THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

STUDY OF THE ARRANGEMENT AND BEHAVIOR OF THE RETICULAR FIBRILS OF THE SPLEEN IN THE LEUKEMIAS

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

DOCTOR OF PHILOSOPHY

BY

WILMA JEANNE GREEN

Oklahoma City, Oklahoma

1958

STUDY OF THE ARRANGEMENT AND BEHAVIOR OF THE RETICULAR FIBRILS OF THE SPLEEN IN THE LEUKEMIAS

APPROVED BY

DISSERTATION COMMITTEE

ACKNOWLEDGMENT

The writer wishes to acknowledge gratefully the encouragement, guidance and assistance of Professors Walter Joel, W. E. Jaques, G. Townley Price, R. E. Eyerer, and other members of the Department of Pathology of the University of Oklahoma School of Medicine. Gratitude is also expressed to Professors F. C. Kelly and L. V. Scott, Department of Microbiology; J. W. H. Smith, Department of Physiology; K. M. Richter and J. F. Lhotka, Department of Anatomy; and A. A. Hellbaum, Department of Pharmacology; for the interest they have shown.

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CHAPTER I

INTRODUCTION

The leukemias and closely related neoplastic diseases of man and animals have been intensively studied since the middle of the nineteenth century. Particular interest in these diseases developed following the classic investigations of Hodgkin, and the publication of Weisses Blut by Virchow (1845). In the century which followed, improvements in the compound microscope and histological technics permitted more illuminating studies to be made of these phenomena. A great mass of knowledge accumulated during this period. Cohnheim, Kundrat, Lubarsch, Arneth, Naegeli, Schilling and many others provided notable contributions. However, to an extent not appreciated by many, there developed such a confusion of terminology, classification and concept that a clearer understanding of these diseases has been greatly retarded. The concept of the reticulo-endothelial system and its role in the dynamics of lymphoid and myeloid tissues was a significant development and added greatly to the sum of all that is known concerning these diseases. However, conflicting statements by respected investigators added confusion to the accepted facts. Much of this confusion has been attributed to the

inability of the investigators to provide a classification based on a study of the cytology and relationship of reticular tissue. Since the reticulum cell has been generally regarded as the stem cell of lymphoid and myeloid elements and the abnormal cells of blood dyscrasias, a study of the characteristics of the reticulum in these diseases appeared to be necessary before a satisfactory classification could be attained. These investigations were undertaken with the intent to inquire into the significance of the arrangement and behavior of the reticular fibrils of the spleen in the leukemias and related neoplastic diseases and to determine if they might provide a basis for a sound classification.

CHAPTER II

REVIEW OF LITERATURE

Tigri and Forster in the middle of the nineteenth century, according to Marshall (1956), were the first to recognize the presence of a framework of stellate cells in the pulp of the spleen. Later, Ranvier and Bizzozero discovered that fibrils were present in association with these elements. For many years it was accepted that the stellate cells were not related to, but overlaid the fibrils. During this period the term reticulum was employed to denote a system of anastomosing fibrils serving as a framework for lymphoid tissue.

In later years, as more extensive and thorough studies of the histological changes accompanying the leukemias and related diseases of lymphoid and myeloid tissues were made, contrary and conflicting observations were reported.

Reed (1902) described what she considered to be a normal reticulum in the early lesions of Hodgkin's disease. She noted that within the reticular foundation of the spleen lymphoid and giant cells were present.

Longcope (1903) observed numerous lymphoid cells within spaces formed by a coarse reticulum in Hodgkin's disease and a thickening of the reticular network of the Malpighian corpuscles in the spleen.

In describing several cases of lymphosarcoma, MacCallum (1907)

reported that in three instances he observed a delicate stroma surrounding masses of small lymphocytes and referred to the reticulum as being inconspicuous and very fine.

A fine fibrillar network was noted by Karsner (1910) in the lesions of Hodgkin's disease.

Mallory (1914) concluded that a lymphoblastoma was an infiltrating tumor and that its stroma was provided by the invaded organ. He described the reticulum as being thinly diffuse.

In describing a case of malignant endothelioma, Foot (1924) stated that the reticulum appeared to run over and through the cytoplasm of the malignant cells forming a coarse-meshed network.

A diffuse hyperplasia of the reticular tissue was observed in splenomegaly by Watson (1926). Ikeda (1926) noted an increased number of reticulum cells in Brill's type of follicular splenomegaly.

In a review of the reticulo-endothelial system, Jaffé (1926) made no mention of the reticular fibrils.

Piney (1926) described two cases of endothelioma in which he observed masses of cells which were separated by branching septa and to the strands of these septa many cells appeared to be attached.

In a case of lymphosarcoma described by Krumbhaar (1927) a fine reticular network supporting large lymphocytes was noted.

Foot (1927b) found the reticulum in the Malpighian bodies of the human spleen to be like that of lymph nodes. The coarse mass of reticulum circumscribing the central arterioles was continuous with the delicate, midzonal reticulum; however, the peripheral reticulum was coarse and compact. He thought that the reticulum of the red pulp

appeared like that of lymphoid reticulum, in which a coarse, irregularly arranged reticulum intimately overlaid the reticulo-endothelial cells.

The effacement of the normal architecture of lymph nodes and spleen by an infiltration of large mononuclear cells was observed in acute monocytic leukemia by Dameshek (1930).

Warthin (1931) believed that a focal proliferation of the reticulum was one of the first marked features of Hodgkin's disease. He observed an abundant reticulum in the lesions of Hodgkin's sarcoma and a very prominent network of coarse fibrils in lymphoblastomas.

A supporting stroma of reticulosis was described by Ross (1933) as consisting of reticular fibrils closely connected with an undifferentiated syncytium. In employing Foot's method of staining reticulum, a finer reticular meshwork was shown to be present in relation to the cells.

Replacement of the normal structure of lymph nodes by a polymorphonuclear tissue and reticulum was noted by Wallhauser (1933) in a case of Hodgkin's disease. He thought that the reticulum was borrowed from the invaded tissue, and cited Sweany who had observed a diffuse hyperplasia of lymph nodes in this disease.

Fitchett and Weidman (1934) found the reticulum of splenic nodules to be greatly thickened in Hodgkin's disease.

The reticulum in leukemic diseases was studied by Callender (1934). He observed that in lymphatic leukemia the reticulum was not increased but that the meshes were more widely separated by the increased numbers of lymphocytic cells. In giant follicular hyperplasia and lymphosarcoma, he described it as being loose meshed. He also observed an increased amount of fibrous tissue in the spleen in myelogenous

leukemia, which appeared to be more evident after irradiation. In monocytic leukemia he described the reticulum as being delicate and closely surrounding the cells. A delicate meshwork of reticulum was described in tissue from cases of reticulum cell sarcoma and Hodgkin's disease.

Klemperer (1934) made no observation of the reticular fibrils of the spleen in his studies of leukemic diseases.

The infiltration of leukemic cells was thought by Jaffé (1935) to effect a separation of the collagenous and elastin fibrils of the trabeculae and to form a fine reticulum for small nests of cells.

Ehrlich and Gerber (1935) described three types of lymphosarcoma. They observed in a reticular type, a small number of coarse, irregular fibers related to the capillary walls, and thought that these were present before the invasion of the tissue by the neoplasm. In an intermediate type, a marked increase of fine argentophilic fibers was described which tended to form an irregular network. The lymphocytic type of lymphosarcoma presented nests of rounded cells delineated by argyrophile fibers, which were considered to be coarser than those of the intermediate type.

In a study of follicular reticulosis Robb-Smith (1938) noted a compression of reticular fibrils to form a sharp ring demarcating the follicles. No increase of reticular fibrils was observed in the follicular lymphoblastoma, or in the remainder of the lymph node. Reticular fibrils were thought to be increased in lymphocytic leukemia, especially after irradiation. Reticular fibrils were not increased in monocytic leukemia. In the three described types of reticulosarcoma it was found that the diffuse syncytial reticulosarcoma produced no new

fibrils, that the trabecular syncytial reticulosarcoma presented fine reticular fibrils, and that in the histioid cell type a considerable increase of reticular fibrils was noted. No increase of reticular fibrils occurred in lymphocytoma or lymphosarcoma.

Watson (1938) described the reticulum of lymphosarcoma as being irregular and believed it to be the reticulum of the tissue and not that of the neoplasm.

Fibrosis of the splenic pulp was described by Richter (1938) as being marked in cases of chronic myelocytic leukemia and as slight in those of lymphocytic leukemia.

Ewing (1940) described lymphosarcoma as being composed of lymphoid cells of variable size lying in an atypical reticular tissue. He observed that silver staining demonstrated a characteristic, fine network of reticular fibrils between the cells.

No increase of reticulum cells was noted by Bell (1941) in leukemia. He described increased numbers of reticular fibrils in Hodgkin's disease and a small amount of stroma resembling that of a normal lymph node in lymphosarcoma.

The reticulum in chronic lymphocytic leukemia was described by Krumbhaar and Stengel (1942) as being increased, normal or decreased. They noted a finely meshed reticulum in monocytic leukemia.

Rappoport and Kugel (1947), however, thought that a marked increase in the number of reticular fibrils was evident in monocytic leukemia.

A great variation in the reticular architecture was described by Jackson and Parker (1947) in Hodgkin's paragranuloma. In some

instances a normal amount of reticulum was present, while in others there was a numerical increase of fibrils in the medullary cords but not in the follicles. They detected an increased amount of reticulum fibrils which wove between single cells or enclosed groups of cells in Hodgkin's granuloma. A like increase was observed in Hodgkin's sarcoma and the fibrils enclosed groups of cells and individual cells. Similar observations of the reticulum in reticulum cell sarcomas were reported. The reticular fibrils of lymphocytomata appeared to be decreased as a result of the distention of the meshwork with the infiltrating cells. The reticulum of lymphosarcomata was considered to be that of a normal lymph node. In giant follicular lymphoma the strands of reticulum around the follicle were thought to compress the pulp. A normal amount of reticulum was described as being present in the giant follicles.

Bilger (1954) detected sparse argentophilic fibers in the germinal centers in Brill-Symmer's disease.

An absence of reticular fibrils in follicular lymphoma was noted by Evans (1956). Irregularly outlined cells contained within a loose network of reticular fibers were described, the more primitive forms of which were usually devoid of argyrophile fibrils. Delicate fibrils, constantly being produced in Hodgkin's disease, fused as the gland became more fibrous. In the paragranuloma the cells were separated into irregular groups by thin strands of reticulum.

Marshall (1956) saw reticular fibrils which formed a ring around the follicles in giant follicle lymphoma. Reticular fibrils were not increased in reticuloses. Frequently an increment of reticular fibrils occurred in Hodgkin's paragranuloma, but were very slight or

absent in the sarcomata of Hodgkin. The syncytial reticulum-celled sarcomata produced no increase of reticular fibrils, but in the fiber forming reticulum-celled sarcomata separate cells lay in a matrix of reticulum.

Richter (1957) noted that reticulum fibers were possibly increased in reticulum cell sarcoma.

Buscinco, Cecchi and Ferraris (1957) observed no alteration in structural outline of reticulum in leukemia, but thought the fibrils appeared thinned.

By the use of an electron microscope, Weiss (1957) found the reticulum of the human spleen to be an interrupted structure beneath the endothelial cells. He was unable to demonstrate a fibrillar component in the reticulum which was composed of finely granular, moderately dense material.

CHAPTER III

STATEMENT OF PROBLEM

This study was undertaken in an effort to determine the changes in the arrangement and characteristics of the reticular fibrils of the spleen in the leukemias and closely related disorders employing newer staining methods which provide greater detail and differentiation.

The reticular cell, generally accepted as the parent cell of the abnormal cells of the various blood dyscrasias, has been studied to a considerable extent, but the reticular fibrils and their arrangement in these states have not been given much attention. Since any knowledge of the arrangement of the cellular components of a tissue is of value in a consideration of the development and regression of morbid processes, it appeared that a study of the pattern and histochemical characteristics of these fibrils in leukemic states might contribute to the sum of knowledge concerning these diseases.

In preparation for this study essentially normal spleens from individuals of the different age groups were selected and examined histologically to observe the changes in the fibrils or fibrillary patterns which developed with aging. Appropriately stained, histological preparations of leukemic spleens were examined and compared with the normal spleens from individuals of the same age to determine the morphological alterations of the fibrils in leukemic states. The first part of this

study is concerned with the changes in amount and arrangement of the reticular fibrils of the spleen in acute, subacute and chronic lymphocytic leukemia. The second part reports the dissimilar patterns of argentophilic fibrils in preparations of the spleen in acute, subacute and chronic myelocytic leukemia. Variation of appearance and occurrence of argyrophile fibrils of the spleen are described in the third portion of this dissertation. The final part recounts the deviation of form and pattern of the reticulum in the spleen in closely related diseases.

CHAPTER IV

MATERIALS AND METHODS

Spleens obtained at autopsy from patients who had died of leukemia, Hodgkin's disease, reticulum cell sarcoma, or lymphosarcoma were used in these studies. Spleens removed from non-leukemic patients of comparable age groups were used as controls. When possible, specimens with a capsule were selected.

After fixation of the specimens in 10 per cent buffered neutral formaldehyde, pieces of tissue were cut approximately 2 mm. thick. These specimens were embedded in paraffin and sections were cut 7 microns thick. In a few instances, due to marked technical difficulties, the sections were cut 8 microns thick. In addition to the usual hematoxylin-eosin stain special stains were used. Goldner's modification of Masson's stain for demonstration of connective tissues (1938), Gomori's methenamine silver stain for reticulin (1937), and the PAS-Hale stain for demonstration of acid and neutral polysaccharides after Ritter and Oleson (1950) were all employed to point out more clearly the alteration of splenic architecture.

Krumbhaar (1939) realized, "truly normal human spleens are practically impossible to obtain." Hellston (1928) noted pronounced individual variations in the spleen, some of which he thought were related to age. Hellman (1926), in his work on normal spleens, found a

greater amount of white pulp in the spleens of younger individuals. Therefore, controls were obtained for every year of age up to the age of twenty years and after that controls for every decade were used.

Foot (1927a) described, "a rather broad, pale band of protoplasmic material overlaid in places by a bundle of reticulin fibrils, beyond which the pale band projects on either side." Consequently, the fibrils which stain light pink in the PAS-Hale stained sections have been designated protoplasmic fibrils.

CHAPTER V

RESULTS

Lymphocytic Leukemia

Acute

In this study, the ages of the patients who died of acute lymphocytic leukemia ranged from 2 months to 68 years, the majority being less than 13 years. Marked variation in the weights of the spleens was noted. The smallest spleen (13 gm.) was found in a 13 month old child while the largest spleen (1120 gm.) was removed from a 57 year old man. Pertinent information on the patients in this study who had acute lymphocytic leukemia can be obtained from Table I.

In the 16 cases studied, different prosectors described the external surface of the spleen as mottled purplish-pink, light reddish-brown, dark reddish-brown, dark red and white, deep red, white flecks over reddish-purple, dark reddish-purple, or deep purple. The pulps were described as dark red, dark reddish-purple, mottled grayish-red, or light reddish-brown. Four spleens were described as slightly diffluent, four were firm, and others were soft, flabby, or rubbery. Malpighian corpuscles were described as normal, minute, not particularly outstanding, small, not identified, or quite prominent. The architecture was readily evident in two spleens and completely replaced in a third

TABLE I

INFORMATION ON PATIENTS WITH ACUTE LYMPHOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
J.L.R	7 yrs.	M	190 gm.	5 mos.
E.R.T.	58 yrs.	M	710 gm.	3 mos.
M.G.W.	5½ yrs.	F	215 gm.	2 yrs.
L.H.	4 yrs.	M	205 gm.	11 mos.
M.H.	68 yrs.	M	150 gm.	24 da.
R.K.	64 yrs.	M	400 gm.	5 da.
C.C.J.	28 yrs.	M	430 gm.	7 wks.
B.S.W.	3½ yrs.	M	150 gm.	9 mos.
B.F.	12 yrs.	F	400 gm.	5 mos.
J.P.F.	13½ mos.	M	13 gm.	5½ mos.
S.A.C.	3 yrs.	F	77 gm.	4 mos.
M.C.H.	4 yrs.	M	100 gm.	11 mos.
L.E.M.	8 mos.	F	34 gm.	1 mo.
C.C.	4 yrs.	F	120 gm.	20 mos.
R.M.	4 yrs.	M	170 gm.	16 mos.
C.W.	31 yrs.	M	440 gm.	4 mos.
W.J.B.	59 yrs.	M	620 gm.	1 yr.
R.L.T.	43 yrs.	M	325 gm.	9 mos.
J.F.	13 yrs.	M	600 gm.	6 mos.
J.C.M.	65 yrs.	F	300 gm.	1 yr.
D.D.S.	57 yrs.	M	1120 gm.	5 mos.
C.M.	2 mos.	F	66 gm.	3 wks.

spleen. In this study, as is usually the case, patients are referred to by their initials.

J.L.R. This 7 year old boy was stricken with acute lymphocytic leukemia 5 months before his death. When compared with normal spleens, the Malpighian corpuscles were decreased almost half in number. Reaction centers were not seen. In an occasional corpuscle the reticular fibrils resembled the normal arrangement. A dense discontinuous network of reticular fibrils in the central portion of the corpuscles separated the cells into small groups. In contrast, there were only a few scattered shreds of reticular fibrils in the central part of a normal Malpighian body. In the periphery of the bodies the thickened, reticular fibrils separated the cells into very small groups. The PAS-Hale stained preparations presented a few protoplasmic fibrils as compared with preparations of normal Malpighian bodies. Reticular fibrils outlined the sinuses in small areas of the red pulp, but in most of the section broken fibrils appeared to be the remainder of the normal reticulum (Fig. 1). There were small vessels with many fine reticular threads running in various directions for a short distance. In small fields there was no vestige of argyrophile fibrils. In the PAS-Hale stained sections, the sinuses of the red pulp were decreased in number and were not delineated as well as the sinuses of a normal spleen.

E.R.T. In a study of histological sections from the spleen of a 58 year old man who had suffered from acute lymphocytic leukemia for 3 months, a decreased number of Malpighian bodies was noted. These Malpighian corpuscles resembled the ones which were seen in the normal spleens from persons of the same age, but the lymphocytes of the

Fig. 1. Acute Lymphocytic Leukemia. Notice the broken fibrils in the red pulp.

