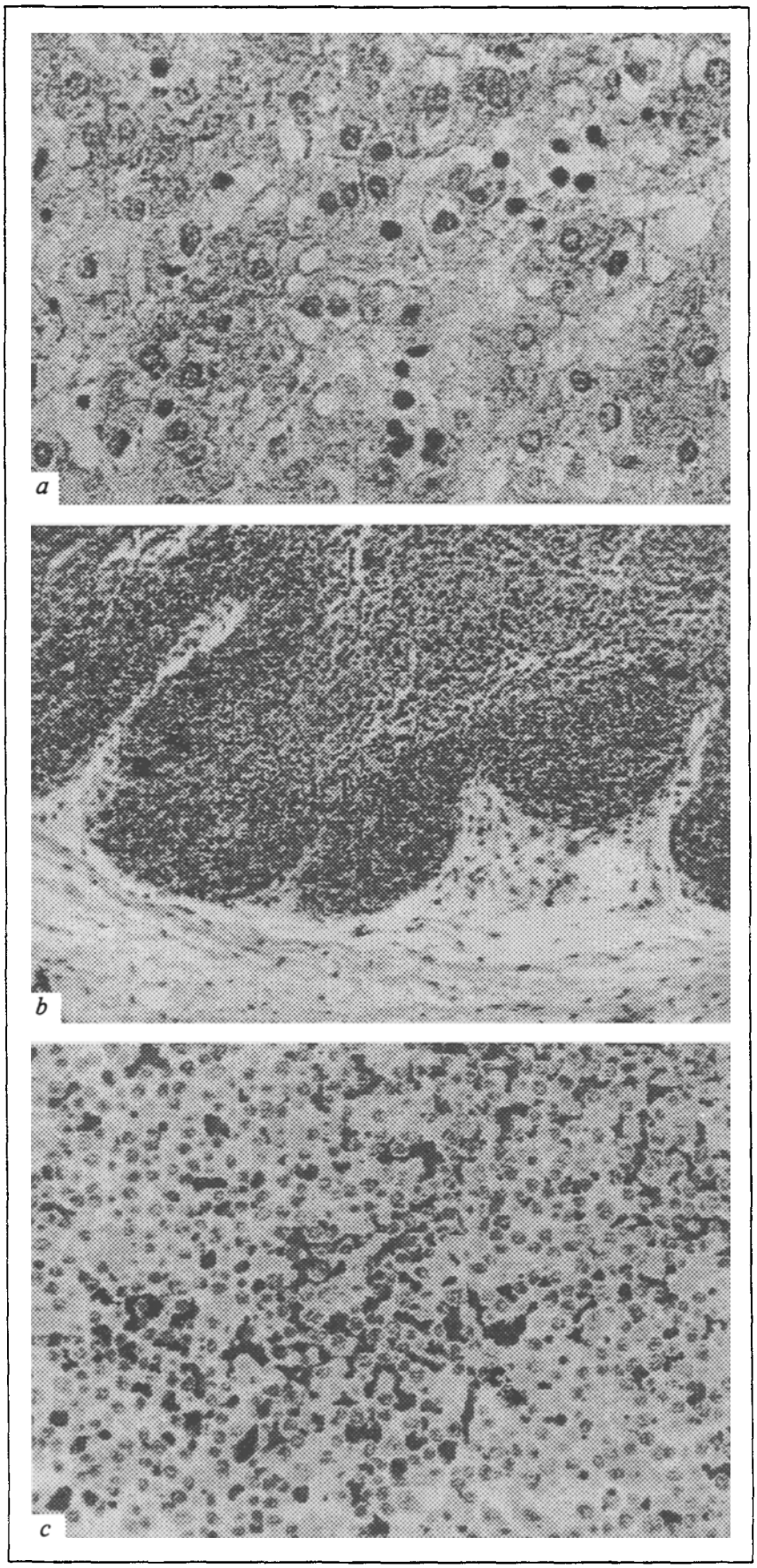


**Fig. 1.** Liver and thymus of a human fetus. *a*) liver of a 32-week fetus from Novozybkov. Vacuolization and necrosis of hepatocytes. Staining with hematoxylin-eosin. ×500. *b*) thymus of a 12-week control fetus. Same staining. ×250. *c*) thymus of a 12-week fetus from Novozybkov. Exocrine secretion of reticuloepithelium. Schiff reaction. ×250.

toluidine blue. The area of hemopoietic islets was calculated using Avtandilov's grid. The results of the calculation were statistically evaluated. In addition, we studied a karyocytogram of the liver from 15 fetuses of 6-12 weeks of gestation obtained in these towns and from 9 control fetuses. Organ prints were fixed with absolute methanol followed by staining with azure II-eosin after Romanowsky-Giemza. At the time of harvesting the material the radiation background was elevated and equal to 80-120 μR/hour in Novozybkov and 18-60 μR/hour in Klintsy, while in Moscow, where the control material was collected, it was within the normal range (10-15 μR/hour).

