

# ONCOLOGICAL CHARACTERISTICS OF A NEW STRAIN OF RAT LYMPHOSARCOMA

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As the number of chemotherapeutic drugs for use against cancer and tested in animals increases, and as biochemical and experimental oncological research is intensified, interest in tumors transplantable into animals increases daily.

The survey made by Pogosyants [2], devoted to the description of tumor strains, gives an extensive list of strains available in Soviet laboratories. Despite the great variety of transplantable tumors in this list, it does not include strains of lymphosarcoma transplantable into rats. Such strains are nowadays widely used in the practice of oncological laboratories abroad [3-5]. We therefore considered it expedient to describe a new strain of lymphosarcoma which we have obtained, which is transplantable into rats.

The tumor was found in a 3½ month old female rat, kept from birth on a diet containing 3,3'-dichlorobenzidine, a substance whose high carcinogenic activity was demonstrated by us in 1958 [1]. The parents of this rat had also received this substance from birth in the same dose (20 mg). Consequently, the animals had been under the influence of a carcinogen throughout their lives.

In the rat which we are describing, a greyish-white neoplasm measuring 6 × 4,5 × 4,5 cm was found in the abdominal cavity above the duodenum and transverse colon, firmly adherent to the mesentery and to its root (Fig. 1). The tumor was invading the retroperitoneal cellular tissue and infiltrating the tissue of the kidneys. Solitary tumor nodules were also observed in the mesentery. The peripheral lymphatic glands, liver and spleen were not enlarged; the bone marrow was pale crimson in color.

Miscoscopic examination of the tumor (Fig. 2) showed that it consists of large and small lymphoid cells, round or irregular in shape, with large round or bean-shaped nuclei usually displacing nearly all the basophilic cytoplasm of the cell, lying in close contact with each other. The moderately hyperchromic nuclei contained one or two nucleoli and delicate chromatin granules, evenly distributed throughout the nucleus. Very many figures of mitotic division of the nuclei were present. Cells of this type were found in large numbers inside the lumen of the vessels in various organs. The tumor infiltrated the kidneys and invaded the pancreas. Areas of perivascular infiltration were found in the lungs. Only in isolated areas of the spleen were small collections of lymphoid cells seen. In the perivascular sheaths in the liver very small foci of lymphoid hemopoiesis were encountered here and there. No lymphoid metaplasia of the bone marrow was observed. The peroxidase reaction gave negative results. From the morphological picture of the changes we were inclined to consider that this lesion was a lymphosarcoma, probably arising from the lymphatic glands at the root of the mesentery or the retroperitoneal cellular tissue, with generalization of the process to involve several organs.

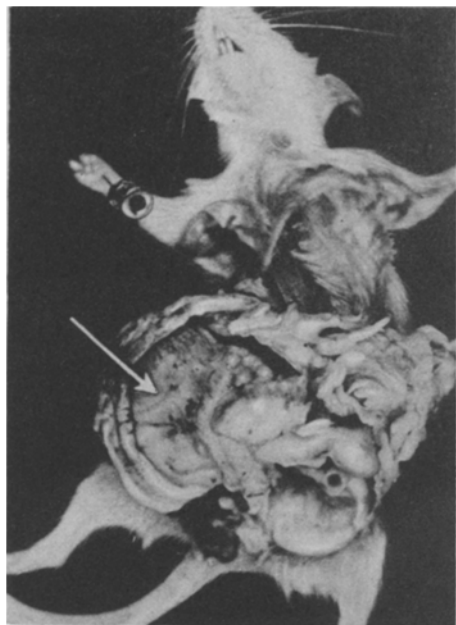


Fig. 1. The rat with the tumor in the abdominal cavity. The neoplasm from which the strain originated.

showed no marked tendency towards widespread invasion of the surrounding tissue, although in some generations invasion of the retroperitoneal cellular tissues was observed. In the first generations the tumor had a doughy consistency, and in later generations it was firmer; the tumor was greyish-white in color, and an opaque fluid of a white color flowed from its cut surface. In the center of the neoplasm small areas of necrosis were observed.