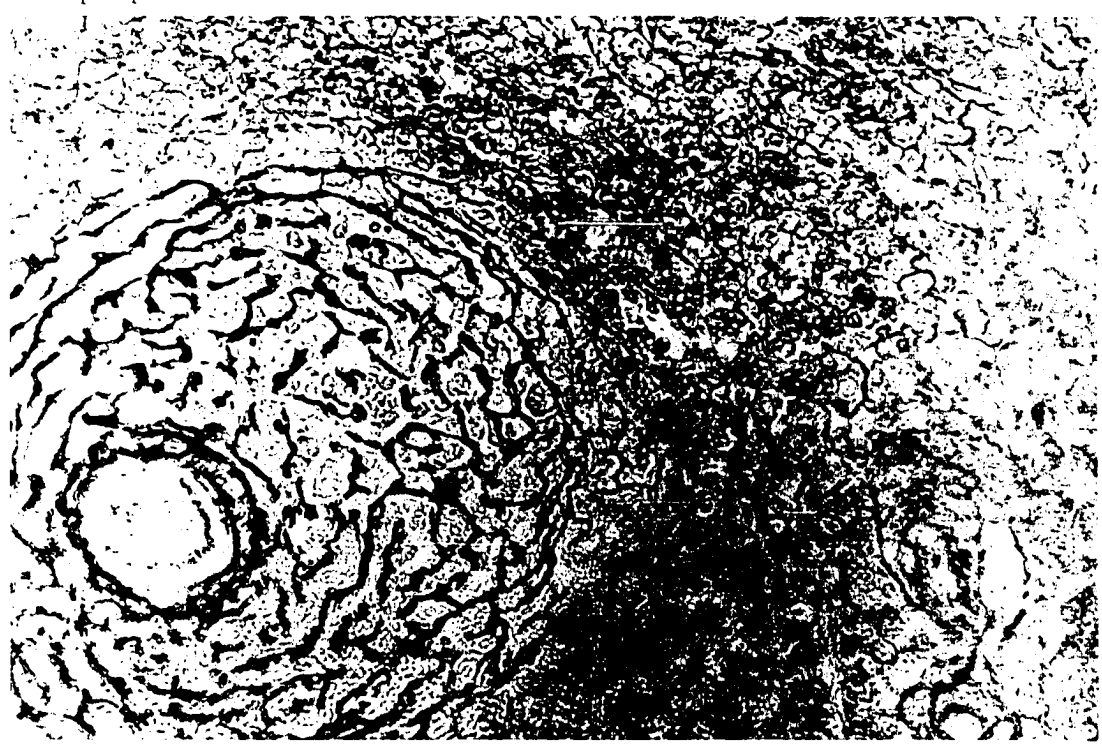

Fig. 2. Acute Lymphocytic Leukemia. Note the Malpighian corpuscle which exhibits an increased number of reticular fibrils.

Malpighian bodies were reduced in amount. Small, eosinophilic, amorphous masses which were slightly larger than a leukemic cell were observed in the Malpighian bodies. The thickened, reticular fibrils which were increased in amount divided the Malpighian corpuscles into small lobules. The arrangement of the protoplasmic fibrils resembled that of a normal Malpighian body. The cells between the widely separated sinuses of the red pulp were encircled individually by reticular fibrils, however, in some fields only an occasional black-stained shred of reticulum was seen. The protoplasmic fibrils duplicated the normal arrangement of the red pulp and definitely did not resemble the pattern of the reticular fibrils.

M.G.W. There were very few Malpighian bodies in the histological sections of the spleen from this 5 year old girl who had been afflicted with acute lymphocytic leukemia for 2 years. Reaction centers were not visible. There were dense, short, fragmented, reticular fibrils some of which were more continuous, but thick and frayed throughout the Malpighian bodies. Protoplasmic fibrils separated nearly every cell from the others of the corpuscles, while only a few delicate fibrils were seen in the periphery of the normal Malpighian bodies. Heavy, frayed, argentophilic fibrils very well outlined a small number of sinuses in the red pulp. Between these sinuses the maze-like arrangement of the reticular fibrils often surrounded individual cells. In the PAS-Hale stained section the pink-stained fibrils were not found in certain areas of the red pulp. When the protoplasmic fibrils could be seen, they were stained faintly and in many instances were broken.

L.H. A normal number of Malpighian corpuscles were found in

the histological sections of spleen from this 4 year old boy who was ill of leukemia for 11 months. Reaction centers were not found. Coarse, reticular fibrils were markedly increased in the outer portion of the Malpighian bodies, as illustrated in Fig. 2. Uneven rows of extremely short, parallel, argyrophile fibrils divided some corpuscles into small compartments. The arrangement of the protoplasmic fibrils was almost identical with that of normal Malpighian bodies. The reticular fibrils were very delicate in the red pulp but were numerically increased. Argentophilic fibrils enveloped single cells, but sinuses were not discernible. Occasionally an extremely fine snarl of black-stained fibrils was seen without relation to blood vessels. Very faintly stained, delicate, protoplasmic fibrils partially demarcated small sinuses.

M.H. The signs and symptoms of leukemia were of short duration (24 days) in this 68 year old man. Malpighian bodies were not decreased in number. Small hyaline masses were found in an occasional corpuscle. Most of the corpuscles simulated normal Malpighian bodies, but a few had heavy threads of reticulum throughout. Sinuses were not observed in the red pulp. Reticular fibrils consisted of short, frayed, broken threads of argentophilic material. Now and then a few heavy, continuous argyrophile fibrils separated small groups of cells with fine fibrils extending between all cells of the group. Protoplasmic fibrils were almost completely absent from the red pulp, but delicate beaded fibrils outlined a few sinuses.

R.K. This 64 year old man suffered from acute lymphocytic leukemia for 5 days before his death. There was a numerical decrease of Malpighian bodies and a decrease in the amount of lymphocytes within

them. The reticular fibrils of the corpuscles appeared almost like those of normal Malpighian bodies. In the PAS-Hale stained sections very delicate, pink-stained, protoplasmic fibrils increased slightly in amount in the corpuscles. Reticular fibrils delicately outlined a few sinuses of the red pulp. Often single, very dense, argentophilic fibrils occurred with short, stubby branches extending almost at right angles. Dense and fine arborizations circumscribed small vessels. Very dense, argyrophile fibrils confined small groups of from five to seven cells, but in other fields only broken strands of reticulum occurred with no semblance of pattern. Delicate, beaded strands and continuous protoplasmic fibrils nicely outlined the sinuses of the red pulp. In some areas dense, pink-stained fibrils separated each cell from the adjacent cells.

C.C.J. In a study of histological sections from the spleen of this 28 year old man who was afflicted with leukemia for 7 weeks a slight decrease in the number of Malpighian bodies was observed. Most of the corpuscles were small but they compared favorably with those of one of the controls. Heavy and frayed, argentophilic fibrils divided the corpuscles into small nests of cells. In the PAS-Hale stained section the corpuscles closely resembled normal Malpighian bodies. The few sinuses that were seen were extremely delicately delineated. Many dense, reticular fibrils separated the cells between these sinuses into small groups. The protoplasmic fibrils of the red pulp closely resembled the normal arrangement, but the fibrils were more delicate. The protoplasmic fibrillary pattern did not conform to the reticular pattern.

B.S.W. Very small Malpighian corpuscles were found in the

sections of spleen from a 3 year old boy who was ill of leukemia for 9 months. Only one reaction center was seen. Coarse, black-stained fibrils divided the corpuscles into small nests of cells. The protoplasmic fibrils of the corpuscles simulated those of normal Malpighian bodies. Reticular fibrils delineated some sinuses of the red pulp very well. Many coarse and fine argentophilic fibrils occurred between these sinuses, and in certain fields nearly every cell was enclosed. Extremely fine networks of argyrophile fibrils extending across cells were seen without reference to blood vessels. The protoplasmic fibrils of the red pulp resembled the normal arrangement. Delicate pink-stained fibrils between the sinuses were not nearly as coarse as the reticular fibrils of comparable areas.

B.F. A 12 year old girl was afflicted with acute lymphocytic leukemia for 5 months. Malpighian bodies in sections of this spleen were very few, very small and without reaction centers. The reticular fibrils were very much like those of normal Malpighian corpuscles. Thickened protoplasmic fibrils were increased in number in the corpuscles. Just beneath the capsule there were more reticular fibrils than elsewhere. Silver-stained fibrils partially separated the cells of the red pulp into very large and small nests. Many areas the size of a high power field contained only a few shreds of reticulum. Tiny areas of extremely fine, argentophilic fibrils seemed related to blood vessels. Protoplasmic fibrils demarcated many small and medium sized sinuses. There was a marked dissimilarity between the reticular and protoplasmic fibrillary patterns.

J.P.F. Most of the Malpighian corpuscles were small in the

histological preparations of the spleen from this 1 year old boy who suffered from acute lymphocytic leukemia for 5 months. The reticular fibrils resembled those of a normal corpuscle, but in a few the fibrils of the outer portion coursed perpendicular to the corpuscular periphery. Protoplasmic fibrils appeared much like those of normal Malpighian corpuscles. The subcapsular and deeper red pulp had much the same reticular fibrillary pattern. There were very delicately delineated sinuses. Very heavy, wide, silver-impregnated fibrils and many fine fibrils separated the cells into small nests or enclosed single cells (Fig. 3). In a few areas extremely fine fibrils extended across cells. The protoplasmic fibrils of the red pulp differed only slightly from the normal arrangement, however, in a few areas pink-stained fibrils surrounded every cell.

S.A.C. In histological sections of spleen from this 3 year old girl who was ill of leukemia for 4 months the Malpighian corpuscles seemed to have about half the normal number of lymphocytes. Connective tissue was slightly increased in the peripheries of the Malpighian corpuscles. The reticular fibrils were coarser than those of normal Malpighian bodies. In the PAS-Hale stained preparation some of the larger corpuscles contained small, homogeneously, eosinophilic-stained masses which were situated very close together. Beneath the capsule the reticular fibrils were not quite as dense as the ones deeper within the section. A few sinuses were delicately outlined. Most of the argentophilic fibrils of the red pulp varied markedly from very fine to coarse. Many times the fine fibrils surrounded single cells, but the coarser ones crossed cells and did not seem to enter into the organization of the tissue. Protoplasmic fibrils nicely but delicately outlined the sinuses of the red pulp. The reticular and

Fig. 3. Acute Lymphocytic Leukemia. Observe the small nests of cells in the red pulp.

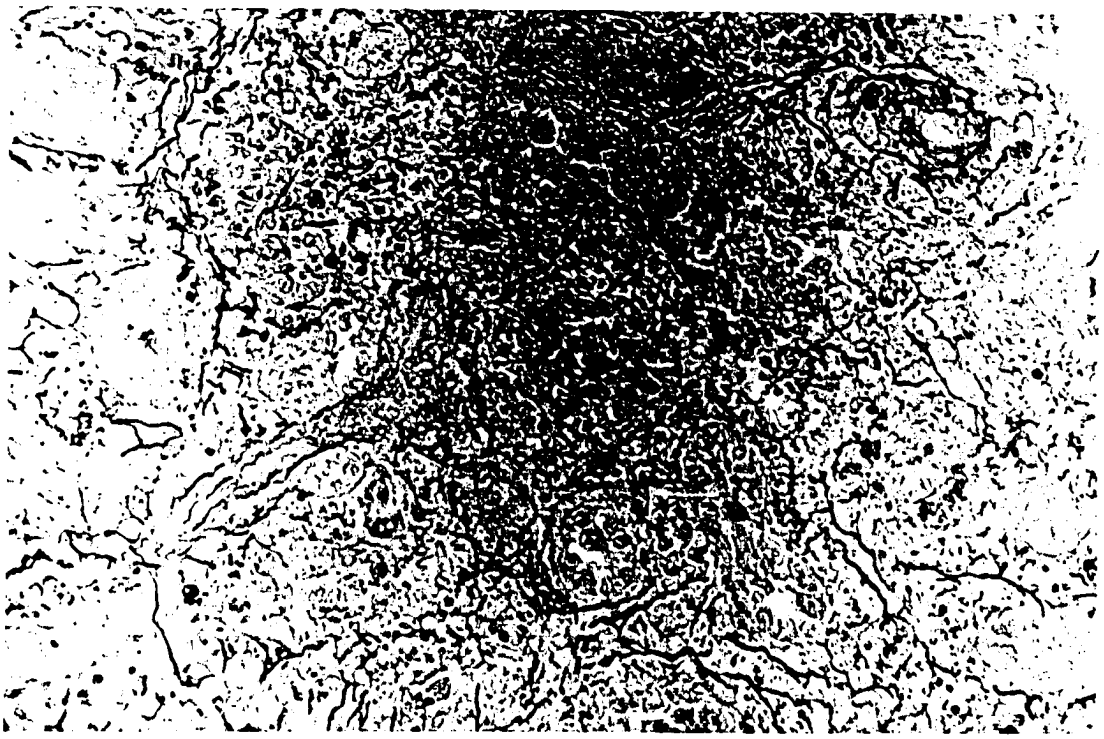

Fig. 4. Subacute Lymphocytic Leukemia. Notice the frayed fibrils arranged in a normal reticular pattern.

protoplasmic fibrils did not conform as to pattern of arrangement.

M.C.H. This 4 year old boy was afflicted with acute lymphocytic leukemia for 11 months. In histological preparations the Malpighian bodies were small and decreased in number. Reaction centers were not found. Many coarse, reticular fibrils divided the corpuscles into nests of cells. Heavy, protoplasmic fibrils were increased in the peripheries of the corpuscles. Beneath the capsule and in many other fields of the red pulp there were only a few shreds of silver-stained fibrils. In other areas small granules and strands of reticular material outlined the sinuses. The arrangement of the protoplasmic fibrils was very similar to that of a normal red pulp. The pattern of the protoplasmic fibrils differed markedly from that of the reticular fibrils.

L.E.M. Some of the Malpighian corpuscles were sharply demarcated in the preparations of the spleen from an 8 month old girl who suffered from acute leukemia for 1 month. Reticular fibrils appeared to be normally arranged in most of the corpuscles, but in a few the heavy fibrils divided the body into small nests of cells. Corpuscular, protoplasmic fibrils closely resembled those of normal Malpighian corpuscles. There were few subcapsular fibrils, but in the remainder of the red pulp a normal amount and arrangement of reticular and protoplasmic fibrils occurred.

C.C. In histological sections of spleen from this 4 year old girl who had leukemia for 20 months the Malpighian corpuscles were markedly infiltrated with leukemic cells. The reticular fibrils of the corpuscles appeared to be normal in amount, size and arrangement. An increased amount of thickened protoplasmic fibrils coursed through the

corpuscles. The scattered, short, reticular fibrils of the red pulp produced no pattern of arrangement, while the protoplasmic fibrils marked out the widely separated sinuses. In areas nearly every cell was surrounded by pink-stained fibrils. The reticular and protoplasmic fibrillary patterns differed markedly.

R.M. This 4 year old boy was afflicted with acute lymphocytic leukemia for 16 months. The decreased number of small Malpighian corpuscles were infiltrated with leukemic cells. The argentophilic fibrils were broken, thick and scattered in the periphery of the corpuscles. The protoplasmic fibrils of some corpuscles appeared like those of normal corpuscles, while in others the coarse protoplasmic fibrils separated the cells into small groups. Below the capsule were a few, short, scattered reticular fibrils. In the deeper tissue many fields had only a few shreds of reticulum, while delicate fibrils divided the cells into small nests in other areas. Protoplasmic fibrils delicately delineated widely dispersed sinuses, and fine pink-stained threads coursed between these sinuses.

C.W. Malpighian bodies seemed normal in size and number in the preparations of the spleen from a 31 year old man who was ill of leukemia for 4 months. Bands of argentophilic material and very wide reticular fibrils separated the cells of the corpuscles into medium sized groups, but the peripheries of the corpuscles were poorly demarcated. In many bodies the protoplasmic fibrillar pattern simulated the normal arrangement, but in a few many heavy, pink-stained fibrils enclosed single cells or small groups of cells. Dense, subcapsular, reticular fibrils surrounded small groups of cells. Very fine, beaded reticular

fibrils marked out the sinuses of the red pulp well. Between these sinuses coarse, argentophilic fibrils encircled individual cells. Sinuses were delineated by thickened, protoplasmic fibrils or granules and short fibrils. Very delicate, pink-stained fibrils occurred between these sinuses.

W.J.B. This 59 year old man was afflicted with leukemia for 1 year. Malpighian corpuscles were represented by follicular arteries which were surrounded by leukemic cells. Dense, reticular fibrils divided the corpuscles into long, narrow compartments, but in a few corpuscles the fibrils simulated a normal arrangement. The corpuscular, protoplasmic, fibrillary arrangement resembled that of the reticular fibrils. Frayed, subcapsular, reticular fibrils demarcated medium sized and small sinuses in certain areas of the red pulp. In other areas coarse, black-stained fibrils separated the cells into diamond-shaped nests. Protoplasmic fibrils divided the red pulp into long compartments. Wide zones of individually encircled cells occurred throughout the preparation.

R.L.T. Malpighian corpuscles were not found in the hematoxylin-eosin stained sections of spleen from a 43 year old man who suffered from leukemia for 9 months. However, coarse, argentophilic fibrils separated the leukemic cells about the follicular artery into small nests - an arrangement very similar to other Malpighian corpuscles in leukemic spleens. At the periphery of these structures the extremely coarse fibrils probably represented connective tissue fibrils. Around the follicular arteries the protoplasmic fibrils simulated the normal arrangement or thickened fibrils were increased in amount. Not many

reticular fibrils were found beneath the capsule. Argentophilic fibrils outlined a few sinuses. Areas of the red pulp in which coarse, reticular fibrils separated the cells into small groups were intermingled with large areas in which very few fibrils occurred. In still other fields shreds and short argentophilic fibrils were insufficient to form a pattern. Protoplasmic fibrils delicately delineated the sinuses of the red pulp.

J.F. The few Malpighian corpuscles did not exhibit reaction centers in the microscopic sections of a spleen from a 13 year old boy who was ill of leukemia for 6 months. In marked contrast to the normal corpuscles with delicate fibrils only in their peripheries, coarse argentophilic fibrils divided the corpuscles into small lobules. Protoplasmic fibrils were increased moderately about the peripheries of the corpuscles. Dense, reticular fibrils which coursed perpendicular to the capsule separated the cells into long narrow nests. Between the nicely outlined sinuses occurred many coarse argentophilic fibrils which encircled every cell. The protoplasmic fibrils demarcated sinuses in the red pulp and occasionally continued around the sinus in spiral formation. Delicate, pink-stained fibrils coursed between these sinuses.

J.C.M. In the study of histological sections of spleen from this 65 year old woman, who was stricken with leukemia 1 year before her death, a normal number of small Malpighian bodies were noted. A marked increase of coarse, reticular fibrils separated the cells of the corpuscles into very small groups, while the protoplasmic fibrils closely resembled the normal arrangement. In the subcapsular and deeper red pulp many frayed, reticular fibrils curled about individual or small groups of cells. Protoplasmic fibrils very delicately outlined sinuses

in the red pulp.

D.D.S. A 57 year old man suffered from leukemia for 5 months. In the splenic preparations the Malpighian corpuscles, which merged into one another, exhibited about half the normal complement of cells. Reticular and protoplasmic fibrillar arrangement compared well with the normal in pattern and density. Coarse, frayed, argentophilic fibrils separated the subcapsular cells and those of the deeper red pulp into very small nests. Snarls of extremely delicate, black-stained fibrils circumscribed small blood vessels. Protoplasmic fibrils delineated well the widely dispersed sinuses of the red pulp. Nearly every cell in many areas was surrounded by coarse pink fibrils.

C.M. Most of the normal lymphocytes had been replaced in the Malpighian bodies of the spleen from this 2 month old girl who was ill of leukemia for 3 weeks. Coarse, reticular fibrils divided the corpuscles into long compartments, while there was only a slight increase of protoplasmic fibrils within the corpuscles. A few delicately outlined sinuses were seen in the red pulp. Coarse, frayed, argentophilic fibrils arranged in a fine-meshed maze separated the cells of the red pulp into very small groups. When the nicely outlined sinuses were close together, protoplasmic fibrils encircled the cells between these sinuses. Between the widely separated sinuses there were no protoplasmic fibrils.