## RESULTS

In regions of permanent low-dose radiation alterations in liver and thymus embryonic development are observed when compared with a region with a normal environment. These alterations are, as a rule, more pronounced in regions with high-level radiation. In the fetal liver the alterations are expressed in destruction of some hepatocytes and reduction in the number of hemopoietic islets. In the liver of control fetuses of 7-8 weeks the lobose structures are still absent, and hepatocytes form cell strands that give the organ a spongelike structure. Multiple blood islets are observed, reflecting active hemopoiesis. Blood islets occupy 39.7% of the whole area of the organ parenchyma. The livers of 7-8-week fetuses obtained from mothers living in the contaminated regions are characterized by a drastic reduction in both quantity and size of blood islets (thus, in Klintsy and Novozybkov they occupy 23.6% and 2.9% of the organ area, respectively). In the 14th week of embryogenesis in the liver of fetuses from contaminated regions vacuolization of the hepatocyte cytoplasm appears, and by the 19th week it demonstrates a further increase. In the 30th week marked vacuolization and partial necrosis of hepatocytes are seen (Fig. 1, *a*).

Study of liver prints revealed that in 6-12-week fetuses the number of erythrokaryocytes was equal in all groups studied; however, in 6-8-week fetuses from contaminated regions a reliable increase of polychromatophilic normoblasts (16.2±6.3% in Novozybkov, 11.2±3.5% in Klintsy, and 4.7±1.7% in Moscow) and a drop of the basophilic megaloblast level (9.1±8% in Novozybkov, 8.1±7.4% in Klintsy, and 18.7±2.6% in Moscow) are noted. By the 9th-12th week the number of oxiphilic instead of polychromatophilic normoblasts increases. Within the hemopoietic liver cells of fetuses from contaminated regions a reliable increase in the number of karyocytes of myeloid lineage is registered at all developmental stages under study (3.8±0.3 in Novozybkov, 6.5±0.4 in Klintsy, and 1.1±0.8 in Moscow).

In the fetuses of parents who live in radionuclide-contaminated regions thymus development is also affected. In control fetuses (born under conditions of a normal radiation environment) a key period of organ formation is established, namely, 11-12 weeks of gestation, when the thymus acquires the structure of the definitive organ (Fig. 1, *b*). Lobule structure and cortical and medullary substance are readily distinguishable, and Hassall bodies begin to appear. All lobules are filled with lymphocytes (mostly small), and up to 80-90% of lymphocytes express receptors of the T-cell system. The total number of lymphocytes further increases; however, the percentage of T cells remains unchanged right up to birth. Small lymphocytes are characterized by a nucleus with a large amount of condensed chromatin and a thin layer of cytoplasm.

Marked alteration are seen in the thymuses of 11-12-week fetuses from radiation-contaminated regions. The discrimination of cortical and medullary substance, as well as the appearance of Hassall bodies are inhibited as a function of the radiation dose; the number of small lymphocytes is drastically diminished against the background of predomination of medium and large forms. In the stroma-forming reticuloepithelium epithelial microtubules with exocrine secretion appear (Fig. 1, *c*). The microtubules are filled with mucoprotein secretion. According to Ageev [1], such microtubules are indicative of pathological processes in an organ.

Thus, in this report we have described for the first time the status of the main hemopoietic organs, liver and thymus, and the karyocytogram of liver prints of fetuses at 6-32 weeks of gestation that were obtained from regions of radiation fallout. Our studies show that permanent residence of parents under conditions of low-dose radionuclide contamination exerts a pathological effect on fetal liver and thymus development that increases in proportion to the increase of the radiation background. At the early stages of embryogenesis hemopoiesis in the liver and lymphocytopoiesis in the thymus are reduced. After 19 weeks of gestation destruction and partial necrosis of hepatocytes are increased. Thymic injury is expressed in hypoplasia and exocrine secretion of microtubule-forming epithelial cells. These processes are absent in the control. A definitive conclusion regarding the nature of changes in the peripheral blood of fetuses from radionuclide-contaminated regions requires additional study of embryonic development

of the bone marrow, which begins to participate in hemopoiesis (in parallel with continuing liver hemopoiesis) in the 12th week.

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