The tumors attained the size of  $9 \times 6 \times 4$  cm. The duration of life of the rats with tumors varied from 12 to 95 days. Most animals, however, perished on the 30th-40th day of the experiment. Transplantation was carried out on the average after 13-16 days. The proportion of successful transplantations varied from 75 to 100% (Table 1).

A homogenate of the tissue of the principal nodule was inoculated in a dose of  $0.5 \text{ cm}^3$  into the subcutaneous cellular tissue of eight rats of both sexes, weighing 70-120 g. Five days later at the site of inoculation in all the animals the skin was elevated by infiltration, which in three rats weighing 70 g was subsequently absorbed. In five rats the tumor continued to grow and reached a large size.

For the subsequent transplantations we used mainly male rats weighing 90-110 g. A suspension of tumor cells in a dose of  $0.5 \text{ cm}^3$  was injected through a wide needle into the subcutaneous cellular tissue of the dorsum of the animal. On the 5th-7th day at the site of transplantation small nodules were found, which increased in size fairly rapidly, invaded the skin and formed ulcers. The tumor was immobile and infiltrated widely into the subcutaneous cellular tissue. In the first 29 generations the tumor had no well defined borders, but it spread far beyond the limits of the site of transplantation, and apparently splitting the subcutaneous cellular tissue into two layers, it covered the entire rat in the form of a muff (Fig. 3), penetrating the deep and the retroperitoneal cellular tissue. Later the character of its growth altered: at the site of transplantation a nodule developed, increased in size progressively and

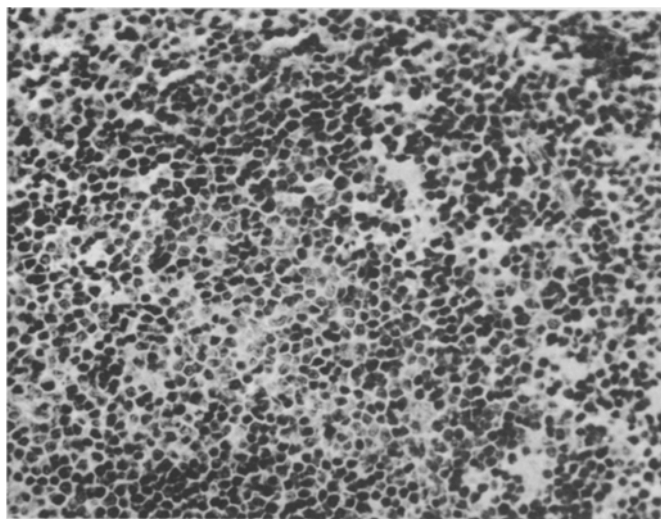


Fig. 2. Microscopic structure of the lymphosarcoma. Magnification  $400 \times$ .

TABLE 1

Results of Transplantation of the New Strain of Rat Lymphosarcoma

Generation	Number of animals				Successful transplants (%)
	included in experiment	with successfully transplanted tumors	with tumors undergoing spontaneous regression	with unsuccessfully transplanted tumors	
1	8	5	3	—	62.5
2	5	4	1	—	80
3	5	3	2	—	60
4	5	4	1	—	80
5	4	4	—	—	100
6	4	4	—	—	100
7	5	5	—	—	100
8	5	4	1	—	80
9	5	5	—	—	100
10	5	5	—	—	100
11	5	5	—	—	100
12	4	3	1	—	75
13	4	4	—	—	100
14	4	4	—	—	100
15	4	4	—	—	100
16	5	5	—	—	100
17	3	3	—	—	100
18	4	4	—	—	100
19	4	4	—	—	100
20	5	5	—	—	100
21	4	4	—	—	100
22	4	4	—	—	100
23	4	4	—	—	100
24	5	5	—	—	100
25	5	5	—	—	100
26	6	6	—	—	100
27	5	5	—	—	100
28	4	4	—	—	100
29	5	5	—	—	100
30	5	4	—	1	80
31	8	8	—	—	100
32	5	5	—	—	100
33	5	5	—	—	100
34	4	4	—	—	100
35	4	4	—	—	100
36	4	4	—	—	100
37	4	3	1	—	75
38	4	4	—	—	100
39	4	3	1	—	75
40	5	5	—	—	100
41	5	5	—	—	100
42	5	5	—	—	100
43	4	4	—	—	100
44	5	4	1	—	80
45	5	5	—	—	100
Total . . . . .	211	198	12	1	93.8