In summary: Malpighian bodies were decreased in amount in the majority of the spleens in acute lymphocytic leukemia. In approximately half of the corpuscles a marked increase of thickened reticular fibrils divided the corpuscles into lobules. In two spleens the reticular pattern resembled that of normal Malpighian bodies. In most of the

combined stained sections slightly thickened protoplasmic fibrils were increased in the corpuscles, while in a few sections they were normally arranged.

An increased amount of argentophilic fibrils delineated a few sinuses of the red pulp, but in some spleens no sinuses were seen. For the most part, reticular fibrils arranged in a maze-like pattern, curled around cells and small groups of cells. However, a few sections of spleen had a decreased amount of reticular fibrils and no pattern could be recognized. On the other hand the protoplasmic fibrils appeared normal in amount and arrangement. Approximately one-third of the sections had a decreased amount of sinuses. In many instances the reticular fibrillary pattern did not conform with the protoplasmic fibrillary pattern.

Subacute

There were only 4 cases of subacute lymphocytic leukemia in this study with ages ranging from $3\frac{1}{2}$ years to 77 years. The spleens varied in weight from 90 gm. of the $3\frac{1}{2}$ year old child to 970 gm. in a 68 year old woman. Germane information on the patients who died of subacute lymphocytic leukemia may be found in Table II.

The external surfaces of the spleens were described as dark bluish-red, bright pinkish-red, mottled red-purple or brownish-purple. The pulps were described as grayish-pink, red-tan or deep reddish-purple. Three spleens were diffluent while the fourth was rather firm. One spleen had very prominent Malpighian corpuscles. The architectural pattern was lacking in another spleen.

D.D.D. The Malpighian corpuscles were very small in microscopic

TABLE II

INFORMATION ON PATIENTS WITH SUBACUTE LYMPHOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
D.D.D.	3½ yrs.	F	90 gm.	11 mos.
H.D.H.	39 yrs.	M	500 gm.	11 mos.
V.R.	68 yrs.	F	970 gm.	1 yr.
L.B.N.	77 yrs.	F	450 gm.	10 mos.

sections of spleen from this 3 year old girl who suffered from subacute lymphocytic leukemia for 11 months. The cells of the corpuscles contained a brown pigment (hemosiderin). A marked increase of argyrophile fibrils divided the corpuscles into small nests of cells, while the normal preparations presented only a few delicate fibrils at the peripheries of the Malpighian corpuscles. The reticular fibrils were wider than usual and appeared to be split. Protoplasmic fibrils simulated the normal arrangement in Malpighian corpuscles. Immediately beneath the capsule and deeper in the section the reticular fibrils were very like the normal arrangement, but the fibrils seemed frayed (Fig. 4). The protoplasmic fibrils nicely outlined the sinuses.

H.D.H. This 39 year old man was stricken with leukemia 11 months before his death. The few recognizable Malpighian bodies were invaded by leukemic cells. The reticular fibrils were broken and slightly heavier than those of normal corpuscles. Reticular fibrils did not demarcate the Malpighian bodies which merged almost imperceptibly with the red pulp. The protoplasmic fibrils in the corpuscles closely resembled the normal arrangement. Under the capsule many fine to moderately coarse, reticular fibrils separated the cells into rows. Sinuses were not recognized, but in areas the black-stained fibrils encircled individual cells. Protoplasmic fibrils delicately outlined the widely separated sinuses and there were a few protoplasmic fibrils between the sinuses in some areas.

V.R. Malpighian bodies were not seen in the histological sections of spleen from this 68 year old woman who had subacute lymphocytic leukemia for 1 year. Probable follicular arteries were surrounded

by leukemic cells. Subcapsular and deeper in the red pulp many coarse and fine reticular fibrils in some areas coursed in a parallel manner, but in other fields formed a partial network. This maze of fibrils separated the cells into small and large groups. Protoplasmic fibrils demarcated the widely dispersed sinuses of the red pulp, however, occasionally there were delicate fibrils between these sinuses. A few structures were found that resembled the arrangement of protoplasmic and reticular patterns in corpuscles. Very delicate, frayed argentophilic fibrils separated cells into small lobules. An increased number of markedly thickened, protoplasmic fibrils contained many small, eosinophilic-stained masses.

L.R.N. This 77 year old woman was ill of lymphocytic leukemia for 10 months. Malpighian corpuscles were not found in histological sections of the spleen. Sinuses were not found in the red pulp, but discontinuous, split, reticular fibrils partially separated the cells into small and medium sized nests, as illustrated in Fig. 5. In broad areas very delicate, argentophilic fibrils encircled every cell. The protoplasmic fibrillary pattern corresponded to the reticular pattern; however, in the areas of individual cell enclosure the thickened protoplasmic fibrils displayed focal increments.

To summarize: The histological sections of spleens of subacute lymphocytic leukemia somewhat resembled those of acute lymphocytic leukemia, but the variation from the normal picture was more marked. In two of the spleens Malpighian corpuscles were not seen, but in one preparation the thickened reticular fibrils were arranged much like those of the corpuscles in acute leukemia. The protoplasmic fibrils in two sections

Fig. 5. Subacute Lymphocytic Leukemia. Observe the very fine reticular fibrils of the red pulp.

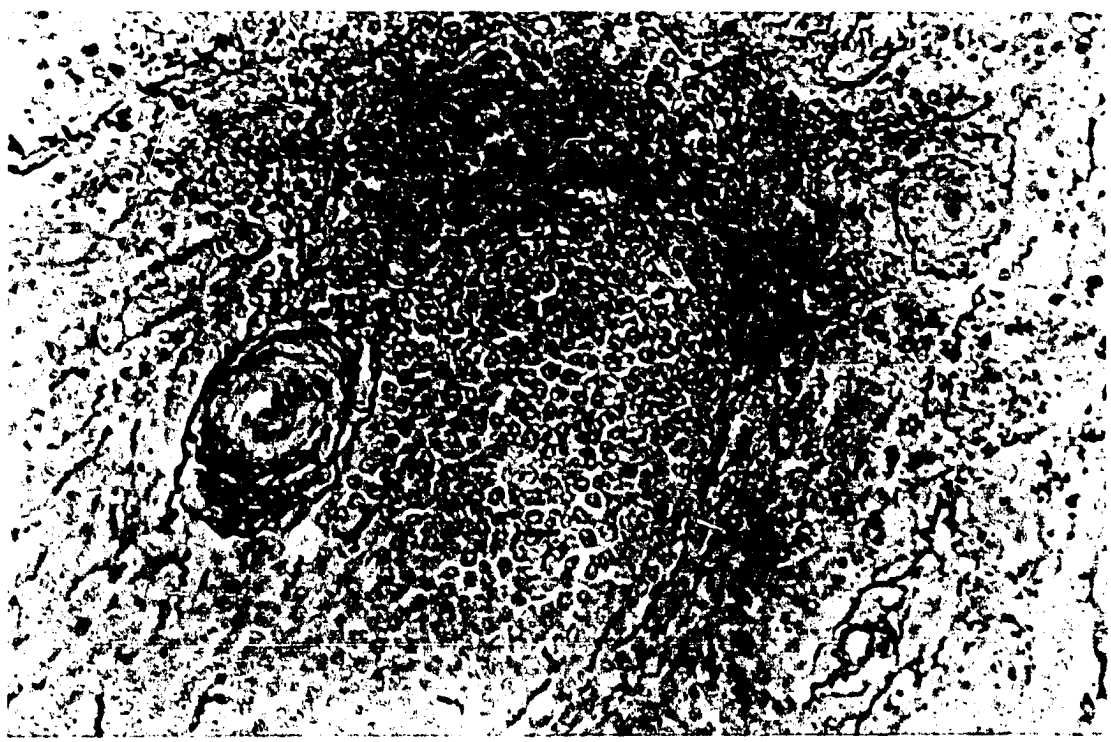

Fig. 6. Chronic Lymphocytic Leukemia. Note the small nests of cells in the red pulp around the Malpighian corpuscle.

of spleen simulated the normal corpuscular arrangement. In one spleen there were very thick protoplasmic fibrils which widened considerably in focal areas.

The red pulps contained few sinuses. In one preparation reticular fibrils were arranged much like the normal pattern. Again, the argyrophile fibrils were arranged in a maze-like pattern and encircled individual or small groups of cells. In one section the protoplasmic fibrils resembled the normal arrangement of red pulp, but in the remainder of the sections the sinuses were widely separated.

Chronic

Of the 26 cases of chronic lymphocytic leukemia, only 8 patients were less than 17 years of age. The splenic weights varied from 100 gm. in a $3\frac{1}{2}$ year old boy to 2600 gm. in a 65 year old man. Only 5 patients had spleens that exceeded 1000 gm. in weight. Relevant information concerning the patients in this study who died of chronic lymphocytic leukemia can be gained from Table III.

The descriptions of the external and cut surfaces of the spleens differed markedly from bluish-gray or light brownish-red to dark purple with many intermediate shades. One spleen had multiple infarcts, while 4 displayed light colored nodules. Thirteen spleens were flabby or diffluent while 7 were firm in consistency. Only 2 spleens were mentioned as having complete loss of architectural pattern. Malpighian corpuscles were described as not seen, obscure or large.

O.S. This 63 year old man suffered from chronic lymphocytic leukemia for 11 years. Many Malpighian corpuscles were small and the

TABLE III

INFORMATION ON PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
O.S.	63 yrs.	M	280 gm.	11 yrs.
M.E.E.	12 yrs.	F	2100 gm.	6 wks.
B.B.	65 yrs.	M	2600 gm.	4 yrs.
A.C.	77 yrs.	F	650 gm.	14 mos.
G.F.	86 yrs.	M	330 gm.	6 yrs.
J.L.	59 yrs.	F	200 gm.	1 yr.
W.L.L.	12 yrs.	M	1400 gm.	1 yr.
C.L.S.	5 yrs.	F	1200 gm.	3 mos.
L.E.	76 yrs.	M	140 gm.	1 yr.
L.L.S.	70 yrs.	M	320 gm.	4 mos.
J.A.J.	4 yrs.	M	355 gm.	2 mos.
B.L.B.	16 yrs.	F	700 gm.	2 yrs.
S.L.M.	4 yrs.	F	150 gm.	1 yr.
M.N.	61 yrs.	M	720 gm.	7 mos.
F.J.	84 yrs.	M	650 gm.	6 mos.
M.B.S.	67 yrs.	F	400 gm.	4 yrs.
R.S.D.	80 yrs.	M	240 gm.	1 yr.
G.J.J.	60 yrs.	M	1200 gm.	5 yrs.
W.L.G.	46 yrs.	M	660 gm.	1 yr.
C.H.M.	64 yrs.	M	400 gm.	5 yrs.

TABLE III (Continued)

Patient	Age	Sex	Weight of Spleen	Duration of Disease
F.B.S.	76 yrs.	M	220 gm.	3 yrs.
P.B.	3½ yrs.	M	110 gm.	16 mos.
T.J.M.	68 yrs.	M	440 gm.	16 mos.
A.B.J.	65 yrs.	M	750 gm.	2 yrs.
D.D.	3½ yrs.	M	100 gm.	9 mos.
L.B.	59 yrs.	M	250 gm.	1 yr.

more normal sized ones had approximately half the normal complement of lymphocytes. Broken, frayed, reticular fibrils were increased markedly in the corpuscles, although the protoplasmic fibrils of the Malpighian corpuscles appeared normal in amount and arrangement. Beneath the capsule the reticular fibrils divided the red pulp into small and medium sized groups of cells. Deep in the section some areas exhibited only reticular shreds, while in other fields very fine, black-stained fibrils surrounded each cell. In occasional areas larger, longer argyrophile fibrils occurred, but were insufficient to establish any type of pattern. Extremely fine arborizations were related to blood vessels. Amidst the delicately delineated, widely separated sinuses, coursed fine, pink-stained fibrils. In some areas the protoplasmic fibrils were almost parallel and seemed to run in spiral formation around the sinus walls.

M.E.E. Only 2 Malpighian bodies were seen in the examined preparations of spleen from this 12 year old girl. The recorded length of her illness is only 6 weeks. Coarse, reticular fibrils divided the corpuscles into many small nests of cells. Heavy protoplasmic fibrils coursed through the Malpighian corpuscles, while in the normal corpuscles a few delicate fibrils occurred at the periphery. Beneath the capsule and deeper in the section the cells were partially separated from each other by frayed, delicate, black-stained fibrils. The arrangement of the protoplasmic fibrils of the red pulp was almost identical with that of the reticular fibrils.

B.B. A few small Malpighian bodies were found in histological sections of spleen from a 65 year old man who suffered from leukemia for 4 years. Heavy reticular fibrils divided the bodies into small groups

of cells, while the normal Malpighian bodies exhibited a few delicate, peripheral fibrils. Many very coarse, protoplasmic fibrils passed through the corpuscles and formed small diamond-shaped compartments. Beneath the capsule delicate, argyrophile fibrils extended perpendicular to the capsule and separated the cells into long rectangular nests. Now and then there was a delicately outlined sinus in the red pulp. In the remainder of the pulp coarse, argentophilic fibrils seemed to enclose partially individual cells and small groups of cells. Protoplasmic fibrils delineated more sinuses than did the reticular fibrils. In other areas delicate pink-stained fibrils separated the cells between these sinuses into small groups.

A.C. The follicular arteries had leukemic cells about them in histological sections of the spleen from a 77 year old woman who was ill of lymphocytic leukemia for 14 months. A marked increase of coarse, discontinuous, argentophilic fibrils separated the cells about the follicular arteries into small groups. Numerous, thickened protoplasmic fibrils occurred throughout these extensively infiltrated Malpighian bodies. The subcapsular reticular fibrils, which had a tendency to course perpendicular to the capsule, separated the cells into small groups. A marked increase of reticular fibrils occurred in the red pulp. Many small areas composed of from 10 to 15 cells seemed encircled and overrun by myriads of extremely fine argentophilic fibrils. Protoplasmic fibrils, occasionally in spiral formation, nicely outlined the sinuses of the red pulp.

G.F. An 86 year old man was stricken by leukemia 6 years before his death. Malpighian corpuscles were not seen in preparations of the

spleen. Fine beaded, reticular fibrils delicately outlined an occasional sinus of the red pulp. An increased amount of argyrophile fibrils separated the cells into long narrow nests. These reticular fibrils were often broken and did not complete the walls of the compartments, however, fragmented reticular fibrils occurred in normal spleens of this age group. In areas there were snarls of extremely fine argentophilic fibrils. The arrangement of the protoplasmic fibrils closely resembled that of the normal red pulp.

J.L. An occasional Malpighian body was noted in the preparations of the spleen from this 59 year old woman who had suffered from leukemia for 1 year. The corpuscles appeared like normal Malpighian corpuscles in the combined and silver-stained preparations. Subcapsular, reticular fibrils coursed parallel to the capsule and separated the cells into small groups. Delicate, wavy, reticular fibrils passed between the cells of the red pulp in certain areas, but were insufficient to establish a pattern. In other areas more fibrils separated the cells into various sized groups. An occasional sinus was delicately delineated. Protoplasmic fibrils delicately demarcated the sinuses of the red pulp.

W.L.L. This 12 year old boy was ill of leukemia for 1 year. The few Malpighian bodies were chiefly replaced by leukemic cells. In the corpuscles divergent, reticular fibrils were increased in density and number. Increased, thickened, protoplasmic fibrils divided the corpuscles into small diamond-shaped compartments, whereas the normal Malpighian bodies had only delicate fibrils at the peripheries. Just beneath the capsule sparse, black-stained fibrils coursed perpendicular to the capsule. Some areas of the red pulp contained delicate,

argentophilic fibrils which were too scattered and too short to simulate the normal arrangement. In other areas coarse, argyrophile fibrils partially separated the cells into small, various-shaped groups. Protoplasmic fibrils delicately outlined the widely dispersed sinuses of the red pulp.

C.L.S. In preparations of the spleen from a 5 year old girl who was afflicted with lymphocytic leukemia for 3 months, leukemic cells almost completely replaced the few Malpighian bodies. Heavy, broken, reticular fibrils were increased only slightly in amount in the corpuscles, while the close, coarse protoplasmic fibrils divided the corpuscles into small diamond-shaped and rectangular compartments. Dense reticular fibrils separated the cells of the subcapsular tissue and red pulp into long narrow and small round nests. In some areas very fine fibrils coursed parallel to the coarser fibrils, but in other areas the fine fibrils extended across the coarser argentophilic fibrils. A maze-like arrangement of protoplasmic fibrils separated the cells of the red pulp into round and oblong nests.

L.E. This 76 year old man was stricken with leukemia 1 year before his death. There was approximately one-half the normal number of Malpighian bodies in the histological sections of the spleen. Many dense, reticular fibrils divided the corpuscles into very small compartments which often accommodated only one cell. Thickened, protoplasmic fibrils occurred throughout the Malpighian bodies. Delicate and coarse, silver-impregnated fibrils surrounded various sized groups of cells in the red pulp and subcapsular tissue. Fine argentophilic fibrils formed tangled snarls which extended across cells. In a few areas of the red

pulp protoplasmic fibrils delineated sinuses, but in many fields thick fibrils surrounded individual cells.

L.L.S. The very few Malpighian bodies were chiefly replaced by leukemic cells in splenic preparations from a 70 year old man who suffered from leukemia for 4 months. Dense, reticular fibrils divided the bodies into small nests of cells. A very normal, protoplasmic fibrillar pattern was seen in the Malpighian corpuscles. Many dense and fine argyrophile fibrils occurred in the red pulp and subcapsular tissue, and separated the cells into various sized and shaped groups. In small areas so many extremely fine fibrils encircled vessels that the tissue appeared gray. Protoplasmic fibrils delicately demarcated the widely separated sinuses of the red pulp. The reticular fibrillary pattern did not conform with the protoplasmic fibrillary pattern.

J.A.J. A 4 year old boy was afflicted with leukemia for 2 months. The few Malpighian corpuscles were divided into small nests by heavy, frayed, silver-impregnated fibrils. The protoplasmic fibrils of the corpuscles appeared to be normal in arrangement and amount. Reticular fibrils nicely but delicately demarcated sinuses in the red pulp and subcapsular tissue. The cells between these sinuses were separated into very small groups by dense, wide, reticular fibrils. Protoplasmic fibrils outlined the widely dispersed sinuses of the red pulp. Often the cells between the sinuses were individually surrounded by protoplasmic fibrils.

B.L.B. A 16 year old girl was stricken with leukemia 2 years before her death. An approximately normal number of Malpighian bodies were markedly infiltrated with leukemic cells. Heavy reticular fibrils

divided the corpuscles into small compartments, but the thickened protoplasmic fibrils in the Malpighian bodies were increased in number. Between the delicately but well demarcated sinuses of the red pulp, dense, argyrophile fibrils surrounded many small groups of cells. Often every cell was encircled by ill-defined fibrils. The widely separated sinuses of the red pulp were faintly outlined by protoplasmic fibrils, however, many thickened protoplasmic fibrils coursed between these sinuses.

S.L.M. There seemed to be a normal number of Malpighian corpuscles in the microscopic sections of spleen from a 4 year old girl who was ill of leukemia for 1 year. Many corpuscles were small and some were markedly infiltrated with leukemic cells. Dense, reticular fibrils divided the corpuscles into large lobules, but the arrangement of the protoplasmic fibrils simulated that of normal Malpighian bodies. Beneath the capsule argentophilic fibrils tended to run parallel to the capsule. Thick and delicate reticular fibrils separated the cells of the red pulp into small groups or very fine fibrils coursed around vessels and cells. Protoplasmic fibrils well delineated the widely dispersed sinuses, and between these sinuses many delicate protoplasmic threads encircled individual cells.

