Malignant tumors of the hematopoietic tissue in the rabbit are rare. Feldman (1) records a case of lymphosarcoma. Schultze (2) reports the occurrence of a sarcoma which he succeeded in transplanting. Some of the animals which were given tumor transplants developed a leukemia, and Schultze (3) observed that "the same agent may cause sarcoma, sarcomatosis, and leukemia in the rabbit." Jianu and Netta (4) record the occurrence of a generalized sarcoma in a rabbit which had been inoculated with an emulsion of a lymph node from a case of Hodgkin's disease in man, but they believed the sarcoma to be a coincidence rather than due directly to the material which they had inoculated. Polson (5) reports a case of lymphosarcoma which he did not regard as of the Hodgkin's type. We have been unable to find in the literature any instance of neoplasia in the rabbit corresponding to the gross and histopathological lesions to be reported in this paper.

During the past ten years we have used many hundreds of rabbits in our experimental work on tuberculosis, the large majority of these having been raised in our own breeding colony. Except for the case recorded here and two carcinomata of the uterus in old breeding does, no evidence of malignancy has been observed. Since our stock consists in large part of hybrids, it is not possible to trace the ancestry of the rabbit in which the tumor occurred.

A hybrid doe of black and white stock was given a single intravenous injection of heat-killed *Brucella abortus* in February 1932, and was kept to determine how long after the initial appearance of complement-fixing and agglutinin antibodies these immune substances could be demonstrated. The rabbit was kept in a cage by itself throughout the period of observation, and was handled only for the withdrawal of small samples of blood from an ear vein at infrequent intervals. The sole observation of note from 1932 to 1936 was a complete loss of hair and a marked degree of emaciation in 1933. Such a condition has been recorded in other animals and has *per se* no relation to the injection of *Br. abortus*. The animal fully recovered and appeared in good condition thereafter. It died in March 1936, a little over four years after inoculation.

Necropsy, which was done several hours after death, showed a most unusual condition, which was not understood at that time. In the lungs were a few small grayish spots which on microscopic examination proved to be foci of fungus infection. Mycelia were demonstrated in the lesions. The heart was enlarged, firm, and for the most part reddish-gray in color. The entire left ventricle, the major portion of the right ventricle, and both auricles were involved in the pathological process. A slightly cloudy pericardial fluid was present.

The liver was normal in size and shape. The major part of the organ was of normal color and consistence. Scattered throughout the organ were a small number of firm, grayish spots, grossly not unlike tubercles.
The spleen was much enlarged and extended downward into the pelvis. Except at its upper pole, where it was involved in a retroperitoneal tumor, the organ was free and had a smooth, slightly thickened capsule. The spleen was nodular to the touch. Section showed reddish-gray nodules set in a dark red pulp. Malpighian corpuscles were not prominent. The organ measured $10 \times 2 \times 1$ cm. in its greatest dimensions.

The gastro-intestinal tract was normal aside from the distal portion of the appendix, which was involved in a retroperitoneal tumor. This retroperitoneal mass involved, also, the mesentery, pancreas, both adrenals, and the ureter on the left side. It extended along the aorta for practically the entire length of the abdomen and was on the whole homogeneous in appearance, fairly firm and of a gray color. There were enlarged lymph nodes in the mesentery and around the pyloric end of the stomach.

The kidneys appeared grossly normal.

The genital organs were normal.

The bone marrow of the femur was firm and reddish-gray in color.

The left ureter on section was found to be 3 mm. in diameter, firm, and of a reddish-gray color.

The mediastinal lymph nodes were more prominent than normal but were not greatly enlarged or especially firm.

Microscopic examination of the tissue revealed the following salient points. The pathological lesions in the lymph nodes, spleen, liver, heart, adrenals, and retroperitoneal tissue in some areas strongly resembled Hodgkin's disease and in other places gave the picture of a rapidly growing lymphosarcoma. The whole picture was at times seen in a single section of tissue. The bone marrow of the femur was markedly hyperplastic, with an increase of large (mammalian type) and small (thrombocyte type) megakaryocytes. Mitotic figures were easily found.

The histologic picture in sections of the left ureter was most unusual. Erythrogenic, leukogenic and megakaryogenic centers were present, as well as areas which resembled the sarcomatous tissue seen in other organs. Small areas of erythropoiesis were also found in the lymph nodes, spleen, and in tissue about the appendix. Sections of the appendix showed infiltration of that organ with tumor tissue and also ulcers which penetrated deep into the serosa.

Areas of necrosis were present in the adrenals, lymph nodes, and the retroperitoneal tumor where it had invaded fat tissue. There were small areas of fibrosis in the heart, liver and retroperitoneal tissue, but this was not a prominent feature. Eosinophils were rare.

Blood counts were not done on this rabbit during life. From the blood within the heart and blood vessels in the various organs it was evident that a leukemic condition was not present. A differential count of the heart blood (400 cells counted) gave 80 per cent neutrophils, 8 per cent lymphocytes and 12 per cent mononuclears. This type of blood count is common in human cases of Hodgkin's disease.

No transplants of the tumor and no bacteriological studies were made, as the nature of the pathological process was not appreciated at the time the autopsy was done.

