in the chicken from which Strain 5 took its origin. The cells that infiltrate the nerves are mainly lymphocytes of small and medium size, and the infiltration has the characteristics of a neoplasm. Moreover, neurolymphomatosis is often associated with lymphomatous infiltrations of viscera such as ovary, lung and heart, but the liver is seldom infiltrated. These characteristics differentiate neurolymphomatosis from the most common type of lymphomatosis of chickens which is associated with great enlargement of the liver caused by infiltration with large round cells like lymphocytes; this disease may be called hepatolymphomatosis. Hepatolymphomatosis is not associated with paralysis. Lymphomatosis caused by our Strain 2[5] is characterized by the presence of numerous large basophile lymphocytes in the blood and the same large cells often infiltrate nerves and ganglia.

There are several agents that cause leukosis and their characteristics remain constant throughout numerous animal passages. To the 2 types of agents of leukosis described in previous communications[5] a third type of agent may be added, namely that which produces neurolymphomatosis. The agent causing hepatolymphomatosis has not yet been discovered.

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Transmission of Myeloid Leukemia in Mice.*

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Myeloid leukemia, the most common type of leukemia in man, is rare in animals. A survey of this disease leaves doubt whether myeloid leukemia has ever been observed in domesticated animals (Jármai[1]). It has been described in mice by Simonds,[2] although neither the bone marrow nor blood smears were available to him.

Myeloid leukemia was rarely found among our mice until a large number of them had been exposed to a single dose of approximately 400 r-units of X-rays or to smaller doses repeated at approximately

5 *J. Exp. Med.*, 1933, **58**, 253.

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1 Jármai, K., *Ergebn. allg. Path. u. path. Anat.*, 1934, **28**, 227.

2 Simonds, J. P., *J. Canc. Res.*, 1925, **9**, 329.

TABLE I.

	No. of Mice	
	Irradiated	Control
Mice over 8 months of age examined post mortem	385	481
Died with myeloid leukemia	21	2
Died with mediastinal lymphosarcoma	62	9
Died with either lymphoid or myeloid leukemia	118*	37*
Died with malignant tumors other than lymphosarcoma	23	40

* These figures include those of the second and third groups.

monthly intervals. Table I contains a preliminary survey of this experiment and shows the frequent occurrence of myeloid leukemia and mediastinal lymphosarcoma among the irradiated mice as compared to the unirradiated, closely related control mice.

Increase of spontaneous lymphomatosis in mice by exposure to X-rays was observed by Krebs, Rask-Nielsen and Wagner.[3] Aubertin[4] called attention to the frequent occurrence of myeloid leukemia in X-ray workers.

The mouse from which the first strain of myeloid leukemia of mice took its origin was an unirradiated male mouse (No. Ar117). At the age of 16 months, the spleen of this mouse was greatly enlarged while the lymph nodes were of normal size or only slightly enlarged. The leukocyte count was 105,000. The most significant feature of the differential count was the presence of 9.5% of immature myeloid cells with coarse basophile granules in the blood. Neutrophile polynuclear leukocytes were 31%, neutrophile myelocytes and metamyelocytes 20%, eosinophile granulocytes 0.5%, cells like monocytes 17%, cells like monocytes with basophile cytoplasm 11.5%, lymphocytes 10.5%. At post mortem examination the liver, bone marrow, and spleen showed extensive infiltrations by myeloid cells with basophile granules and the same cells filled the sinuses of many lymph nodes. Many of these myeloid cells were in the process of mitotic division.

TABLE II.

	Injection	No. in Group	No. successful Inject.	No. unsuccessful Inject.
Unrelated to mouse with spontaneous disease; irradiated*	Intravenous	4	3	1
Unrelated; irradiated	"Intrasplenic"	4	4	0
Related; not irradiated	Intravenous	8	1	7
" " "	"Intrasplenic"	4	0	4

*With 400 r-units of X-rays 24 hours before inoculation.

[3] Krebs, C., Rask-Nielsen and Wagner, A., *Acta radiologica,* Suppl. to Vol. 10, 1930.

[4] Aubertin, C., *Bull. off. Soc. Franc. d'electro. et de radiol.,* 1931, **40**, 218.

The spleen of this mouse was cut up in the presence of Locke's solution, filtered through a small piece of cotton and injected into 20 mice as shown in Table II.

After shaving the skin of mice over the splenic area and moistening the skin with alcohol, the spleen becomes visible. With a 27 gauge needle inoculation was attempted into the spleen through the intact abdominal wall. In all 4 irradiated mice gray tumors developed about the spleen and in the subcutaneous tissue at the site of injection, and these tumors were composed of immature myeloid cells with coarse basophile granules.

After intravenous inoculation the spleens of the injected irradiated mice were found to be much enlarged within from 13 to 18 days after the injection. Post mortem examination showed that this organ was almost completely replaced by immature myeloid cells with coarse basophile granules, and diffuse infiltration with these cells caused great enlargement of the liver. The lymph nodes were only slightly enlarged.

Subpassages were readily made by intravenous or subcutaneous inoculation of emulsions of cells obtained from the infiltrated spleen. Of the 46 irradiated mice injected intravenously, 42 developed myeloid leukemia in the course of the first 4 subpassages. After subcutaneous inoculation tumors developed at the site of injection. After intravenous inoculation the systemic disease that was produced was characterized by extensive infiltrations of several organs, chiefly, spleen, liver and bone marrow, with cells similar to those that infiltrated the organs of the mouse with the spontaneous disease. Many of these cells were in the process of mitotic division. They appeared in the circulating blood of all mice inoculated intravenously and leukemia was associated with very severe anemia. *E. g.*

No. R 3143 was inoculated 24 hours after irradiation, and 18 days after injection the leukocyte count was 34,000, of which 94.5% were the immature, presumably malignant myeloid cells with coarse basophile granules. The erythrocyte count was reduced to 494,000, the lowest erythrocyte count we have observed in mice.

These experiments indicate (a) that the myeloid leukemia studied by us is transmissible, (b) the leukemic myeloid cells, like the leukemic lymphocytes,[5] have the characteristics of neoplastic cells and multiply but do not mature into normal leukocytes, (c) they produce systemic disease after intravenous inoculation and form tumors (myelomata) after subcutaneous injection.

[5] *Cf.* Furth, J., Seibold, H. R., Rathbone, R. R., *Am. J. Canc.*, 1933, **19**, 521.