M.N. Very few Malpighian bodies were recognized in the histologic sections of spleen from this 61 year old man who suffered from leukemia for 7 months. Many very wide bands of reticular fibrils were found in the central portion of the corpuscles although the peripheral fibrils were fine. The protoplasmic fibrils appeared much like those of normal corpuscles. Beneath the capsule and deeper in the red pulp, many coarse and a few fine argyrophile fibrils separated the cells into small

groups. Reticular fibrils delicately outlined the widely dispersed sinuses of the red pulp. Protoplasmic fibrils simulated the normal arrangement of well outlined sinuses in the red pulp. The fine fibrils between these sinuses enclosed individual cells.

F.J. An 84 year old man was stricken with leukemia 6 months before his death. Malpighian bodies were markedly diminished in number. The arrangement of the reticular fibrils differed from that seen in any other corpuscles. Very coarse, reticular fibrils in the central third of the bodies diminished considerably in the middle third, while in the periphery an increased number of fine fibrils occurred. Argentophilic fibrils very faintly outlined a few sinuses. In some fields many delicate fibrils passed between cells and groups of cells, but very fine, close, silver-impregnated fibrils extended across cells in other fields. The arrangement of the protoplasmic fibrils very closely resembled that of a normal spleen.

M.B.S. Normal appearing Malpighian bodies were seen in microscopic sections of spleen from a 67 year old woman who was afflicted with leukemia for 4 years. An increased amount of dense, reticular fibrils coursed through the corpuscles, while the protoplasmic fibrils were very similar to the normal arrangement. The reticular and protoplasmic fibrillary patterns in the red pulp very closely resembled those of normal spleens.

R.S.D. Poorly defined Malpighian bodies seemed to merge with each other in the preparations of spleen from this 80 year old man who was ill of leukemia for 1 year. The arrangement of the reticular and protoplasmic fibrils resembled those of normal corpuscles. The

subcapsular tissue and red pulp did not exhibit as many reticular fibrils as preparations from younger aged persons, but compared favorably with the normal spleens of the corresponding age. The protoplasmic fibrils of the red pulp were normal in arrangement and amount.

G.J.J. Malpighian bodies were markedly infiltrated with leukemic cells in the sections of spleen from a 60 year old man who suffered from leukemia for 5 years. Many corpuscles retained a normal amount of reticular fibrils, while others acquired a moderate quantity of thick, reticular fibrils. The protoplasmic, fibrillary pattern closely resembled that of normal corpuscles. In the subcapsular tissue and red pulp, many fields resembled the normal arrangement, but the reticular fibrils were thicker than those of normal spleens. Argentophilic fibrils circumscribed every cell in other areas. The nicely outlined sinuses occasionally presented a spiral arrangement of the protoplasmic fibrils.

W.L.G. A 46 year old man was ill of leukemia for 1 year before his death. Malpighian bodies were decreased in number and extensively infiltrated by leukemic cells. A decided increase of coarse, frayed, reticular fibrils divided the corpuscles into long, diamond-shaped nests of cells. The arrangement of the thickened, protoplasmic fibrils in the corpuscles resembled that of the reticular fibrils. Between the few delicately outlined sinuses of the red pulp, many coarse and fine reticular fibrils separated the cells into various sized nests (Fig. 6). Extremely fine fibrils extended from one coarse fibril to another. Fine arborizations surrounded minute blood vessels. The red pulp demonstrated a very normal appearing protoplasmic fibrillary pattern.

C.H.M. Only one Malpighian body was found in the preparations from the spleen of a 64 year old man who was ill of leukemia for 5 years. Malpighian bodies were not found in the silver-stained sections. An increased number of thick protoplasmic fibrils divided the Malpighian body into large diamond-shaped compartments. In some areas of the red pulp reticular fibrils were neither plentiful enough nor close enough together to form any pattern. Black-stained, wavy, twig-like fibrils surrounded groups of cells in other fields of the red pulp. Dense, reticular fibrils beneath the capsule separated the cells into small nests. Fine protoplasmic threads coursed between the sinuses of the red pulp, which were delineated by delicate, beaded fibrils.

F.B.S. This 76 year old man had endured leukemia for 3 years. The few Malpighian bodies were markedly infiltrated with leukemic cells. No corpuscles were found in the silver-stained preparation. Thickened, protoplasmic fibrils coursed through the corpuscles. Very coarse, reticular fibrils separated the cells of the red pulp and subcapsular tissue into large and small groups. In some fields tiers of fibrils were separated by single rows of cells. Between the widely dispersed sinuses of the red pulp, delicate protoplasmic fibrils encircled every cell.

P.B. In the histologic sections of this spleen from a 3 year old boy who was afflicted with leukemia for 16 months, one reaction center was found in a Malpighian body. The arrangement of the reticular fibrils was very like the normal pattern, but the protoplasmic fibrils were slightly increased within the corpuscles. Argentophilic fibrils separated the cells of the red pulp into large rectangular shaped

groups, however, many fields had only scattered fibrils. Fine protoplasmic fibrils coursed between the widely separated, delicately outlined sinuses of the red pulp.

T.J.M. Malpighian bodies were infiltrated with leukemic cells in the preparations of the spleen from a 68 year old man who was ill of leukemia for 16 months. The reticular fibrils of the corpuscles were normal or diminished in amount. Especially near the follicular arteries the protoplasmic fibrils were thickened. The arrangement of the coarse, broken, reticular fibrils, beneath the capsule and in the red pulp, resembled that of one of the normal sections which did not have very many fibrils, as illustrated in Fig. 7. In general there was no pattern of arrangement of the argentophilic fibrils of the red pulp, but an occasional large sinus was poorly delineated. Protoplasmic fibrils demarcated well the sinuses of the red pulp. Now and then a spiral configuration of the protoplasmic fibrils occurred around a sinus.

A.B.J. Large, poorly defined Malpighian corpuscles seemed to merge with each other in the microscopic sections from the spleen of a 65 year old man who had leukemia for 2 years. A few reticular fibrils in the central portion of the corpuscles and none in the periphery was much like the normal arrangement in spleens of a comparable age. The protoplasmic, fibrillary pattern closely resembled that of normal Malpighian corpuscles. Coarse, branching, argyrophile fibrils extended between the poorly delineated sinuses. Many broken and frayed fibrils, which seemed to be made of small granular masses of reticulum, appeared as if they were disintegrating. Now and then one of the many nicely delineated sinuses of the red pulp appeared to be surrounded by a

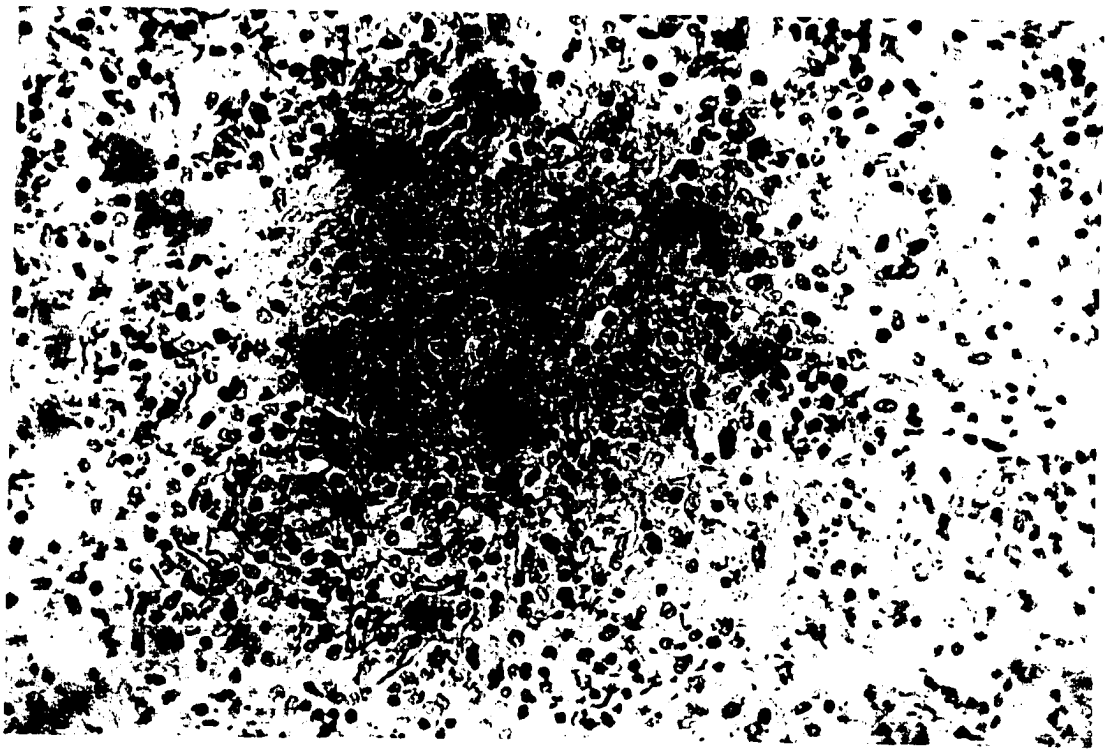

Fig. 7. Chronic Lymphocytic Leukemia. Note the numerically diminished fibrils in the red pulp.

Fig. 8. Acute Myelocytic Leukemia. Observe the maze-like arrangement of the reticular fibrils.

spiral configuration of the protoplasmic fibrils.

D.D. This 3 year old boy suffered from leukemia for 9 months. Coarse, frayed, reticular fibrils occurred throughout the corpuscles. In the combined stained preparations, the corpuscles seemed to contain reaction centers, yet many coarse protoplasmic fibrils occurred in the peripheries. The small number of subcapsular, reticulin fibrils had a tendency to course perpendicular to the capsule. Between the small, well outlined sinuses of the red pulp, coarse, wavy, frayed, argentophilic fibrils separated the cells into small groups. Protoplasmic fibrils exhibited a varied and mixed pattern. In some areas the protoplasmic fibrils appeared normal in amount and arrangement, while in other areas quite broad fibrils were focally increased in width. Protoplasmic fibrils surrounded nearly every cell in still other areas.

L.B. An approximately normal number of Malpighian bodies were found in preparations of the spleen from this 59 year old man who was ill of leukemia for 1 year. The reticular fibrils of the corpuscles closely resembled the normal arrangement, but thickened protoplasmic fibrils were increased in the corpuscular peripheries. Coarse, reticular fibrils separated the subcapsular cells into small nests, but individual cells were encircled in the red pulp. The sinuses of the red pulp were heavily outlined by argentophilic fibrils. The array of protoplasmic fibrils was very normal in appearance. Spiral arrangements of the protoplasmic fibrils around some of the sinuses were seen.

To summarize: The majority of the sections of chronic lymphocytic leukemia had a marked reduction in number and/or size of Malpighian corpuscles. Dense, often frayed and broken, reticular fibrils divided

most of the corpuscles into small compartments. Protoplasmic fibrils were thickened in the corpuscles. In a few preparations the reticular pattern resembled the normal arrangement, but markedly thickened protoplasmic fibrils were found in the corpuscles of other sections of these spleens.

The red pulp presented a very varied picture. Every spleen, except one, exhibited an increase of reticular fibrils, however, they differed considerably. Occasionally reticular fibrils appeared as scattered shreds or coarse, frayed and broken strands without pattern formation. Argentophilic fibrils were very fine and formed a small-meshed net surrounding single cells. In some microscopic sections coarse and fine, argyrophile fibrils were intermixed to form a coarse or fine maze which partially surrounded groups of cells. Some reticular fibrils appeared to be split and the fine threads passed across cells. Protoplasmic fibrils in some sections still displayed a normal pattern of arrangement. However, in many sections there was a marked reduction in the number of sinuses with delicate protoplasmic fibrils between the cells. In certain other sections the protoplasmic fibrils had much the same arrangement as the reticular fibrils. In one spleen fields of normal appearing pulp were interspersed with fields in which thickened protoplasmic fibrils surrounded every cell.

Myelocytic Leukemia

Acute and Subacute

In the cases of acute and subacute myelocytic leukemia the ages ranged from 6 to 71 years. The weights of the spleens varied from

150 gm. to 920 gm. The single case of subacute myelocytic leukemia was included with those of acute myelocytic leukemia. Pertinent information on the patients in this study who had acute or subacute myelocytic leukemia may be found in Table IV.

The external surfaces of these spleens were described as varying shades of dark red. Infarcts were noted in one spleen. The pulps were described as dark red, deep purple-red, red-brown, homogeneous red or multiple areas of light tan. Six spleens were diffluent and 2 were firm. Malpighian corpuscles were described as fairly distinct, not evident, quite prominent, prominent or evident.

R.B. A decreased number of Malpighian bodies were noted in the preparations of spleen from a 49 year old man who had suffered from acute myelocytic leukemia for only 4 weeks. The reticular fibrils of the Malpighian bodies resembled the normal arrangement, but in an occasional body there was a slight increase of reticulum. The protoplasmic fibrillary pattern closely resembled the reticular fibrillary pattern of the corpuscles. Beneath the capsule and in the red pulp were widely separated sinuses. Fine, black fibrils coursed among the cells and partially divided them into moderate sized nests. The protoplasmic fibrils delicately outlined the sinuses of the red pulp.

M.S. An apparently normal number of Malpighian corpuscles were found in the preparations of spleen from this 71 year old woman who was ill of acute myelocytic leukemia for 6 months. A normal amount of reticular and protoplasmic fibrils occurred in the corpuscles, but they were diminished in a few corpuscles. Black-stained fibrils delicately demarcated an occasional sinus. Coarse reticular fibrils,

TABLE IV

INFORMATION ON PATIENTS WITH ACUTE AND SUBACUTE MYELOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
R.B.	49 yrs.	M	730 gm.	4 wks.
M.S.	71 yrs.	F	420 gm.	6 mos.
J.W.H.	65 yrs.	M	150 gm.	3 mos.
E.E.S.	57 yrs.	M	220 gm.	2 wks.
M.S.	41 yrs.	F	400 gm.	6 mos.
J.L.	60 yrs.	M	520 gm.	3 mos.
B.J.T.	19 yrs.	F	840 gm.	6 mos.
J.J.	44 yrs.	M	270 gm.	4 mos.
G.H.	46 yrs.	F	420 gm.	2 mos.
C.F.	16 yrs.	M	920 gm.	6 mos.
C.R.	6 yrs.	M	210 gm.	11 mos.
T.V.	19 yrs.	F	540 gm.	1 mo.

which were arranged in a maze-like manner, separated the cells of the red pulp into small nests. Very fine, argyrophile fibrils surrounded small blood vessels. Protoplasmic fibrils delicately outlined the sinuses of the red pulp.

J.W.H. A 65 year old man was afflicted with myelocytic leukemia for 3 months. In the silver and combined stained preparations the corpuscles appeared like those of normal spleens. Small and large sinuses in the red pulp were outlined delicately by granules or short, parallel, reticular fibrils. Discontinuous, frayed, coarse, argentophilic fibrils that were arranged in maze formation coursed between the cells of the red pulp. The delicately outlined sinuses indicated a normal arrangement in the protoplasmic fibrillary pattern.

E.E.S. A few Malpighian corpuscles were found in the preparations of spleen from a 57 year old man who was afflicted with acute myelocytic leukemia for 2 weeks. The reticular and protoplasmic fibrillary patterns of the corpuscles resembled the normal arrangement. Coarse, discontinuous, argentophilic fibrils partially separated the cells of the red pulp into medium sized nests. Very fine arborizations of black-stained fibrils circumscribed the small vessels. The protoplasmic fibrils faintly outlined the sinuses of the red pulp.

M.S. This 41 year old woman suffered from acute myelocytic leukemia for 6 months. The Malpighian bodies were reduced in number and were infiltrated by leukemic cells. Some corpuscles had a normal reticular pattern, but others were divided into small groups of cells by markedly increased, argentophilic fibrils. The protoplasmic fibrils of the corpuscles closely resembled the usual arrangement. A few sinuses

in the red pulp were delicately outlined by reticular fibrils. The cells of the red pulp were partially separated into small nests by a maze of coarse, frayed reticular fibrils with an occasional area of very fine fibrils, as illustrated in Fig. 8. Beneath the capsule and deeper in the red pulp coarse, straight, black-stained fibrils extended between the sinuses. Protoplasmic fibrils delineated well the sinuses of the red pulp and in small areas each cell was surrounded by wide protoplasmic fibrils.

J.L. Normal appearing Malpighian corpuscles were seen in the histological sections of spleen from this 60 year old man who was ill of leukemia for 3 months. The reticular and protoplasmic fibrils closely resembled those of normal corpuscles in amount and arrangement. Subcapsular, reticular fibrils had a tendency to course parallel to the capsule. Wavy, broken, frayed, coarse argentophilic fibrils almost completely outlined the sinuses of the red pulp. A few of the well demarcated sinuses manifested the spiral arrangement of the protoplasmic fibrils.

B.J.T. A 19 year old woman was stricken with acute myelocytic leukemia 6 months before her death. The few Malpighian corpuscles were infiltrated with leukemic cells. A marked increase of coarse, short, parallel reticular fibrils divided the Malpighian bodies into small groups of cells. The protoplasmic fibrils of the corpuscles simulated the normal arrangement. Beneath the capsule and in the red pulp the coarse, argentophilic fibrils partially separated the cells into various sized nests (Fig. 9). In very small areas fine fibrils extended from one coarse fibril to another. Black-stained fibrils surrounded every

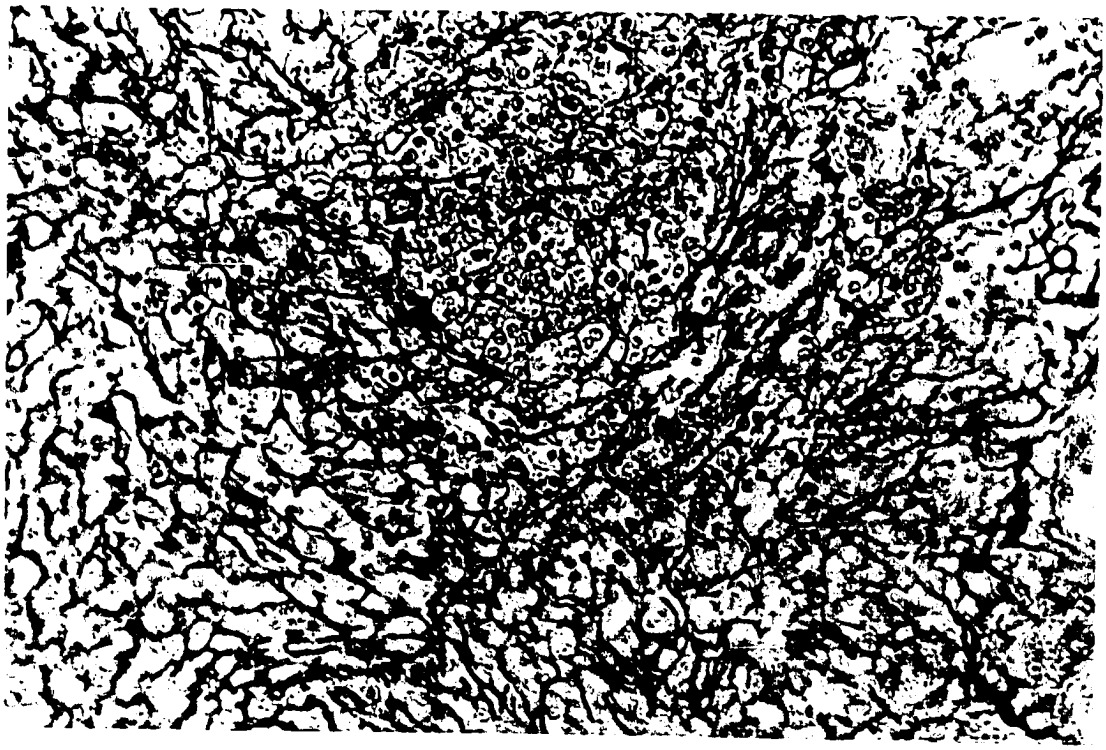

Fig. 9. Acute Myelocytic Leukemia. Observe the various sized nests of cells in the red pulp.