**DISCUSSION**

Malignant tumors in the rabbit are rare and, as previously stated, we have been unable to find a record of any neoplasm in that animal which corresponds to the condition described above. We do not believe that the inoculation of the heat-killed *Br. abortus* had any direct bearing upon the pathological condition under discussion, since other rabbits treated in the same way and living as long have shown no such lesions.

From our study of this animal we believe that we are dealing with a case of Hodgkin's disease which in part suggests a lymphosarcoma. In other papers (6, 7) we have suggested that Hodgkin's disease in man is but one type of malignancy of the bone marrow in which the megakaryocyte is pri-
PLATE I

FIGS. 1-3. SAME SECTION OF MARROW TISSUE

Fig. 1 shows a leukogenic area. Compare with Fig. 2. Note mitotic figure near upper border, a little left of center.

The majority of cells in Fig. 2 we interpret as small (thrombocyte type) megakaryocytes. Note the "birdseye" appearance of many of the cells. Some of those in the lower left quadrant have two or three nuclei. Attention is called to the granular debris, which is interpreted as platelet material, between the cells, and to the tendency for the "birdseye" cells to have an irregular outline. Note the difference in the size and appearance of the cells in Figs. 1 and 2.

Fig. 3 shows a group of large (mammalian type) megakaryocytes; also the small thrombocyte type.

FIG. 4. MULTIPLE MITOTIC FIGURE IN A MEGAKARYOCYTE IN THE FEMUR MARROW

FIG. 5. A MITOTIC FIGURE SIMILAR TO FIG. 4, IN THE SPLENIC PULP

Such figures were also found in the heart and lymph nodes.

FIG. 6. A MEGAKARYOCYTE IN THE MARROW CONTAINING A DOZEN NEUTROPHILS

This phenomenon, present only in the large megakaryocytes, was seen not only in the marrow but also in the lymph nodes and spleen.

(All photomicrographs were taken at a magnification of 600, and the same technic was used throughout.)
PLATE II

FIG. 7. NORMAL LYMPHOID TISSUE IN THE "CORDS" OF A LYMPH NODE
Compare with Fig. 8.

FIG. 8. AN AREA OF RAPIDLY GROWING TUMOR FROM THE SAME SECTION OF LYMPH NODE AS FIG. 7
Two mitotic figures are present in the upper right hand quadrant. Note the irregular fuzzy outline of the cells and several "birdseye" nuclei.

FIG. 9. A NORMAL GERMINAL CENTER IN THE SPLEEN
Compare with Fig. 10.

FIG. 10. A GERMINAL CENTER OF THE SPLEEN FROM THE SAME SECTION AS FIG. 9, WHICH IS IN LARGE PART REPLACED BY TUMOR TISSUE
Note mitotic figure in upper center and the similarity of the majority of the cells to those shown in Fig. 8.

(All photomicrographs × 600)
PLATE III

FIG. 11. AN AREA IN THE PULP OF THE SPLEEN FROM THE SAME SECTION AS FIG. 9
This area shows various phases of the megakaryocyte from the small (thrombocyte) to the large (mammalian) type. Note the considerable amount of granular débris between the cells. This we interpret as blood platelets. Such a picture was more common in the spleen than in any other organ outside the marrow.

FIG. 12. AN ERYTHROGENIC AREA IN A SECTION OF THE URETER
See text. Similar areas, though smaller, were found in lymph nodes, in the spleen, and in tumor tissue involving the omentum and mesentery.

FIG. 13. AN AREA OF RAPIDLY GROWING TUMOR TISSUE IN THE HEART MUSCLE
There are two mitotic figures near the center of the illustration. Note the similarity of the tumor cells in this picture to those shown in Fig. 8.

FIG. 14. AN AREA OF TUMOR IN THE HEART, WHERE THERE WAS LESS CELLULARITY AND SOME FIBROSIS
Note large megakaryocyte and compare with Figs. 3, 11, and 15. In other areas of the heart there were foci of fibrosis with very little tumor tissue left.

FIG. 15. SECTION OF LYMPH NODE SHOWING THE LARGE TYPE OF MEGAKARYOCYTE
Compare with Figs. 14, 11, and 3. In some lymph nodes such cells were common, while in others they were scarce or absent.

(All photomicrographs × 600)
marily involved. The pathological picture in this rabbit is in agreement with such a concept. The sarcomatous aspect we believe represents the more rapidly growing areas of primitive marrow cells which have not undergone differentiation. The finding of erythrogenic, leukogenic, and megakaryogenic areas in unusual locations, as for instance the ureter, signify to us the maturation potentialities of the primitive or "stem" cell so abundant in the sarcomatous areas of the tumor tissue.

If this is a case of Hodgkin's disease, as we are inclined to believe it is, then this disease can occur spontaneously in the rabbit and it would appear that that animal may be suitable for the experimental investigation of Hodgkin's disease. Should human Hodgkin's material be used in such a study, it is evident that a condition similar to the one described above will have to be reproduced before any judgment as to the nature of the disease can be made. To date no published experimental data correspond even closely to the pathological picture which we have described.

The only malignant neoplasms which we have seen in rabbits have been in females, all over four years old. It is possible that, as in our laboratory, the great majority of animals are used in experiments which terminate before the age of two years. It may be for this reason that spontaneous neoplasms have not been more frequently encountered in this species.

References