potension with bradycardia and azotemia. In one obese female a psychoneurotic crisis seemed to have been precipitated; it persisted after the diet was discontinued. This regime is tolerated in warm as well as cold seasons.

Preliminary studies suggest that the results obtained by treating essential hypertension with a diet low in sodium may prove to be better than those achieved by surgical procedures (Table I). This is true particularly in patients with far advanced heart and eye ground changes. The response seems to be similar in degree to that observed by Kempner[4] who uses drastic restriction of fluid (700 to 1000 cc), protein (20 g), fat (5 g), as well as sodium (200 mg), thus suggesting that his results, as previously pointed out,[5] may be primarily due to sodium restriction. Compared to that used by Grollmann *et al.*,[5] who obtained a significant reduction in blood pressure in 2 of 6 hypertensive patients, our diet appears less inconvenient, more palatable and contains about half as much sodium.

These observations confirm the early findings of Allen and Sherrill[6] in the treatment of arterial hypertension and the later observations of Schemm[7] in the management of heart failure. It should be emphasized, however, that failure may be expected unless the strictest cooperation and a complete understanding over a long period of time exists between patient, dietitian and physician.

It is suggested that rigid restriction of sodium seems to have a definite place at the present time, in the management of hypertensive vascular disease. These observations, in addition may have a more important bearing on the pathogenesis of this condition.

The authors wish to express their appreciation to Dr. L. H. Newburgh and Dr. Frank N. Wilson for their aid in carrying out this study.

4 Kempner, W., *Nor. Car. Med. J.*, 1945, **6**, 62.

5 Grollman, A., Harrison, T. R., Mason, M. F., Baxter, J., Crampton, J., and Reichsman, F., *J. A. M. A.*, 1945, **129**, 533.

6 Allen, F. M., and Sherrill, J. W., *J. Metab. Research*, 1922, **2**, 429.

7 Schemm, F., *Ann. Int. Med.*, 1944, **21**, 937.

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Heterologous Transmission of a Human Lymphoma.

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Greene[1] was the first to transplant a human tumor into an animal by passage through the anterior chamber of the eye. Since 1939, at the suggestion of Dr. Lawrence Weld Smith, numerous attempts were made in this laboratory to transplant human tumors into animals by previous passage through tissue culture without any success. The work was resumed by the author and changes were made in the tissue culture medium and the type of mice used.

The tissue used for inoculation was obtained from a lymphnode of a patient whose diagnosis elsewhere had been "lymphosarcoma or aleukemic leukemia." The diagnosis on section here was "possible lymphosarcoma, leukemia cannot be excluded." Bone marrow examination did neither prove nor disprove the diagnosis of leukemia. The tumor was inoculated into a tissue culture medium consisting of the patient's own plasma, mouse embryo extract and Tyrode's solution at pH around 7.6. Growth was profuse and consisted mainly of lymphocytes, occasional blast forms and a few fibroblasts and reticulocytes. A small number of mitoses were noted.

1 Greene, H. S. N., and Murphy, E. D., *Cancer Research*, 1945, **5**, 269.

As mentioned above the patient's own plasma was used. In fact it had been observed in the study of tissue cultures in the past year, that certain tumors but more so those originating in the lymphnodes, grew more readily when the autogenous plasma was used instead of the habitual chicken plasma.* That there is a factor in the serum and plasma of cancerous patients peculiar to them has been noted by many research workers and some have used it to develop diagnostic tests.[2-4] Another change made in the preparation of the medium was the use of mouse embryo extract instead of calf embryo extract.

After 5 days the tissue culture was removed to a petri dish and cut into fragments measuring about 1 mm in size. Waste products (practically none), plasma clot and the tissue growth were included. Tyrode's solution was added so that each animal received .3 cc of suspension including 6 fragments of the tissue growth. No attempt was made to count the number of cells inoculated. Injection was done in the lower left quadrant part subcutaneously and part into the peritoneal cavity. The entire procedure was done under aseptic conditions. The animals used were a cancer-susceptible hybrid strain of female mice, 5 to 10 days postpartum. The control mice received a similar tissue culture medium without the cells.

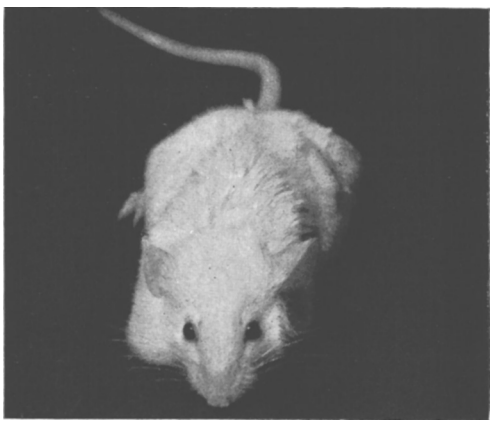

FIG. 1.
Mouse showing metastatic adenocarcinoma to the neck.