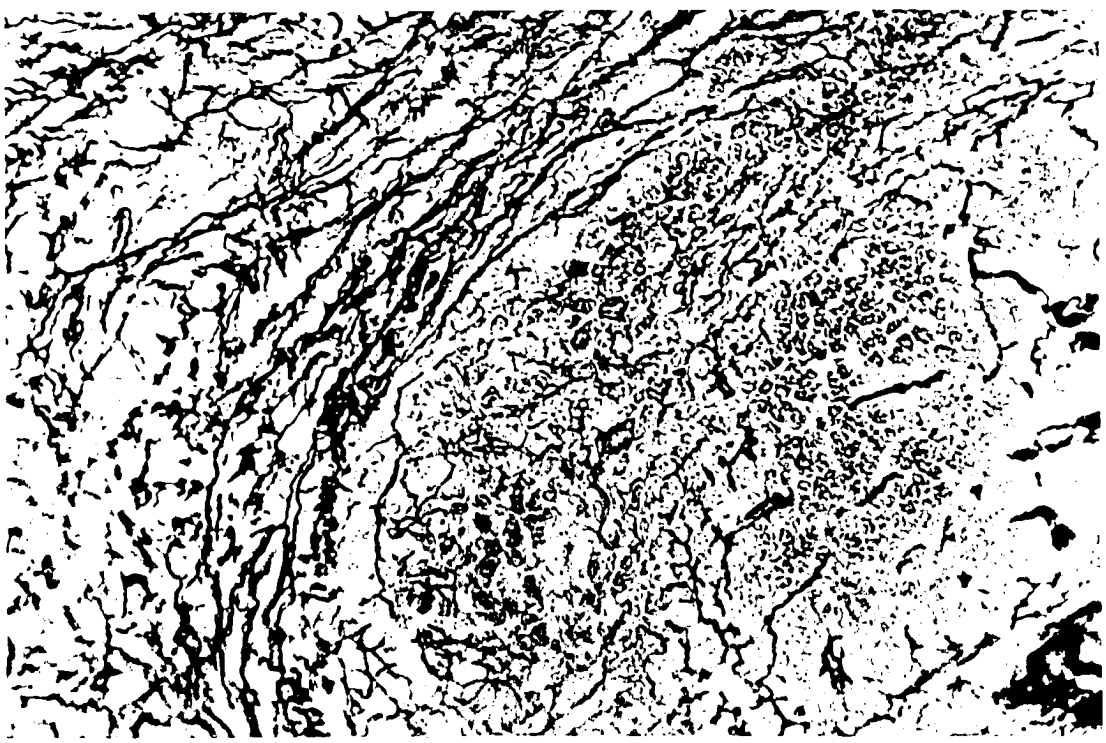

Fig. 10. Chronic Myelocytic Leukemia. Note the marked increase of reticular fibrils in the red pulp with a slight increase in the Malpighian corpuscle.

cell in some fields. In general the arrangement of the protoplasmic fibrils resembled that of a normal pulp, but every cell in occasional small areas was surrounded by protoplasmic fibrils.

J.J. Malpighian bodies were normal in size and number in the preparations of the spleen from a 44 year old man who was afflicted with acute leukemia for 4 months. Some corpuscles contained a normal amount of reticular fibrils, but others were divided into small nests of cells by coarse, argentophilic fibrils. The protoplasmic fibrillary arrangement of the corpuscles was of the usual appearance. The coarse, argentophilic fibrils between the nicely delineated sinuses separated the cells individually or into small groups. Fine arborizations had no relation to blood vessels. Protoplasmic fibrils delicately demarcated the sinuses of the red pulp.

G.H. Several reaction centers occurred in the sharply demarcated Malpighian bodies of the microscopic sections of a spleen from a 46 year old woman who suffered from leukemia for 2 months. The argentophilic and protoplasmic fibrils were arranged normally within the corpuscles. The coarse, broken, reticular fibrils of the subcapsular tissue and the red pulp were too scattered to form a pattern. In the combined stained sections protoplasmic fibrils nicely delineated the sinuses of the red pulp.

C.F. The 4 recognizable Malpighian bodies were markedly infiltrated with leukemic cells in the preparations of the spleen from this 16 year old boy who had leukemia for 6 months. The increased reticular fibrils in the corpuscles were too discontinuous to form compartments. The normal corpuscular arrangement was closely simulated by

the protoplasmic fibrils. In the red pulp scattered, broken, coarse, argentophilic fibrils and longer, frayed ones were arranged in a maze-like pattern. Granules of argentophilic material outlined a small number of sinuses in the red pulp. In the combined stained sections the sinuses were delineated partially but very delicately by protoplasmic fibrils. Protoplasmic fibrils enclosed single cells in some areas.

C.R. Small Malpighian bodies were almost replaced by leukemic cells in the preparations of the spleen from this 6 year old boy who suffered from leukemia for 11 months. A few large Malpighian corpuscles appeared to be normal and contained reaction centers. The reticular fibrils were moderately increased in amount in the small corpuscles, but the protoplasmic fibrils simulated the normal in arrangement. In some areas many sinuses were delicately outlined by continuous, argentophilic fibrils or granules; however, numerous other areas had only a few sinuses. Delicate and coarse, reticular fibrils separated the cells of the red pulp into small irregular groups and often single cells were enclosed. Occasional very fine arborizations did not seem to have any relation to blood vessels. The protoplasmic fibrils were arranged in a very normal pattern with sinuses which were delicately outlined by pink-stained fibrils.

T.V. This 19 year old woman was afflicted with subacute myelocytic leukemia for 1 month. There was a marked decrease of Malpighian bodies which appeared like the normal in the reticular and protoplasmic fibrillar arrangement. In the subcapsular tissue and red pulp delicate and coarse argentophilic fibrils in maze arrangement, partially separated the cells into various sized groups. Very fine

arborizations of reticular fibrils were around small vessels. Protoplasmic fibrils delicately outlined the widely dispersed sinuses of the red pulp.

In the summary of the above cases it was found that the Malpighian bodies were numerically decreased in approximately two-thirds of the spleens. In less than half of the spleens there was an increase of reticular fibrils within the corpuscles. A normal amount and arrangement of the protoplasmic fibrils of the corpuscles occurred in nearly every splenic preparation.

The red pulp presented an increased amount of argentophilic fibrils with a few delicately outlined sinuses. The cells were separated into small and large groups by coarse, frayed, broken, argyrophile fibrils in maze-like formation. Many of the PAS-Hale stained sections exhibited a normal appearance with the sinuses being delicately delineated by protoplasmic fibrils. However, a third of the spleens displayed very widely separated sinuses and wide zones in which every cell was surrounded by thick protoplasmic fibrils.

Chronic

The ages of the patients dying from chronic myelocytic leukemia ranged from 38 through 84 years. All except 3 spleens weighed more than 1000 gm. Relevant information on the patients in this study who died of chronic myelocytic leukemia may be obtained from Table V.

The capsular surfaces of the spleens varied greatly and were described as dark purple, mottled pink-tan and light brown, dark red and light tan, reddish-purple and yellowish-tan, red with light gray plaques,

TABLE V

INFORMATION ON PATIENTS WITH CHRONIC MYELOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
C.L.M.	48 yrs.	F	1360 gm.	18 mos.
H.M.	59 yrs.	F	1010 gm.	3 yrs.
H.W.	38 yrs.	M	2010 gm.	4 yrs.
H.T.	49 yrs.	F	2050 gm.	11 mos.
M.H.T.	84 yrs.	F	1270 gm.	2 yrs.
I.B.A	63 yrs.	F	400 gm.	2½ mos.
L.A.C.	54 yrs.	F	2280 gm.	9 mos.
J.S.	43 yrs.	M	2130 gm.	2 yrs.
F.M.	55 yrs.	M	2950 gm.	2 yrs.
L.L.	79 yrs.	M	1000 gm.	5 yrs.
G.K.	73 yrs.	M	360 gm.	3 yrs.
P.J.B.	77 yrs.	M	640 gm.	2 yrs.

dark purple mottled with yellowish-brown or purple with whitish spots. Five spleens were the sites of infarcts. The pulps were described as reddish-brown or reddish-purple. Three organs were firm and 2 were friable. Four spleens showed no evidence of normal architecture, but 1 had a comparatively well preserved architectural pattern. Malpighian corpuscles were not seen in 5 spleens.

C.L.M. A 48 year old man was ill of chronic myelocytic leukemia for 18 months. A few Malpighian bodies were almost replaced by leukemic cells, while others were necrotic centrally with a few lymphocytes in the peripheries. The corpuscles, which merged imperceptibly into the red pulp, were divided into small compartments by many short, parallel, reticular fibrils. In the PAS-Hale stained preparations the necrotic areas manifested a hazy pink background with heavy pink fibrils coursing through it. Pink-stained masses and protoplasmic fibrils masked the architecture in other corpuscles. Fine to very coarse, argentophilic fibrils separated the cells of the red pulp into various sized nests. Now and then fibrils coursed parallel and so close together that they crossed cells. Occasionally a delicately outlined sinus was seen. The finely delineated sinuses of the red pulp displayed protoplasmic fibrils in spiral formation. Pink-stained fibrils surrounded every cell in many small areas.

H.M. One structure was found in the infarct that was apparently a Malpighian body in the preparations of the spleen from a 59 year old woman who had leukemia for 3 years. The infarcted area demonstrated a remarkable preservation of reticular fibrils. In the red pulp and subcapsular tissue frayed, coarse, black-stained fibrils

partially separated cells into various sized groups, often encircling single cells. Fine fibrils occurred close together in many fields. Occasionally a sinus was found outlined delicately by reticular fibrils. The widely dispersed sinuses of the red pulp were faintly delineated by protoplasmic fibrils.

H.W. Malpighian corpuscles were not found in the histological sections of spleen from this 38 year old man who suffered from chronic myelogenous leukemia for 4 years. Many heavy, frayed, reticular fibrils separated the cells of the red pulp into groups. In numerous small areas very fine fibrils were extended between the coarser fibrils and across the cells. In small areas these fibrils were so fine and close that the tissue appeared gray. In the combined stained sections sinuses were delicately delineated by protoplasmic fibrils. In some fields very fine, protoplasmic fibrils had much the same arrangement as the fine reticular fibrils.

H.T. Malpighian corpuscles were not recognized in the preparations of the spleen from this 49 year old woman who was afflicted with leukemia for 11 months. The red pulp and subcapsular tissue appeared alike, with sinuses being outlined by coarse reticular fibrils. In the greater portion of the section many coarse, frayed, argentophilic fibrils, arranged in a fine meshed maze, partially enclosed single cells. Very fine fibrils extended across cells. Protoplasmic fibrils presented about the same pattern as did the reticular fibrils, however, a few sinuses were well outlined. Where the reticular fibrils decreased in size and increased in number, the protoplasmic fibrils thickened, and increased in number so that these areas looked like a pink matrix with

entrapped cells.

M.H.T. An 84 year old woman was stricken with myelocytic leukemia 2 years before her death. A slight increase of reticular fibrils occurred in the few Malpighian bodies, while the protoplasmic fibrils appeared normal in arrangement. Subcapsular, coarse, reticular fibrils tended to course parallel to the capsule. Many coarse, argyrophile fibrils passed in all directions through the red pulp and separated the cells into various sized nests (Fig. 10). Extremely fine fibrils extended across cells and between the coarser fibrils. The PAS-Hale stained sections presented normal appearing, widely separated sinuses which were delicately outlined by protoplasmic fibrils.

I.B.A. Malpighian bodies were numerically decreased in the preparations of the spleen from a 63 year old woman who suffered from leukemia for 2½ months. Coarse, reticular fibrils were moderately increased in the corpuscles, but the protoplasmic fibrils simulated the normal arrangement. The subcapsular fibrils, which coursed perpendicular to the capsule, became scattered, short, coarse fibrils in the red pulp where occasionally they enclosed groups of cells. Extremely fine, reticular arborizations had no relation to blood vessels. Protoplasmic fibrils delicately outlined the sinuses of the normal appearing red pulp.

L.A.C. A few Malpighian bodies were found in the histological sections of spleen from this 54 year old woman who had leukemia for 9 months. Malpighian corpuscles could not be identified in the silver or combined stained sections. An occasional sinus of the red pulp was delicately outlined. Many coarse, frayed, reticular fibrils formed a maze which enclosed small groups of cells (Fig. 11). In a few areas

Fig. 11. Chronic Myelocytic Leukemia. Notice the maze-like arrangement of the reticular fibrils.

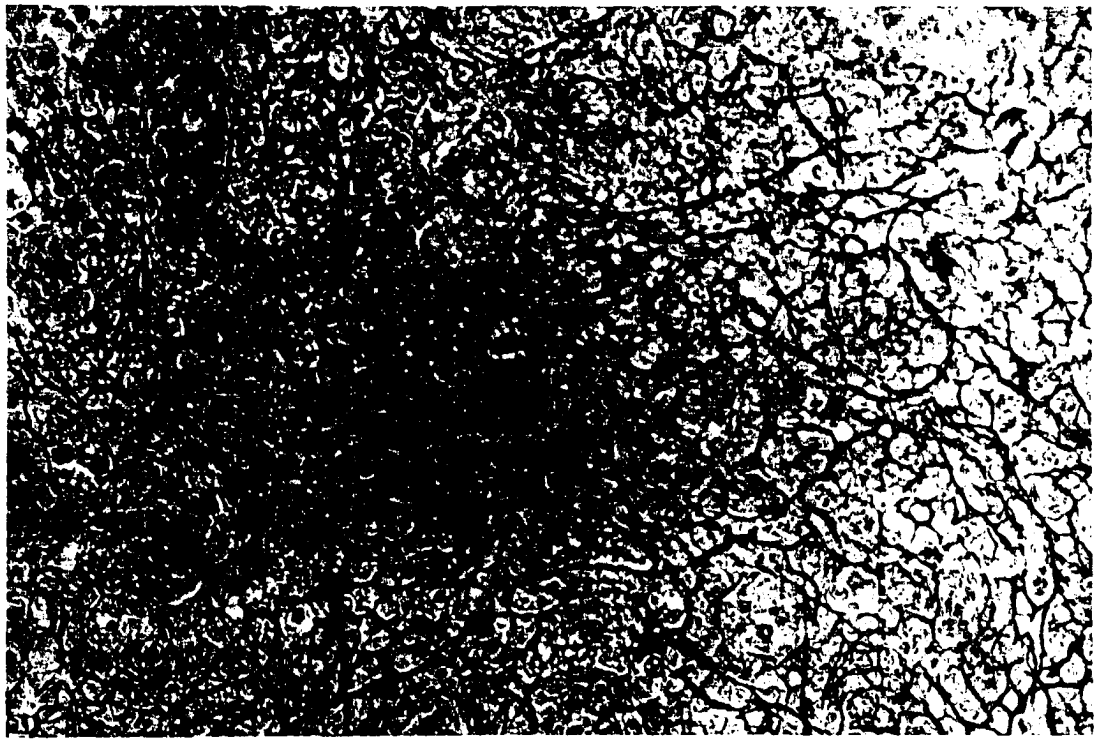

Fig. 12. Acute Monocytic Leukemia. Note the sinuses and the maze pattern of the reticular fibrils.

very fine fibrils extended from one coarse fibril to another. Between the delicately outlined, widely separated sinuses of the red pulp protoplasmic fibrils encircled almost every cell.

J.S. A 45 year old man was ill of chronic myelocytic leukemia for 2 years. Many short, coarse, reticular fibrils overran and masked the architecture of the few Malpighian bodies. Corpuscles were not recognized in the PAS-Hale stained sections. Many coarse and fine, black-stained fibrils, which seemed to be composed of granules arranged like a strand of beads, separated the cells of the red pulp into various sized groups. Very fine, argentophilic fibrils coursed so close together that the structures beneath were not visible in many small areas. Protoplasmic fibrils faintly demarcated a few sinuses, but in most of the section pink-stained fibrils continued between the cells.

F.M. This 55 year old man suffered from myelocytic leukemia for 2 years. Malpighian corpuscles were not identified in the silver and combined stained preparations. Subcapsular, reticular fibrils were broken into short, coarse strands. A maze of coarse, black-stained fibrils separated the cells of the red pulp into small groups. A few sinuses were delicately outlined by protoplasmic fibrils and many pink-stained fibrils separated the cells of the red pulp into small nests. The protoplasmic fibrils coursed close together in small areas and exhibited thickened, eosinophilic masses.

L.L. A few Malpighian corpuscles were seen in preparations of the spleen from a 79 year old man who suffered from leukemia for 5 years. Many coarse, frayed, reticular fibrils separated the cells of the corpuscles into small nests. A normal appearing, protoplasmic, fibrillary

pattern occurred in the Malpighian bodies. An occasional sinus was outlined by black-stained granules of reticulum. A maze of coarse, reticular fibrils separated the cells of the red pulp into small groups or partially encircled single cells. Beaded, delicate, protoplasmic fibrils delineated the sinuses in a normal manner.

G.K. This 73 year old man was ill of chronic myelocytic leukemia for 3 years. The decreased number of Malpighian bodies presented an almost normal pattern of reticular and protoplasmic fibrils. Fine and coarse, reticular fibrils separated the cells of the red pulp into large and small groups with a few cells being encircled individually. Very small areas of fine arborizations were not related to blood vessels. Now and then a well demarcated sinus was found. Between the faintly outlined, widely dispersed sinuses of the red pulp, a few protoplasmic fibrils coursed among the cells.

P.J.B. This 77 year old man suffered from myelocytic leukemia for 2 years. The slightly infiltrated Malpighian bodies were separated into many small compartments by coarse, reticular fibrils. The protoplasmic, fibrillary arrangement simulated that of normal corpuscles. Heavy, argyrophile fibrils, with finer ones running between them, occurred in some areas of the red pulp, but in other fields broken, delicate fibrils partially separated the cells into groups. Some of the well delineated sinuses presented a spiral configuration of the protoplasmic fibrils.

To summarize: In every section of chronic myelocytic leukemia there was a numerical reduction or total loss of Malpighian corpuscles. These corpuscles displayed a marked increase of reticular fibrils, which

in one instance were so heavy as to mask the architecture of the corpuscles. A normal appearing, protoplasmic, fibrillary pattern of the corpuscles occurred in some splenic preparations with no corpuscles found in other sections.

