and in the development of a comprehensive theory of protein structure. These are fields of great activity in biochemistry, and in all of them the demand is for accuracy and more accuracy.

The employment of a method of calculation which introduces needless error without any compensating advantage is strongly to be condemned. This is not the time for a backward step, for a relaxation of the standards of accuracy or for the introduction of a new complication into an already sufficiently complex situation.

Attention is drawn to this matter because several papers have recently appeared in which the use of the proposed method of calculation has apparently escaped the vigilance of the referees, and more are to be anticipated.

H. B. VICKERY
CONNECTICUT AGRICULTURAL EXPERIMENT STATION,
NEW HAVEN, CONN.

H. T. CLARKE
COLLEGE OF PHYSICIANS AND SURGEONS,
COLUMBIA UNIVERSITY

RELATIONSHIPS OF LYMPHOCYTES AND CANCER[1]

FINDING a direct correlation between the amount of lymphoid tissue in the intestine and the incidence of spontaneous mammary tumors in several pure strains of mice[2] suggested the idea that the lymphocyte might contribute to the growth of tumors or possibly even to instigate them. Lymphocytes have been considered in many studies on cancer, but practically all the experiments have been designed from the viewpoint that this cell and the lymphoid tissue has a part in immunity to tumor transplants. The conclusions obtained have not been consistent, one group of investigators maintaining that the lymphocyte is a factor to immunity; the other, that this cell has no part.

The approach used here is based upon histological association between the presence of lymphocytes and tumors and also upon correspondence in the growth and incidence of tumors and conditions that result in an increase or decrease in the number of lymphocytes within a tissue or throughout the body as a whole.

Mammary tumors. Records of metastases of mammary carcinoma in women and data obtained from animal experiments indicate a connection between mammary tumors and the presence of lymphocytes. Metastases of mammary carcinoma occur most frequently in lymph nodes, organs normally composed chiefly of lymphocytes. In addition, lymphocytes are present in metastases to the liver,[3] in neoplastic foci developed from burst lymphatics[3] and between the elastic connective tissue and the epithelium containing neoplastic cells in Paget's disease of the nipple.[4]

Animal experiments indicate several histological associations between lymphocytes and mammary tumors. The mammary tumor inciter in mice has been found in the milk, blood, spleen, thymus, lactating mammary tissue and breast tumors of certain strains high in their incidence of spontaneous mammary tumors.[5, 6] No cell is as numerous in all these fluids and organs as is the lymphocyte; it is a dominant histological element in the spleen and thymus gland. Furthermore, lymphocytes occur in the milk of many animals and have also been identified in the stomach contents of nursing mice. After centrifuging milk diluted with saline, the lymphocytes occur chiefly in the sediment, very few remaining in the supernatant fluid. The milk factor in mice has been found to be concentrated in the sediment.[7]

Breeding in pure strains of mice shows another connection between the incidence of spontaneous mammary tumors and lymphocytes. For example, strain dba has only 51 per cent. tumor incidence in virgins, but 85 per cent. in the breeding females; strain A shows a more marked difference by having less than 5 per cent. in virgins and 84 per cent. in breeding females.[8] One prominent histological change in the mammary gland during pregnancy and lactation is the presence of quantities of lymphocytes. There are masses of lymphocytes in the mammary gland of mice belonging to line dba during various stages of pregnancy and lactation.[9]

Lymphocytosis. The term "lymphocytosis" as used here will apply not only to an increase in the circulating lymphocytes, but also to an increase in the number of lymphocytes within an organ or tissue.

Data exist to show that one inciter of tumors is irritation, whether it be caused by chemicals, physical factors, radiation or possibly by certain parasites and viruses. Regardless of its source, irritation produces histological changes involving the attraction of the white blood cells. Lymphocytes are present at neoplastic foci caused by irritation.

The increase in blood lymphocytes that occurs in some unbalances of the endocrines and in some in-

[1] The author is a recipient of a Finney-Howell Research Fellowship.

[2] M. A. Kelsall. Paper in press.

[3] W. S. Handley, "Cancer of the Breast and Its Treatment." New York: Hoeber. 1922.

[4] G. L. Cheatle and M. Cutler, "Tumors of the Breast." Philadelphia: Lippincott.

[5] J. J. Bittner, *Trans. and Stud., College of Physicians of Philadelphia*, 4 ser., 9: 129–142, 1941.

[6] G. W. Woolley, L. W. Law and C. C. Little, *Proc. Nat. Acad. Sci.*, 29: 22, 1942.

[7] C. P. Barnum, Z. B. Ball, J. J. Bittner and M. B. Visscher, SCIENCE, 100: 575, 1944.

[8] C. C. Little, "Biology of the Laboratory Mouse." Philadelphia: Blakiston. 1941.