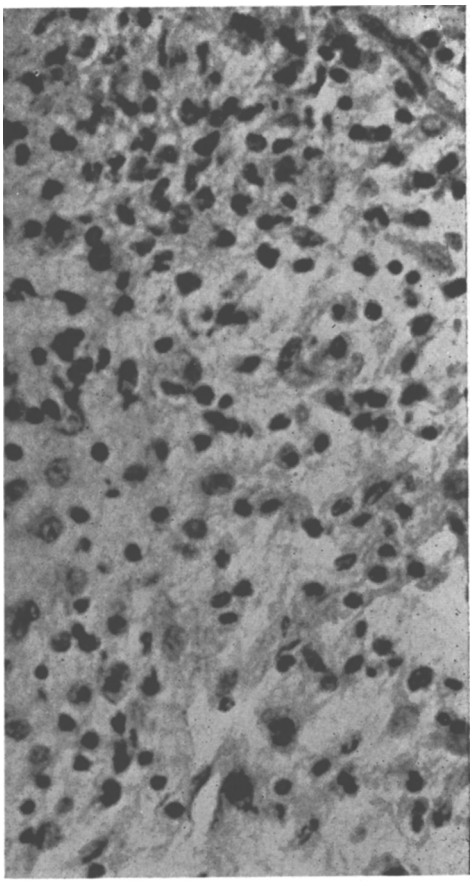

FIG. 2.
Primary tumor growth at the site of inoculation of mouse one (Fig. 1). × 200.

Three weeks later one of 4 mice developed a nodule at the site of inoculation. Six weeks later the tumor measured one cm in diameter and was firm and adherent to the skin. At this time a second tumor developed in the neck on the opposite side of the primary tumor (Fig. 1). The mouse was operated on under ether anesthesia and the left lower quadrant tumor removed. It was moderately firm, hemorrhagic and adherent to the skin and underlying tissues.

On section the upper surface of the tumor nearest to the region of inoculation, was seen

* Paper in preparation.

[2] Mendeleeff, *P. Bull. d. l'Ass. Fr., p. l'Et. du Cancer*, 1938, **26**, 1.

[3] Carratala, A. T., *Bol. Inst. de med. exp. para el estud. y trat. d. Cancer*, 1944, **21**, 183.

[4] Roskin, G., *Am. Rev. Sov. Med.*, 1946, **4**, 111.

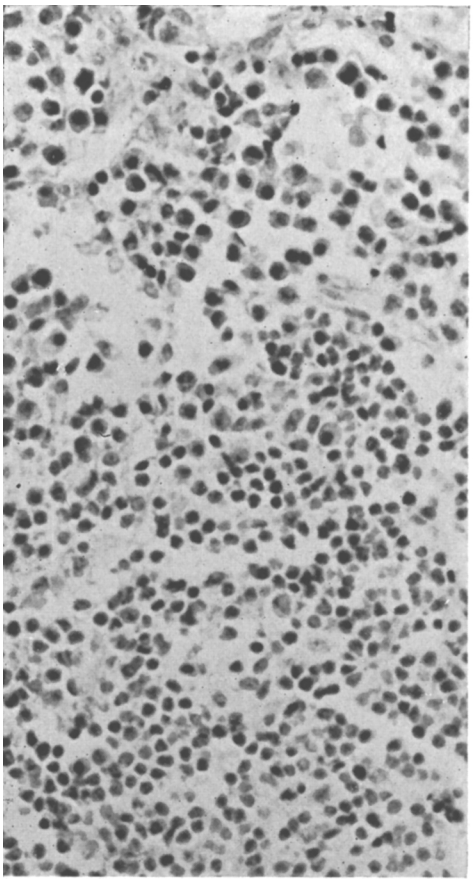

FIG. 3.
Human lymphoma, diagnosis questionable. × 200.

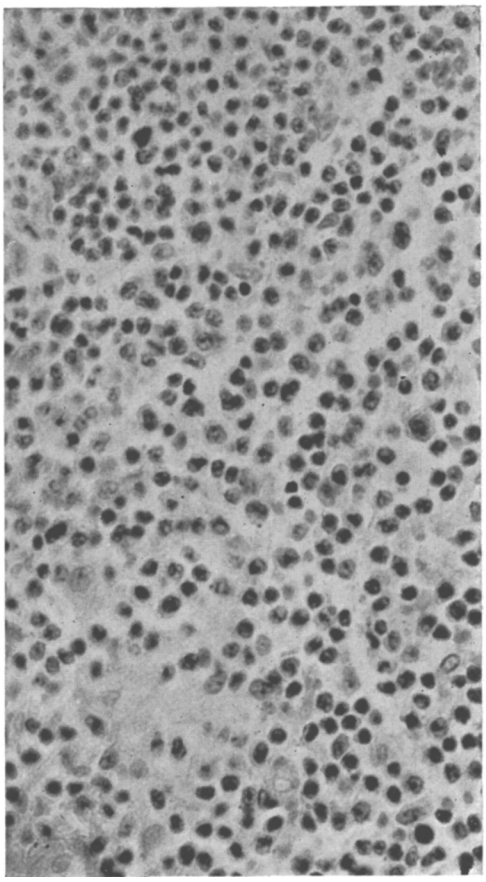

FIG. 4.
Primary tumor growth at the site of inoculation in mouse two. Note similarity with human tumor. × 200.

to consist of a fine network of reticulum-like stroma infiltrated with lymphoid cells, similar to those observed in the human tumor (Fig. 2 and 3). Adjacent to it and forming part of it was breast tissue. The lining epithelial of the acini had undergone malignant alteration so that the greatest mass of the tumor was formed by an adenocarcinoma in which little stromal element was present. Atypical mitoses were encountered.