A marked variation of the red pulp was found in the preparations. These differences were not quite as conspicuous as those of chronic lymphocytic leukemia. Nearly every section demonstrated an increased amount of reticular fibrils which were quite coarse. An occasional sinus was delicately outlined by fibrils or granules of reticulum. A maze-like pattern of argentophilic fibrils separated the cells of the red pulp into various sized groups. Often nearly every cell was partially encircled in the whole section or in parts of a section. Extremely fine, reticular fibrils paralleled the coarser ones or crossed them. The reticular fibrils occasionally were frayed and in one instance were composed of many small granules. Between the delicately outlined sinuses protoplasmic fibrils often individually enclosed cells.

Monocytic Leukemia

Acute

The ages of the 17 patients, who had monocytic leukemia, ranged from 12 months to 86 years. Splenic weights varied from 50 gm. to 1440 gm. Germane information on the patients in this study who had monocytic leukemia can be found in Table VI.

There was great variation in the descriptions of the external surfaces of the spleens. This marked diversity was exemplified by the following: mottled milky, pale tan-red, light gray, grayish-purple,

TABLE VI

INFORMATION ON PATIENTS WITH ACUTE MONOCYTIC LEUKEMIA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
O.B.	62 yrs.	F	185 gm.	4 wks.
B.B.	33 yrs.	M	470 gm.	3 mos.
A.D.	43 yrs.	F	900 gm.	6 wks.
C.E.G.	71 yrs.	M	240 gm.	12 mos.
J.M.H.	66 yrs.	M	520 gm.	8 mos.
E.M.	47 yrs.	M	370 gm.	10 mos.
D.M.	76 yrs.	F	110 gm.	3 mos.
C.B.	42 yrs.	M	175 gm.	1 yr.
L.V.M.	11 yrs.	M	150 gm.	2 wks.
L.W.J.	33 yrs.	M	780 gm.	1 yr.
J.S.E.	12 mos.	M	50 gm.	7 wks.
E.P.H.	60 yrs.	M	200 gm.	7 mos.
K.A.R.	10 yrs.	M	500 gm.	9 mos.
C.W.	86 yrs.	M	260 gm.	3 mos.
G.R.B.	65 yrs.	M	370 gm.	6 mos.
E.T.	46 yrs.	M	1440 gm.	10 mos.
L.S.	13 yrs.	M	970 gm.	9 mos.

dirty gray, dark reddish-purple, light gray-green, bluish-purple or dirty grayish-brown. One spleen displayed gray-white flecks, while another contained pale, hard nodules. Some spleens were soft and diffluent while others were firm. The pulps were described as deep purple, dark reddish purple, deep red, chocolate brown, mottled purple and brown or dark red with contrasting lighter red. Malpighian corpuscles were indistinct, not discernible, quite small, faintly visible or not prominent. A markedly altered architectural pattern was found in 2 spleens, but it was intact in another spleen.

O.B. Some of the Malpighian bodies showed reaction centers in the histological sections of the spleen from this 62 year old woman who was ill of acute monocytic leukemia for 4 weeks. The reticular and protoplasmic fibrillary patterns resembled those of normal corpuscles. In some very normal appearing areas of the red pulp delicately outlined sinuses occurred between which were coarse, wavy, reticular fibrils in lattice formation. However, in many fields coarse fibrils, which had short branches attached at right angles, proceeded in a reasonably straight line. Many fine fibrils separated the cells into very small groups of 3 or 4 cells. Subcapsular fibrils coursed in every direction. The sinuses of the red pulp were delineated well by protoplasmic fibrils.

B.B. A diminished amount of lymphocytes were seen in the Malpighian bodies of the preparations of the spleen from a 33 year old man who suffered from leukemia for 3 months. Corpuscles were not found in the silver-stained section. The protoplasmic, fibrillary pattern resembled the normal arrangement. Between partially and completely delineated sinuses, scattered threads of reticulum coursed among the

cells. Subcapsular fibrils were scattered and broken. Widely separated sinuses were outlined faintly by protoplasmic fibrils.

A.D. A marked numerical decrease of Malpighian bodies was observed in the histological sections of spleen from this 43 year old woman who had monocytic leukemia for 6 weeks. An occasional reaction center was found in the corpuscles. Reticular fibrils were slightly increased in width, while the protoplasmic, fibrillary pattern of the corpuscles resembled the normal arrangement. Beneath the capsule a few coarse, argentophilic fibrils continued perpendicular to the capsule. A small number of sinuses in the red pulp were outlined very delicately by reticular fibrils. Fine, argyrophile fibrils and a few coarse ones occurred in the red pulp, but there were not enough to form a clear pattern. Some fields were almost devoid of reticular fibrils. Coarse and fine arborizations circumscribed the small vessels. Protoplasmic fibrils delicately delineated the sinuses of the red pulp.

C.E.G. A 71 year old man suffered from monocytic leukemia for 12 months. The reticular and protoplasmic fibrillary arrangement of the Malpighian corpuscles appeared normal with the exception of a few large corpuscles which contained a moderate increase of thick protoplasmic fibrils. Coarse reticular fibrils occurred between the well delineated sinuses of the red pulp. Very fine arborizations were found around the small vessels. Peculiar round formations of diminishing, concentric circles of reticular fibrils had radiating fine threads separating the cells. Protoplasmic fibrils nicely demarcated the sinuses of the red pulp.

J.M.H. Malpighian bodies were numerically diminished in the

microsconic sections of spleen from a 66 year old man who was afflicted with leukemia for 8 months. Coarse, argentophilic fibrils occurred in the central portions of the corpuscles and were accentuated in the peripheries. However, a few had a normal appearance. The pattern of the protoplasmic fibrils resembled that of normal corpuscles. In the red pulp and subcapsular tissue, a normal amount of sinuses were outlined by granules and delicate fibrils of reticulum. Many coarse, argentophilic fibrils arranged in a maze-like pattern separated the cells of the red pulp into various sized nests (Fig. 12). Very fine threads in many areas crossed the cells and partially masked the architectural pattern. Fine arborizations surrounded small blood vessels. The well delineated sinuses of the red pulp occasionally demonstrated a spiral configuration of the protoplasmic fibrils. In a few areas the cells between the sinuses were individually enclosed by pink-stained fibrils.

E.M. The small Malpighian corpuscles were extensively infiltrated with leukemic cells in the preparations of the spleen from this 47 year old man who was ill of leukemia for 10 months. Heavy, reticular fibrils divided the corpuscles into long narrow nests. Numerically increased, thickened protoplasmic fibrils occurred throughout the corpuscles. Many fine, frayed, argentophilic fibrils separated the cells of the red pulp between the delicately demarcated sinuses into small nests. Often individual cells were surrounded. In the combined stained sections the sinuses were outlined delicately by beaded protoplasmic fibrils.

D.M. Malpighian corpuscles, which were slightly infiltrated by leukemic cells, were found in the microscopic sections of spleen from

a 76 year old man who had monocytic leukemia for 3 months. Increased, thickened, reticular and protoplasmic fibrils traversed the corpuscles (Fig. 13). Between the many well outlined sinuses coarse and fine argentophilic fibrils separated the cells of the red pulp into small groups with individual cells being encircled. A few configurations of concentric circles occurred in which divergent fibrils separated the cells (Fig. 14). Protoplasmic fibrils outlined the sinuses of the red pulp in a normal manner.

C.B. A 42 year old man was afflicted with leukemia for 1 year. The numerically decreased Malpighian bodies were infiltrated by leukemic cells. A moderate increase of coarse, reticular fibrils partially divided the corpuscles into compartments, while thickened, protoplasmic fibrils separated almost all the cells. Fine, discontinuous, argentophilic fibrils were found between the few sinuses of the red pulp. In a very normal red pulp sinuses were demarcated by protoplasmic fibrils.

L.V.M. This 11 year old boy was stricken with monocytic leukemia 2 weeks before his death. A normal reticular pattern was observed in some Malpighian corpuscles but others were partially divided into compartments by coarse fibrils. In the combined stained sections a band of thick, protoplasmic fibrils divided the corpuscle into inner and outer portions, neither of which produced pink-stained fibrils. Between the delicately outlined sinuses of the red pulp occurred coarse and fine, argentophilic fibrils. Small areas of extremely fine, latticed fibrils were occasionally seen. Protoplasmic fibrils, which outlined the sinuses, were often arranged in spiral formations. Pink-stained fibrils surrounded each cell in various areas.

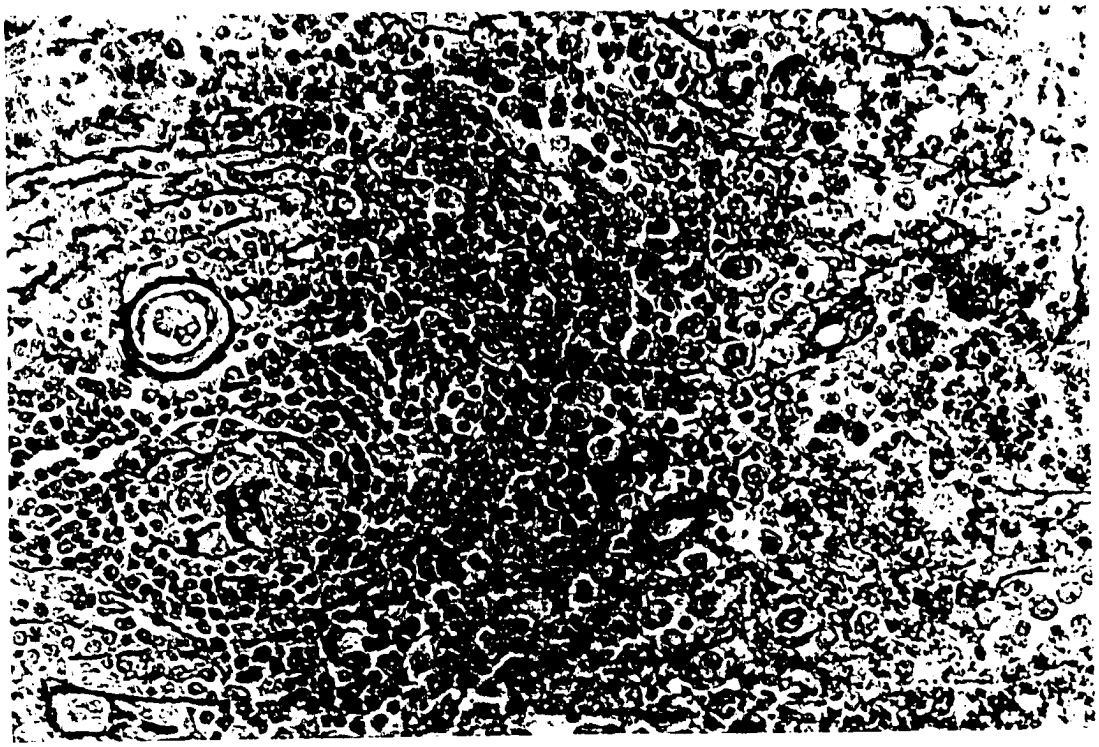

Fig. 13. Acute Monocytic Leukemia. Observe the numerically increased reticular fibrils in the Malpighian corpuscle.

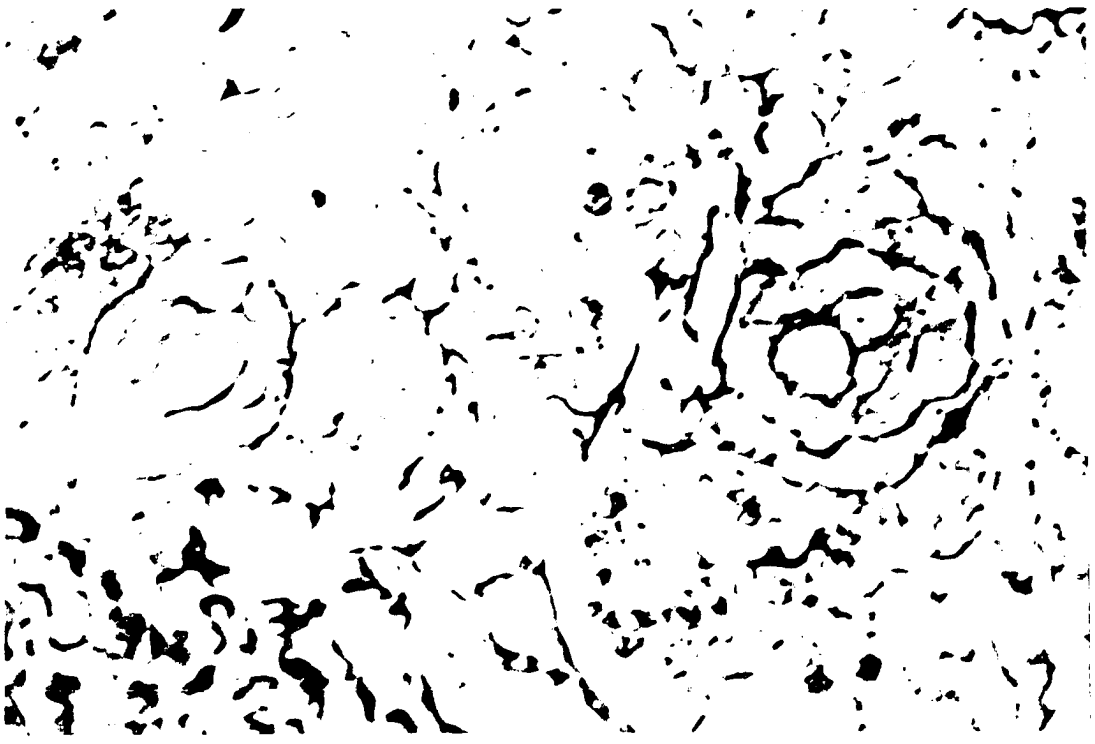

Fig. 14. Acute Monocytic Leukemia. Notice the round bodies which were found in the red pulp.

L.W.J. A few Malpighian corpuscles were noted in the preparations of the spleen from a 33 year old man who was ill of leukemia for 1 year. A very marked increase of coarse fibrils partially masked the corpuscular structure, while other corpuscles simulated the normal arrangement. A slight increase of protoplasmic fibrils was seen in the peripheries of the bodies. Beneath the capsule fine fibrils separated the cells into small groups (Fig. 15). Between the nicely outlined sinuses of the red pulp, fine, reticular fibrils separated the cells into small nests. Beaded protoplasmic fibrils faintly delineated the widely separated sinuses.

J.S.E. This 1 year old boy suffered from acute monocytic leukemia for 7 weeks. A normal amount of protoplasmic and reticular fibrils, which barely outlined the bodies, occurred in the Malpighian corpuscles. A very few delicately outlined sinuses were seen. In some areas coarse, reticular fibrils separated the cells of the red pulp into small and medium sized groups, while scattered, broken fibrils occurred in other areas. Small vessels were enclosed by very fine arborizations. Areas of the red pulp, in which sinuses were nicely delineated by protoplasmic fibrils, were intermingled with fields that manifested only a few shreds of pink-stained fibrils.

E.P.H. A 60 year old man was afflicted with monocytic leukemia for 7 months. Numerous broken, reticular fibrils in the central portions of the corpuscles increased considerably at the peripheries. A few reticular fibrils were found in other corpuscles. Occasionally a few protoplasmic fibrils occurred in Malpighian bodies, but most of them had none. A few reticular fibrils were found beneath the capsule. Between

Fig. 15. Acute Monocytic Leukemia. Note the reticular fibrils which separate the subcapsular cells into small nests.

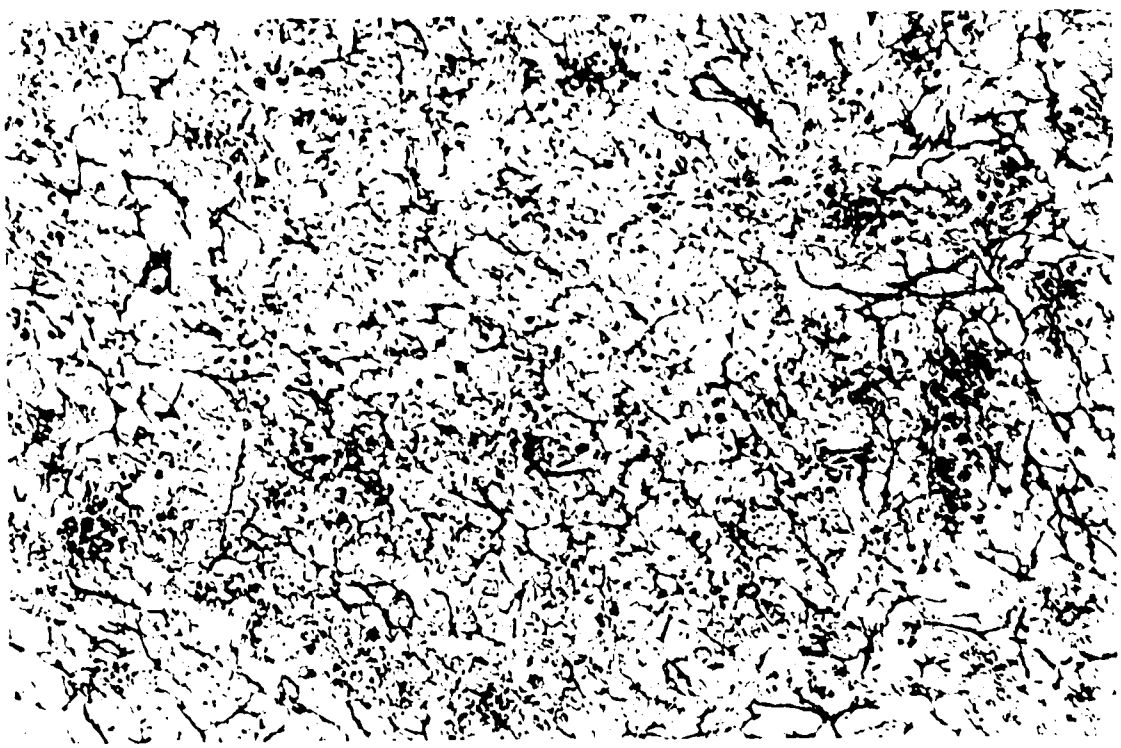

Fig. 16. Acute Monocytic Leukemia. Observe the maze-like arrangement of the reticular fibrils of the red pulp.

the delicately outlined sinuses of the red pulp very coarse, argentophilic fibrils separated the cells into small groups. In certain areas the reticular fibrils were composed of numerous granules and seemed to be disintegrating, while large areas had only a few shreds of reticulum. The protoplasmic fibrils of the red pulp were normal in arrangement.

K.A.R. In the preparations of the spleen from this 10 year old boy who was ill of leukemia for 9 months, the numerically diminished Malpighian bodies had been chiefly replaced by leukemic cells. Many coarse, argyrophile fibrils enclosed nearly every cell of the corpuscles in diamond-shaped compartments, while a slight increase of thickened, protoplasmic fibrils occurred in the peripheries of the corpuscles. Many coarse, broken, reticular fibrils partially separated the cells of the red pulp into medium sized groups. An occasional sinus was delicately outlined. Beneath the capsule many coarse, reticular fibrils surrounded single cells or separated them into small groups. Protoplasmic fibrils demarcated the sinuses of the red pulp in a very normal manner.