[9] E. Fekete, personal communication, 1945.

fectious diseases also indicates a positive relationship between lymphocytes and tumor growth. The sex hormones are known to be a factor in tumor production; unbalance of the sex hormones has been found to stimulate growth of lymphoblastic tissue.[10] Lymphocytosis occurs in some stages of syphilis, a fact that may account for the greater incidence of carcinoma of the lip in syphilitics.[11]

Lymphopenia. Not only are there correlations between an increase in the number of lymphocytes and increased incidence and growth of tumors, but there are also correlations between a decrease in the number of lymphocytes and decreased incidence and growth of tumors.

Chronic inanition decreases both the blood lymphocytes and the growth of tumors. Stern and Willheim state that "the prevailing majority of authors have expressed the opinion that food restriction is followed by depression of neoplastic growth."[12] Animal experiments give evidence to prove that the amount and kind of food affects the incidence of tumor development. No tumors occurred in C3H mice placed upon a diet in which the carbohydrates and fat were reduced to one third.[13] Inanition has been found by many authors to reduce the number of circulating lymphocytes and to cause involution of lymphoid organs.

Furthermore, observations have frequently been made that primitive societies are less well nourished and have a lower incidence of cancer[14] and also that cancer is less frequent among people having progressive tuberculosis,[14] a condition found by Sabin[15] to be accompanied by lymphopenia. However, the statistical significance of these observations has not been established.

The therapeutic effect of radiation agrees with the idea that a reduction in lymphocytes reduces tumor growth. Mottram[16] found that x-rays over a wide range of intensity caused a 50 per cent. decrease in the number of circulating lymphocytes, and Michels[17] found that the lymph nodes underwent fatty involution following x-rays.

Nucleus of the Lymphocyte. The most obvious characteristic of the small lymphocyte is its enormous nucleus in proportion to the amount of cytoplasm. No other cell in adults has a nucleus nearly as large in proportion to the cytoplasm except sperm, cells that are known to initiate the division of another cell. Basophilic staining reveals that most lymphocytes have larger nucleoli and contain more nucleic acid than most cells. Staining also shows that there are two kinds of small lymphocytes varying in their degree of basophilic staining. Stowell[18] thoroughly reviews the literature on the role of thymonucleic acid in tumors and concludes that a disturbance of the nucleoproteins forms the basis for an "intracellular cause of neoplasia." The lymphocyte may have a part in modifying nucleoproteins and be the source of the greater amount of thymonucleic acid found in carcinomas.[19]

There may also be a relationship between normal growth processes and quantitative chemical changes initiated by lymphocytes on the one hand, and abnormal growth and abnormal lymphocytosis on the other. The thymus gland has long been thought to have a part in normal growth; at the present time thymocytes are considered to be the same as lymphocytes. Lymphoid tissue involutes with age, the decrease being particularly coincident with the attainment of mature growth in the case of the thymus gland. In addition, those tissues of the adult that are most active mitotically contain large numbers of lymphocytes. The bone marrow continues production of blood cells throughout life and contains quantities of lymphocytes. During pregnancy the mammary gland of the adult is also subjected to rapid growth, a change accompanied by the invasion of lymphocytes into this organ.

Summary. Lymphocytes are present in metastases of mammary carcinomas, in tissues containing the mammary tumor inciter and at neoplastic foci caused by irritation. Unbalance of sex hormones stimulates lymphoblastic tissue and increases tumor incidence. Inanition and radiation reduce the number of circulating lymphocytes and also the growth and occurrence of tumors. The nucleus of the lymphocyte is considered to be a possible factor causing a disturbance of the nucleoproteins.

MARGARET A. KELSALL
ROSCOE B. JACKSON MEMORIAL LABORATORY,
BAR HARBOR, MAINE

[10] D. Marine and S. H. Rosen, *Proc. Soc. Exp. Biol. and Med.*, 44: 61, 1941.
[11] C. Ryall, *Brit. Med. Jour.*, 2: 697, 1913.
[12] K. Stern and R. Willheim, "Biochemistry of Malignant Tumors." Brooklyn: Reference Press. 1943.
[13] M. B. Visscher, Z. B. Ball, R. H. Barnes and I. Siversten, *Surgery*, 11: 48, 1942.
[14] H. Gilford, "Tumors and Cancers." London: Selwyn and Blount. 1925.
[15] F. R. Sabin, *Amer. Rev. of Tuberculosis*, 25: 153–171, 1931.
[16] J. Mottram, *Jour. Path. and Bact.*, 34: 800–801, 1931.
[17] N. A. Michels, *Amer. Jour. Anat.*, 57: 439–501, 1935.
[18] R. E. Stowell, *Cancer Research*, 5: 283–294, 1945.
[19] R. E. Stowell and Z. Cooper, *Cancer Research*, 5: 295–301, 1945.

WHAT IS EDUCATION AND WHAT IS DISPENSABLE?

THE suggestions offered by H. M. Dadourian[1] include two ideas which seem quite opposite. I fully

[1] H. M. Dadourian, SCIENCE, 101: 612, 1945.