It must be emphasized that we observed no significant changes in the morphological picture of the tumor in the course of 45 generations (until November 10, 1959). The nodules consisted of the same young lymphoid cells which were described in the tumor in the original rat.

The animals which died or were sacrificed at late stages of the experiment merely showed signs of exhaustion. The liver, spleen and lymphatic glands were not enlarged. Here and there in the liver were seen small collections of young lymphoid cells in the perivascular sheaths; in the spleen were seen foci of increased proliferation of reticulum cells and of infiltration with lymphoid cells.

TABLE 2

Blood Count (mean of 8 counts) in Rats with Transplanted Lymphosarcoma (new strain)

Rat	Erythroblasts	Leucocytes (thousands/ $\text{mm}^3$ )	Neutrophils (in %)			Eosinophils	Lymphocytes	Monocytes
			juvenile	stab cells	segmented			
Control	—	$12 \pm 1.3$	—	7	12	1	75	5
Experimental	6	$13 \pm 3$	2	5	7	4	72	4

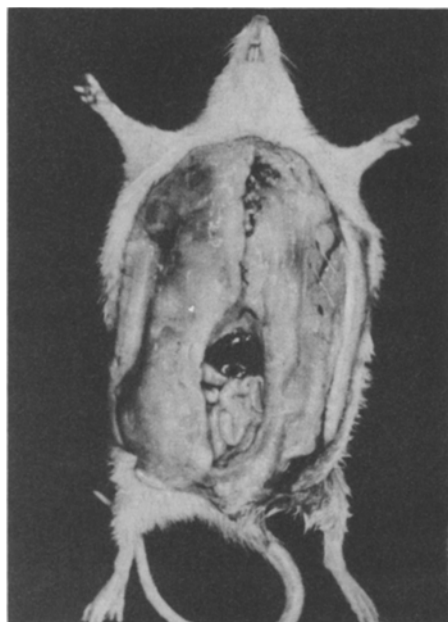


Fig. 3. A rat on the 49th day after subcutaneous transplantation (5th generation). The tumor is infiltrating the subcutaneous cellular tissue.

On comparing the blood and marrow films of healthy and experimental animals we were unable to detect any appreciable increase in the number of lymphoid cells in the experiment. As is clear from Table 2, only a slight shift in the leukocyte formula to the left and an increase in the number of erythroblasts were observed.

An attempt at transplantation using blood and homogenate of liver and spleen (taken from rats with a subcutaneous tumor), carried out three times on 21 rats, on two occasions did not give positive results, although in one case two of five rats developed lymphosarcoma at the site of injection of the homogenate.

A new transplantable strain of rat lymphosarcoma has been obtained and observed in 45 generations. The findings described indicate that this strain of tumor possesses certain distinctive features, including the fact that in some rats, in addition to the development of a neoplasm in the subcutaneous cellular tissue, generalization of the process may occur.

#### SUMMARY

The author describes a new strain of rat lymphosarcoma. The initial tumor was detected in the abdominal cavity of a female rat which was fed 3,3'-dichloro-

benzidine from birth. When transplanted the tumor took in 75-100% of the cases. Generalization of the process occurred occasionally in subcutaneous transplantation. In a number of cases (averaging 5.7%) "spontaneous" regression was observed.

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\*Original Russian pagination. See CB translation.