C.W. This 86 year old man was stricken with monocytic leukemia 3 months before his death. A normal reticular pattern was found in a few Malpighian corpuscles, but in others many coarse fibrils separated almost every cell. The protoplasmic fibrillary pattern resembled that of a normal corpuscle. The sinuses of the red pulp were nicely outlined. Many very coarse and some fine, reticular fibrils passed between and often encircled every cell. Very fine arborizations circumscribed small vessels and occasionally seemed to be around a few cells. Sinuses of the red pulp appeared to be demarcated normally by protoplasmic fibrils.

G.R.B. A 65 year old man was afflicted with leukemia for 6 months. A normal arrangement of reticular and protoplasmic fibrils occurred within the corpuscles. In the red pulp and beneath the capsule coarse, reticular fibrils were insufficient to form a pattern. The protoplasmic fibrils closely simulated the reticular fibrillary pattern.

E.T. Very few Malpighian corpuscles were noted in the preparations of the spleen from this 46 year old man who was ill of leukemia for 10 months. Many coarse, reticular and protoplasmic fibrils divided the bodies into small nests of cells. Numerous coarse, argentophilic fibrils in maze formation separated the cells of the red pulp and subcapsular tissue into small groups (Fig. 16). The protoplasmic fibrils faintly outlined sinuses.

L.S. A 13 year old boy was afflicted with leukemia for 9 months before his death. Malpighian corpuscles were divided into long diamond-shaped compartments by coarse, argyrophile fibrils while the protoplasmic fibrillary arrangement resembled that of normal corpuscles. Between widely separated, delicately outlined sinuses, coarse, reticular fibrils in maze configuration partially separated the cells of the red pulp into small groups. The protoplasmic fibrils clearly delineated the sinuses in a normal manner.

In summary: In approximately half of the cases of monocytic leukemia Malpighian corpuscles were numerically reduced or not recognized. More than half of the splenic preparations manifested a marked increase of coarse, reticular fibrils which divided the corpuscles into small groups of cells. The majority of the sections displayed a fairly normal amount and arrangement of protoplasmic fibrils, but some presented

an increase of thickened fibrils.

Reticular fibrils of the red pulp in nearly half of the sections were normal in amount and arrangement; however, some variation from the normal occurred. Nearly every cell was surrounded by argentophilic fibrils in some areas, but not many sinuses were found. Reticular fibrils varied greatly from coarse to fine and from sharply demarcated to frayed. Some peculiar, round formations consisted of concentric circles of coarse, reticular fibrils and fine divergent threads which separated every cell in the configuration. A maze-like arrangement of coarse, argyrophile fibrils occurred in other microscopic sections. A very normal arrangement of the protoplasmic fibrils occurred in these splenic preparations. Between the numerically decreased sinuses every cell was surrounded by protoplasmic fibrils. A maze-like pattern of the protoplasmic fibrils occurred in the histological sections of one spleen.

Related Diseases

Lymphosarcoma

The ages of patients with lymphosarcoma ranged from 16 months to 77 years. The weight of the smallest spleen was 150 gm. while the largest weighed 480 gm. Relevant information about the patients in this study who died of lymphosarcoma may be found in Table VII.

The external surfaces of these spleens were described as purple or reddish-purple. Two spleens were firm and 3 were diffluent. The pulps were described as red with white dots, light reddish-brown with a grayish infiltration, dark purple, dark red, reddish-purple, or pale with mottled dark areas. Malpighian corpuscles were evident, not seen, or hardly visible.

TABLE VII

INFORMATION ON PATIENTS WITH LYMPHOSARCOMA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
W.F.M.	72 yrs.	M	390 gm.	3 yrs.
M.D.P.	16 mos.	M	480 gm.	3 mos.
E.W.	76 yrs.	F	150 gm.	2 mos.
L.J.	46 yrs.	F	310 gm.	5 mos.
T.R.P.	55 yrs.	M	300 gm.	6 mos.
A.D.C.	16 yrs.	F	150 gm.	7 mos.
F.G.	56 yrs.	M	350 gm.	1 yr.
E.O.V.	77 yrs.	M	180 gm.	6 mos.
E.J.	71 yrs.	M	460 gm.	4 mos.

W.F.M. Small Malpighian bodies were found in the preparations of the spleen from this 72 year old man who suffered from lymphosarcoma for 3 years. A normal arrangement of reticular fibrils occurred in the small corpuscles. The central portion of the larger corpuscles were divided into medium sized groups of cells by coarse, argentophilic fibrils, while the peripheral cells were separated into small nests by frayed, coarse fibrils or were individually enclosed by fine fibrils. Thickened, protoplasmic fibrils occurred around the follicular arteries but the remainder of the corpuscular cells were separated into groups by delicate pink fibrils. Between the well demarcated sinuses of the subcapsular and deeper red pulp coarse, reticular fibrils separated the cells into very small lobules. The protoplasmic fibrils of the red pulp were arranged in a normal manner.

M.D.P. This 16 month old boy was ill of lymphosarcoma for 3 months. Dense reticular fibrils or extremely short, coarse, parallel fibrils divided the Malpighian corpuscles into small nests of cells with the periphery being divided into long, diamond-shaped compartments. Thick, protoplasmic fibrils divided the corpuscles into medium sized groups of cells. Coarse and fine, argentophilic fibrils coursed at random through the subcapsular and red pulp, and separated the cells into very small and large groups. In some areas of the red pulp protoplasmic fibrils outlined sinuses, but in other areas every cell was surrounded by pink-stained fibrils.

E.W. A 76 year old man was afflicted with lymphosarcoma for 2 months. A marked increase of coarse, reticular fibrils separated the cells of the Malpighian bodies into small groups, while the protoplasmic

fibrils of the bodies were thickened and increased in amount. The subcapsular and deeper red pulp appeared very normal with well outlined sinuses and fine to coarse, reticular fibrils which separated the cells into small groups. Protoplasmic fibrils also resembled the normal arrangement. The capsule was markedly involved by the tumor. Reticular fibrils separated cells and occasionally formed Malpighian corpuscle-like structure (Fig. 17).

L.J. This 46 year old woman was stricken by lymphosarcoma 5 months before her death. The reticular and protoplasmic fibrils were slightly thickened, but otherwise resembled the arrangements in normal corpuscles. Broken, coarse, argentophilic fibrils were scattered through the subcapsular tissue and red pulp, but were insufficient to form a pattern. Protoplasmic fibrils delicately outlined a few sinuses, but the short fibrils closely resembled the arrangement of the reticular fibrils.

T.R.P. This 55 year old man endured lymphosarcoma for 6 months. The reticular fibrils in the Malpighian bodies appeared to have a normal arrangement, but many protoplasmic fibrils separated the cells of the corpuscles into extremely small nests. Between the delicately outlined sinuses of the subcapsular tissue and red pulp, fine, wavy argentophilic fibrils separated the cells into various sized groups. Some fibrils were extremely fine and lay close together or surrounded individual cells. Protoplasmic fibrils simulated the normal arrangement in most of the red pulp, but in a few areas every cell was surrounded by pink-stained fibrils.

A.D.C. This 16 year old girl suffered from lymphosarcoma for

Fig. 17. Lymphosarcoma. Notice the reticular fibrils which are arranged in a corpuscle-like formation.

Fig. 18. Reticulum Cell Sarcoma. Note the marked increase of fine and coarse reticular fibrils.

7 months. Fine, frayed, broken, reticular fibrils occurred in the Malpighian corpuscles, but there was a marked increase of thick, protoplasmic fibrils which divided the corpuscle into very small compartments. Coarse and fine, reticular fibrils ran unrestrainedly through the red pulp and partially enclosed large groups of cells. In some areas there were only a few reticular fibrils or an occasional sinus. Protoplasmic fibrils nicely delineated the sinuses of the red pulp.

F.G. A few Malpighian corpuscles were found in the preparations of the spleen from a 56 year old man who suffered from lymphosarcoma for 1 year. Broad, black bands and coarse, reticular fibrils partially separated the cells of the corpuscle into medium sized groups. Very coarse fibrils in the periphery of the corpuscles surrounded nearly every cell. Many argentophilic fibrils at the periphery of other corpuscles separated the cells into long, narrow compartments. Protoplasmic fibrils were not seen in the central portion of the bodies, but there was an increased number of fibrils at the periphery. The reticular fibrillary pattern of the red pulp appeared very normal with sinuses nicely outlined. Between these sinuses coarse, argentophilic fibrils coursed among the cells. The protoplasmic fibrils were arranged very much like those of a normal red pulp.

E.O.V. A 77 year old man was afflicted with lymphosarcoma for 6 months. Coarse, argyrophile fibrils were scattered in the central portion of Malpighian bodies, while in the periphery many fibrils enclosed nearly every cell. The protoplasmic fibrillar arrangement of the corpuscles was very much like that of the reticular fibrils. Coarse, argentophilic fibrils occurred between the well outlined sinuses of the

red pulp. Sinuses were delineated well by protoplasmic fibrils and in some fields nearly every cell was encircled by pink-stained fibrils.

E.J. A 71 year old man who was stricken by lymphosarcoma 4 months before his death. There was a slight increase of coarse, reticular fibrils around vessels of the corpuscles and at the periphery of the bodies, while the protoplasmic fibrils were of normal appearance. Broken, frayed, argentophilic fibrils outlined sinuses and partially separated cells into small groups in the subcapsular tissue and red pulp. Delicate fibrils and granules of protoplasmic material outlined the sinuses of the red pulp.

To summarize: A decreased number of Malpighian corpuscles were observed in one-third of the spleens from patients with lymphosarcoma. In the majority of the spleens coarse, reticular fibrils divided the corpuscles into various sized groups of cells. Thickened protoplasmic fibrils were found in the corpuscles in most of the sections.

The red pulps of most of these sections were normal in appearance, with coarse argentophilic fibrils occurring between the well outlined sinuses. In one spleen broken, coarse, scattered, reticular fibrils without pattern formation were found. Coarse, argyrophile fibrils throughout the red pulp of another spleen separated the cells into varying sized and shaped groups. A normal sinus pattern of protoplasmic fibrils occurred in some areas, while in others pink fibrils enclosed every cell.

Reticulum Cell Sarcoma

The ages of the 3 patients with reticulum cell sarcoma were

34, 63, and 81 years respectively. The organs were not large and the only spleen which might be increased in size weighed 340 gm. Pertinent information concerning the patients in this study who had a reticulum cell sarcoma can be obtained from Table VIII.

The capsular surfaces of the spleens were described as blue-gray or dark reddish-brown. The prosector noted only irregular grayish areas on the surface of the third spleen. All 3 spleens were diffluent with a brown or brownish-red pulp. One spleen showed metastatic nodules measuring 6 to 8 mm. in diameter. No Malpighian corpuscles were discernible.

B.K. Small Malpighian corpuscles were found in the preparations of the spleen from a 34 year old man who was ill of reticulum cell sarcoma for 20 months. The pattern of reticular and protoplasmic fibrils closely resembled those of normal corpuscles. Coarse, reticular fibrils outlined smaller sinuses than are usually seen in spleens. The protoplasmic fibrils of the non-tumorous portion of the red pulp were almost identical to those of normal spleens. In the tumor nodules many frayed, reticular fibrils coursed close together and often crossed cells, but they did not appear to come from or run through the cells (Fig. 18). The greater portion of the cells were individually separated, while a dense network separated the remaining cells into small groups. Many fine and some coarse, protoplasmic fibrils were arranged in a pattern which simulated that of the silver-impregnated fibrils.

C.D. A 63 year old man suffered from reticulum cell sarcoma for 1 year. Malpighian corpuscles seemed unaffected and very closely resembled the normal for the age as to reticular and protoplasmic fibrils.

TABLE VIII

INFORMATION ON PATIENTS WITH RETICULUM CELL SARCOMA IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
B.K.	54 yrs.	M	320 gm.	20 mos.
C.D.	63 yrs.	M	100 gm.	1 yr.
M.L.B.	81 yrs.	M	60 gm.	10 mos.

The remaining red pulp also manifested a normal protoplasmic and reticular fibrillary pattern. The tumor in this section was not nodular but was more diffuse and arranged in many small masses. A very fine network of reticular fibrils separated almost every tumor cell from the others. In some areas of the combined stained preparations there were no protoplasmic fibrils while in other areas tumor nests were delicately outlined by pink-stained fibrils. In this spleen the reticular pattern definitely did not follow the arrangement of the protoplasmic fibrils in the tumor.

M.L.B. An 81 year old man was afflicted with lymphosarcoma for 10 months. There were vessels which might be follicular arteries, but they had no surrounding lymphocytes. Delicately outlined sinuses were immediately adjacent to the follicular arteries. A normal spleen had a similar reticular fibrillary arrangement. The protoplasmic pattern also resembled that of a normal spleen. In the tumor many fine thread-like reticular fibrils continued close together and crossed cells, but in other areas the tumor cells were separated into nests by a coarse network of wavy and frayed fibrils. The arrangement of the protoplasmic fibrils in the tumor closely resembled that of the reticular fibrils. In many instances these tumor nests were approximately the size of the splenic sinuses.

To summarize: The non-tumorous portion of the spleens in reticulum cell sarcoma manifested a normal protoplasmic and reticular fibrillary arrangement. In the tumors many frayed, argentophilic fibrils coursed close together and crossed cells. The protoplasmic fibrillary pattern simulated the reticular fibrillary pattern.

Hodgkin's Disease

All the cases of Hodgkin's disease in this study were 47 years of age or older. Spleens ranged in weight from 150 to 600 gm. Relevant information on the patients in this study who died of Hodgkin's disease may be found in Table IX.

The capsular surfaces were described as bluish-gray-red, gray-white, reddish-blue, grayish-blue, or dark reddish-purple. Three spleens were diffluent and another was firm. Malpighian corpuscles were very prominent, not evident, or of average size. In 2 spleens there was complete loss of architectural pattern.

E.W. Malpighian corpuscles were not recognized in the preparations of the spleen from a 56 year old woman who suffered from Hodgkin's disease for 8 months. In the Hodgkin's nodules numerous coarse, frayed, reticular fibrils were arranged in a fine-meshed maze, and partially surrounded small groups or individual cells. A few delicate, protoplasmic fibrils were found at the periphery of the nodules. There were structures in which many thickened, pink-stained fibrils separated cells into small nests much like the arrangement of the abnormal Malpighian bodies of leukemic spleens. The reticular and protoplasmic fibrils closely resembled the arrangements found in normal red pulps.

R.L.C. A few Malpighian corpuscles were noted in the histological sections of spleen from a 55 year old man who was ill of Hodgkin's disease for 4 years. A decrease of lymphocytes was observed in the Malpighian corpuscles. The protoplasmic and reticular fibrillary arrangement in the corpuscles appeared much like that of the normal

TABLE IX

INFORMATION ON PATIENTS WITH HODGKIN'S DISEASE IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
E.W.	56 yrs.	F	550 gm.	8 mos.
R.L.C.	55 yrs.	M	240 gm.	4 yrs.
E.R.	48 yrs.	M	580 gm.	10 mos.
H.L.C.	70 yrs.	M	150 gm.	3 mos.
T.W.K.	56 yrs.	M	190 gm.	6 mos.
G.D.G.	47 yrs.	M	600 gm.	2 yrs.

corpuscles. Coarse and fine, broken, argentophilic fibrils partially separated the cells of the red pulp and the subcapsular tissue into groups of cells, but in some fields there were practically no fibrils. Occasionally, fine threads coursed very close together. A very normal, protoplasmic fibrillary arrangement with some spiral formations occurred in the red pulp.

E.R. A 48 year old man was afflicted with Hodgkin's disease for 10 months. The architecture of this section was almost destroyed, and only a few Malpighian bodies were seen. In Gomori's silver-stained, and the PAS-Hale stained preparations, it was impossible to differentiate corpuscles from Hodgkin's nodules. Consequently, they will be described together. Many coarse, frayed, reticular fibrils formed a fine-meshed maze which partially enclosed small groups of 2 or 3 cells (Fig. 19). Immediately around the vessels the argentophilic fibrils were extremely coarse and close together. A slight increase of delicate, protoplasmic fibrils coursed through the nodules. A normal arrangement of reticular and protoplasmic fibrils occurred in the red pulp with the exception of a few areas in which the cells were individually encircled.

H.L.C. A few small Malpighian corpuscles were found in the preparations from the spleen of a 70 year old man who was a victim of Hodgkin's disease for 3 months. Many coarse, reticular fibrils throughout the bodies aligned the cells in rows at the periphery. In the PAS-Hale stained sections Malpighian corpuscles and Hodgkin's nodules were very much alike. Centrally there were thick protoplasmic fibrils with focally widened areas, while delicate fibrils surrounded every cell in the periphery. Many coarse, broken, argentophilic fibrils and short,

Fig. 19. Hodgkin's Disease. Note the marked increase of fibrils in the nodule and the normal appearing adjacent sinus.

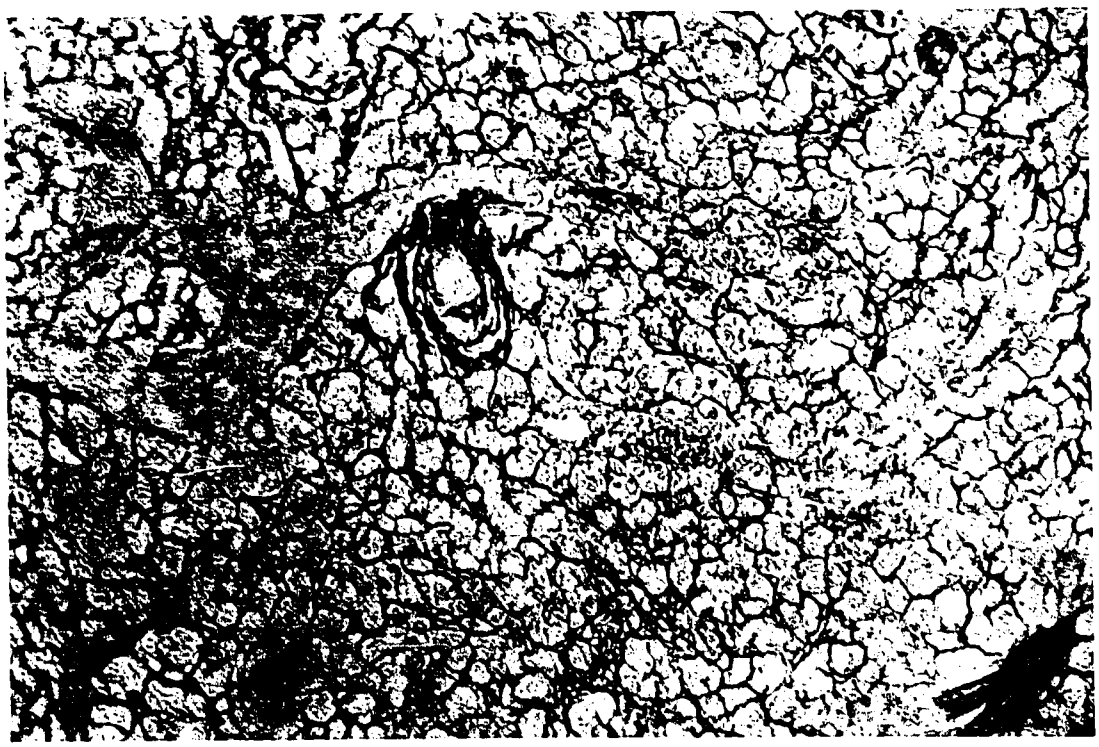

Fig. 20. Congenital Leukemia. Notice the marked increase of reticular fibrils between the sinuses.

black-stained bands were interspersed throughout the Hodgkin's nodules. Very fine fibrils encircled every cell in the periphery of the nodules. The reticular pattern of the red pulp could not be differentiated from the Hodgkin's nodules for they seemed to merge imperceptibly. In the combined stained sections widely separated sinuses were well outlined by protoplasmic fibrils. Nearly all of the pulp cells were individually surrounded by thickened, pink-stained fibrils.