A week later the neck tumor was operated on and this was likewise adenocarcinoma such as was found in the first tumor. Another tumor with rapid development now appeared on the back on the same side as the neck tumor. It was freely movable. The mouse was beginning to lose weight and was found dead 9 weeks after inoculation. The third tumor was likewise a carcinoma but much less differentiated than the previous ones. There was practically no stroma but sometimes a few round cells were noted in between the tumor cells.

The second mouse developed a nodule at the site of inoculation 6 weeks after the injection. It was yellowish grey in color and had a delicate vascular pedicule arising from the parietal peritoneum. The liver was markedly enlarged and was studded with delicate salmon pink nonelevated areas. On section the tumor nodule was similar in appearance to the human tumor presenting the same difficulty in diagnosis (Fig. 4). The liver was infiltrated throughout by the tumor cells (Fig. 5).

The third mouse developed a tumor about 6 weeks after inoculation but this was more a thickening of the subcutaneous tissue. The

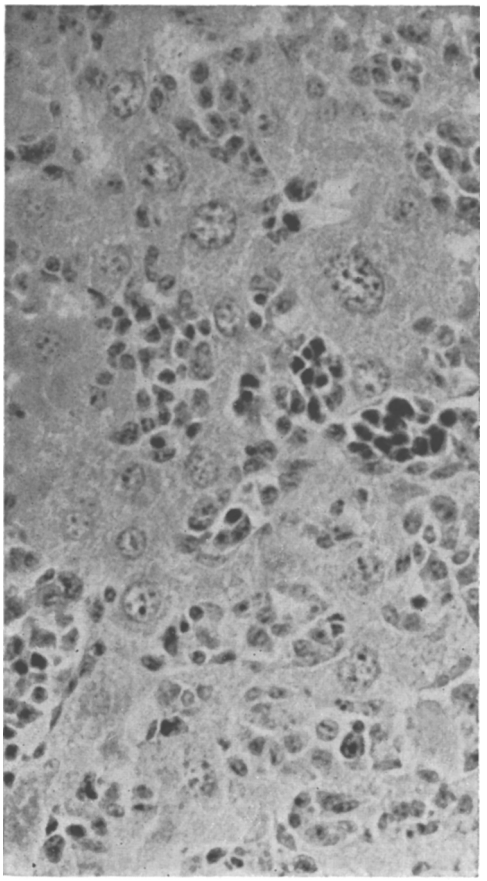

FIG. 5.
Metastasis to the liver of tumor shown in Fig. 4. × 200.

mouse was killed. The liver was slightly enlarged but grossly showed no evidence of tumor. On section the subcutaneous thickening was found to be actually formed by squamous pearls and normal breast tissue. Some of the cells were distorted and there was a marked hyperkeratosis. The picture suggested precancerous alterations.

The fourth mouse died 3 days after inoculation of intestinal obstruction due to mechanical perforation at the time of inoculation. One control mouse died 7 weeks later of pneumonia. The other 2 remained well.

Transmission of the carcinoma developed in the first mouse to other mice has been repeated thrice without much difficulty. Transmission of the lymphoma of the second mouse has not been entirely successful though not without interest. Direct transmission was unsuccessful. It was found expedient to pass this tumor back to tissue culture. Of the 8 animals then inoculated with the tissue culture 3 have shown disturbances in the white blood cell count. Of these 2 show a normal white count but the differential count reveals 86% lymphocytes none of which were abnormal. One mouse showed a white count of 32.000 with no apparent change in the differential count. Control blood counts were done and the variations always present taken into account. On all tumors, tissue cultures and other procedures bacterial studies were made. They were always negative.

Discussion. The diagnosis of the lymphoma has been and still is a difficult problem to the pathologist. Its transmission to animals has remained unsuccessful. In the above experiments it has been shown that under certain specified conditions it may be possible to transplant such a tumor and induce in the adjacent tissues a tumor of a different nature. It is true that the growth of the transplant was reduced yet sufficient to elicit tumor growth at the site of inoculation. Simultaneous growth of an undetermined lymphoma and an epithelial tumor at the same site had never been observed by the author in man. Recently Dr. Simpson brought to me a slide for examination in which such a tumor co-existed at the same site with a squamous cell carcinoma the latter metastasizing independently to the liver. I believe the growth and induction of these tumors under the above mentioned conditions is due to a concomitant action. This will require further verification.

Summary. Under specified conditions a human unclassified lymphoma was transmitted to mice by previous passage through tissue culture.† An unclassified lymphoma was produced in the mouse and an adenocarcinoma was induced in the adjacent breast tissue demonstrating the lability of these tumors.

† Since this paper has been written another very similar case has occurred.