T.W.K. A 56 year old man was ill of Hodgkin's disease for 6 months. A normal reticular and protoplasmic fibrillary arrangement occurred in the Malpighian corpuscles. Only one Hodgkin's nodule was recognized in which wide, frayed and broken, reticular fibrils formed a maze. There were small eosinophilic masses and protoplasmic fibrils in the central portion of the Hodgkin's nodule. A very normal protoplasmic and reticular fibrillary pattern was found in the remaining red pulp.

G.D.G. The architecture of the spleen was destroyed and Malpighian corpuscles were not found in the histological sections of spleen from this 47 year old man who was afflicted with Hodgkin's disease for 2 years. Frayed, reticular fibrils divided the Hodgkin's nodules into small nests of cells. Occasionally, threads were so fine and so close together that the area appeared gray. Many delicate and some very wide protoplasmic fibrils divided the nodules into small nests of cells. The protoplasmic and reticular fibrillary arrangements in the red pulp closely resembled those of normal spleens.

In summary: Marked variation appeared in the Hodgkin's nodules. A marked increase of reticular fibrils were coarse and frayed, forming a fine mesh; or fine, argentophilic fibrils were very close

together; or coarse, short, wide bands of reticulum were interspersed with coarse, broken fibrils. The protoplasmic fibrils showed almost as much variation as the reticular fibrils. Nodules demonstrated only delicate pink threads at the periphery, increased thickened fibrils, or heavy protoplasmic fibrils forming large meshes in the central portion and changing to fine meshes at the periphery.

In a few sections Malpighian corpuscles were not found. Reticular and protoplasmic fibrils resembled those of normal corpuscles or they were thickened and numerically increased.

The architectural pattern in the hematoxylin-eosin stained sections seemed totally destroyed, but the reticular and protoplasmic fibrillar patterns resembled those of normal spleens.

Miscellaneous Group

This miscellaneous group consists of myelofibrosis, very acute, unclassified leukemia, and giant follicle lymphoma. Ages ranged from 9 days to 61 years. Splenic weights varied from 50 gm. to 2565 gm. Germane information concerning the patients of this miscellaneous group may be obtained from Table X.

The capsular surfaces of these spleens were described as light reddish-purple, dark red, purplish-blue, or mottled reddish-purple. Two organs were soft and the others were firm. The pulps were described as dark red, light brown, deep purple-red, or dark reddish-brown. Malpighian corpuscles were not identified, distinct, small, or not prominent. It was noted that one spleen had rather good retention of the architectural pattern.

L.W. Malpighian corpuscles were not recognized in the

TABLE X

INFORMATION ON PATIENTS WITH MISCELLANEOUS DISEASES IN THIS STUDY

Patient	Age	Sex	Weight of Spleen	Duration of Disease
L.W.	9 da.	F	50 gm.	9 da.
R.D.	14 yrs.	M	520 gm.	3 mos.
D.P.	56 yrs.	M	2565 gm.	2 yrs.
D.W.	59 yrs.	F	850 gm.	8 mos.
G.W.	61 yrs.	M	350 gm.	5 mos.

preparations of spleen from this 9 day old girl who had congenital, acute leukemia. However, protoplasmic and reticular fibrillary arrangements about follicular arteries were very much like those of Malpighian bodies. Coarse and fine reticular fibrils separated the cells into small nests or enclosed each cell. Coarse, protoplasmic fibrils occurred between every cell in these structures. Subcapsular reticular fibrils coursed perpendicular to the capsule and separated the cells into small groups. Fine argentophilic fibrils outlined sinuses and separated pulp cells into small nests or encircled single cells (Fig. 20). The protoplasmic fibrils delineated sinuses and often enclosed individual cells.

R.D. A 14 year old boy was ill of acute blastic leukemia for 3 months. A moderate increase of reticular fibrils occurred in the central portions of the corpuscles with several fine strands of fibrils in the peripheries. The arrangement of the corpuscular, protoplasmic fibrils appeared to be normal. In some areas of the red pulp reticular fibrils appeared normal in arrangement, but they were sparse in other areas (Fig. 21). Beneath the capsule coarse fibrils separated the cells into small nests. The protoplasmic fibrils simulated the normal arrangement.

D.P. This 56 year old man suffered from myelofibrosis for 2 years. Corpuscle-like structures demonstrated very broad bands of black-stained material, which was probably connective tissue. In a few of these structures coarse frayed, reticular fibrils separated the cells into small nests. Coarse, protoplasmic fibrils divided the central portion of these structures into nests of cells while the peripheral cells were individually separated. Between the well delineated sinuses

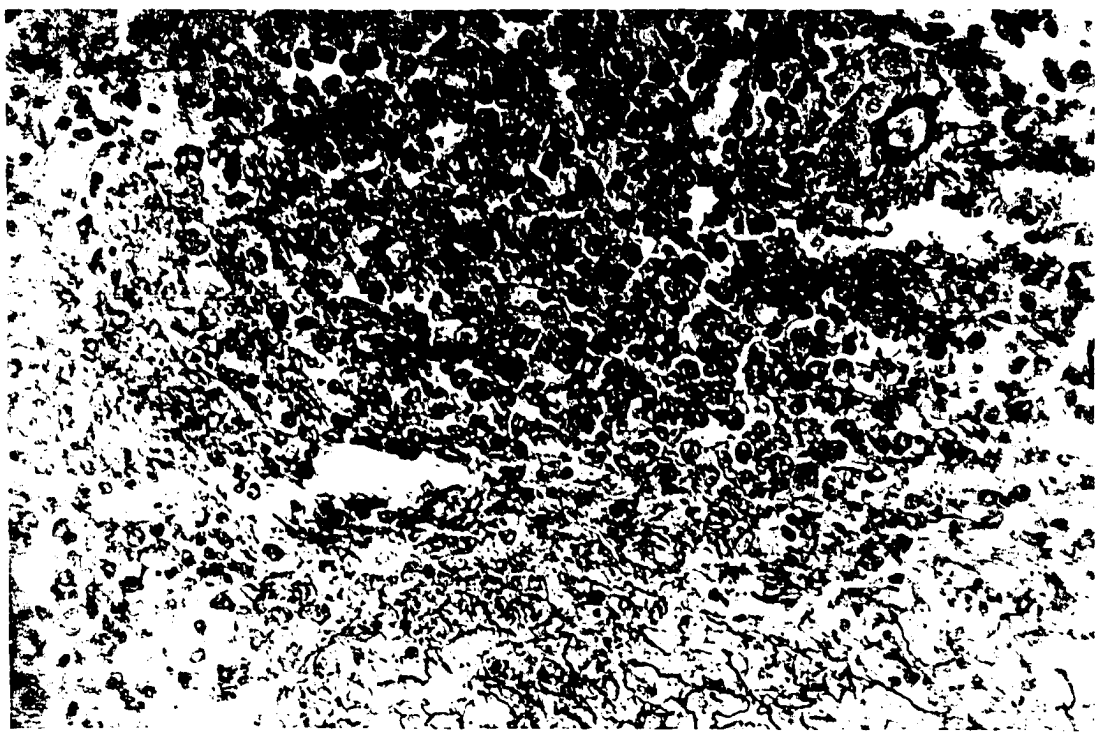

Fig. 21. Acute Blastic Leukemia. Observe the variation in arrangement of the reticular fibrils of the red pulp.

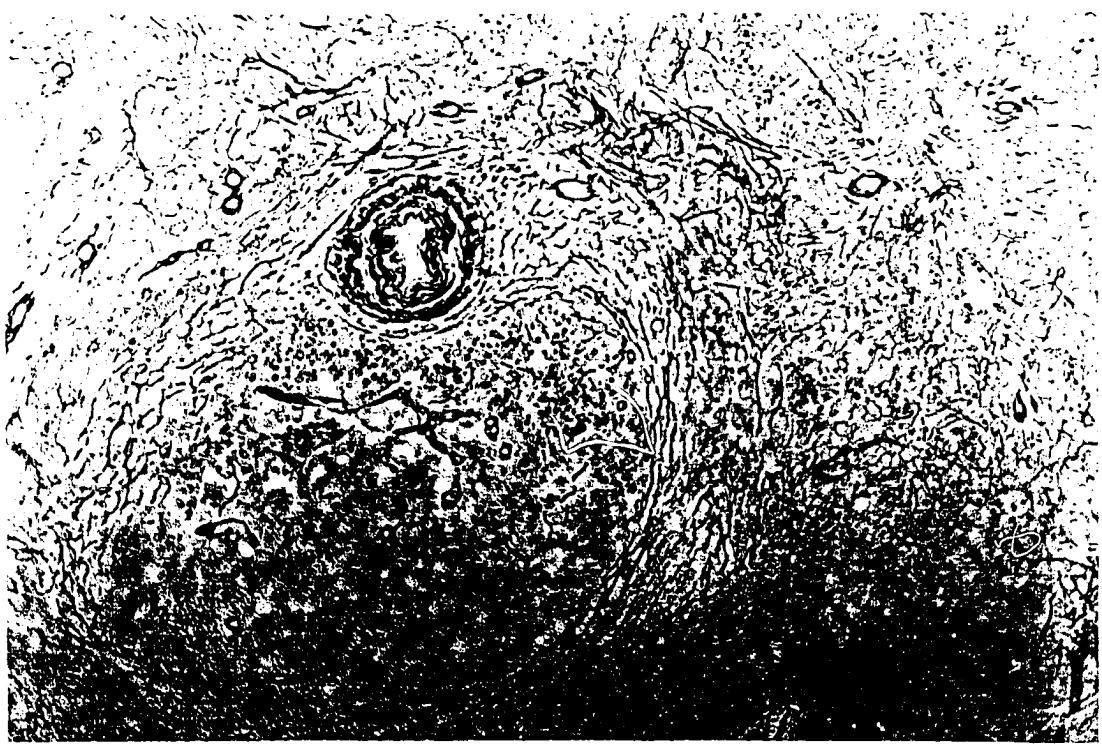

Fig. 22. Giant Follicle Lymphoma. Note the resemblance of this giant follicle to a normal Malpighian body with a reaction center.

of the red pulp, coarse and fine divergent reticular fibrils separated the cells into very large and very small groups. Protoplasmic fibrils outlined sinuses in some areas, but in other areas pink-stained fibrils were not found. In occasional areas every cell was encircled by protoplasmic fibrils.

D.W. Small corpuscles were found in the preparations of spleen from this 59 year old man who was afflicted with myelofibrosis for 8 months. An increased amount of coarse, reticular fibrils traversed the Malpighian bodies. A numerical increase of thickened, protoplasmic fibrils divided the corpuscle into small groups of cells. Many coarse, frayed, argentophilic fibrils formed a fine-meshed maze which encircled small groups or individual cells. Protoplasmic fibrils were not found in some areas of the red pulp; but in other areas there were no protoplasmic fibrils; in still other areas sinuses were faintly outlined. Fine protoplasmic threads coursed between these sinuses.

G.W. Enlarged Malpighian bodies were observed in the preparations of the spleen from a 61 year old man who was afflicted with giant follicular lymphoma for 5 months. Several short, wide bands of black-stained material and a few shreds of reticular fibrils occurred in the central portions of the corpuscles, but an increased number of fibrils occurred in the peripheries. These corpuscles were like very large reaction centers (Fig. 22). In the PAS-Hale stained sections the thickened, protoplasmic fibrils were increased in the peripheries of the corpuscles. Sinuses were outlined delicately by argentophilic fibrils. Coarse, reticular fibrils separated the cells of the red pulp into small nests, or individual cells were surrounded. The protoplasmic fibrils nicely outlined the sinuses of the red pulp.

CHAPTER VI

DISCUSSION

The great difference between the arrangement of reticular and protoplasmic fibrils in many of the spleens clearly indicated that not all the fibrils, which were found in spleens, were argentophilic fibrils. The finding of a normal pattern of protoplasmic fibrils would point to a retention of the original pattern or possibly an ability of abnormal reticulum cells still to form a normal type of protoplasmic fibrils. However, in a few preparations of the spleen the deviation in arrangement of the protoplasmic fibrils from that of normal red pulps denoted an additional loss of function of these abnormal reticulum cells. The finding of fibrils in the spleen, which were not impregnated with silver salts but which were stained pink by the PAS-Hale stain, in the sections was puzzling. Foot (1927a) observed this occurrence in normal spleens, therefore it was not a result of disease. Were the fibrils in different stages of development, or was the chemical structure in some way responsible for the difference in staining, or were there two different types of fibrils within the spleen? To solve this enigma it would be necessary to discover differences between the fibrils other than those of staining and arrangement.

None of the writers previously cited mentioned the reticular fibrils of the Malpighian bodies. In acute and chronic leukemia the

reticular fibrils of the Malpighian corpuscles manifested a marked deviation from the normal arrangement of the reticular fibrils. The lesions of the lymphocytic maladies often seemed to occur first in the Malpighian bodies, but this observation was not made in the myelocytic leukemias. Consequently the site of the first invasion or origin of the diseased state did not provide an explanation for the extensive changes in the reticular pattern of the corpuscles. The numerical increase of dense reticular fibrils within the Malpighian corpuscles may indicate a beginning fibrosis and the older lesions should be found as small round areas of connective tissue, but such structures were not found in the sections of spleen.

The arrangement of the reticular fibrils of the red pulp, in preparations of spleens from individuals who had leukemia or related diseases for a short period of time, was nearly identical with the arrangements of the reticular fibrils of normal spleens. Due to the short duration of the disease and the anaplasia of the leukemic cells, it was probable that the normal appearing reticulum was that remaining in the spleen. In chronic leukemia, with a few exceptions, the pronounced variation in the arrangement and amount of the reticular fibrils in the red pulp was quite constant. The abundant reticular fibrils had to be produced by abnormal reticulum cells which were also producing leukemic cells. The deviation from the normal reticulum was manifested by the numerically diminished sinuses and the maze-like arrangement of the reticular fibrils. If the ability to return to a nearly normal structure, when the framework of the liver was retained (as in acute yellow atrophy), can be translated to the spleen, it must be thought

from this study that the spleen was irreparably changed in chronic leukemia because the reticular framework of the spleen was markedly altered.

Tumor cells are regarded as a new type of cell that may closely resemble the cells from which they were derived. When differentiated, tumor cells may function in a somewhat normal manner. Squamous cell carcinomas form pearls (areas of keratinization) deep in the tumors and islet cell tumors may cause hypoglycemia. In leukemia there was an overproduction of thickened argentophilic fibrils which occurred most regularly in the Malpighian corpuscles and slightly less so in the red pulp. Callender (1934) stated that the reticulum of lymph nodes in lymphocytic leukemia was not increased but was spread apart by the infiltration of leukemic cells. The findings of this dissertation were in disagreement with his report. However, in monocytic leukemia, Callender, Krumbhaar and Stengel (1942) and Rappoport and Kugel (1947) noted a delicate reticulum which surrounded the cells. What was the cause of this abundant formation of argyrophile fibrils? Robb-Smith (1938) mentioned that in leukemia there was possibly a slight increase in fibrils after irradiation. However, of the 97 leukemic cases that were studied only 17 had been irradiated. Other prescribed treatments included specific antileukemic drugs, antibiotics, transfusions and general supportive measures. There was a possibility that some of these drugs may have so affected the cells that they produced an abnormal reticulum. The treatment in these cases varied greatly and no one drug was used in all cases.

Other factors that must be considered are the various enzymes

that regulate the activity of the cells. Had an enzyme of the normal cells of the spleen been replaced by another one or had it been changed by rearrangement of its various radicles in the reticulum cells of the leukemic spleen? Did these enzymes cause the formation of a changed ground substance or only a change in the formation of the fibrils? How much consideration must be given to the electrolytes, oxygen and pH of the leukemic tissues? In this study it was noted in most of the silver-stained sections that the cells of the Malpighian corpuscles of the leukemic spleens were rose colored and that the other cells had a black tinge. This phenomena was seen in only the first two or three rows of cells in the Malpighian corpuscles of normal spleens. What was the cause and significance of this observation? This dissertation answered none of these questions, but more research with newer and perhaps undiscovered methods may enable us to answer some of these questions.

CHAPTER VII

SUMMARY AND CONCLUSIONS

The writer thoroughly agrees with Krumbhaar and Stengel (1942) concerning the spleen in leukemia when they stated, "In general, it may be said that in most items analyzed there was considerably more variation than would be expected from a study of the literature." The descriptions of the external and cut surfaces of the spleens varied greatly as to color and consistency.

In the great majority of the leukemic spleens there was a marked increase of reticular fibrils which divided the corpuscles into medium sized and small groups of cells. In the periphery of the Malpighian bodies, many coarse, argentophilic fibrils separated the cells into small compartments. Often individual cells were enclosed. However, in a small number of specimens a very normal appearing, reticular fibrillary pattern occurred in the Malpighian corpuscles, with a few threads centrally and very fine threads at the periphery, which demarcated the body from the red pulp. Usually these were from spleens in which the duration of the disease was quite short. Some Malpighian corpuscles in which the lymphocytes were completely replaced by leukemic cells retained the altered reticular fibrillary formation; however, other sections manifested a complete loss of the reticular fibrillary configuration. In nearly half of the specimens studied, a normal amount

and arrangement of protoplasmic fibrils appeared in the Malpighian corpuscles. In slightly less than half of the spleens an increased amount of thickened protoplasmic fibrils separated the corpuscles into small nests of cells.

The reticular fibrils varied greatly in amount and arrangement in the red pulp of leukemic spleens. In acute leukemia of very short duration there may be a very normal amount of the argentophilic fibrils. In these spleens the sinuses were delineated well and coarse, silver-impregnated fibrils occurred between them. A few sinuses were outlined in other sections and the cells between them were separated into various sized groups by coarse or fine reticular fibrils. A maze-like arrangement of the reticular fibrils continued between the cells to form small groups and often enclosed individual cells. The reticular fibrils in chronic leukemia had a tendency to be frayed and split. Often the fibrils were very short and too far apart to form any pattern of arrangement. A few specimens exhibited a very small amount of reticular fibrils and closely resembled the spleens of other young children. The protoplasmic fibrillary pattern nicely outlined a normal number of sinuses in about half of the leukemic spleens, while the sinuses were diminished in the remainder of the sections. In a few instances the protoplasmic fibrils resembled the arrangement of the reticular fibrils.

In lymphosarcoma, reticulum cell sarcoma, and Hodgkin's disease, the Malpighian corpuscles of the non-tumorous portions of the spleen somewhat resembled those of leukemic sections, but the red pulp appeared to have a normal amount and arrangement of reticular fibrils. The tumors showed many coarse reticular and thickened protoplasmic fibrils.

From the studies made, it was concluded that:

1. In leukemic spleens, Malpighian corpuscles showed a marked increase in the amount of reticular fibrils with a very distinct alteration of pattern from the normal.

2. The altered reticular fibrillary pattern of Malpighian corpuscles remained for a time after the corpuscles had been extensively infiltrated by leukemic cells and then the fibrils of the corpuscles disappeared.

3. Reticular fibrils of the red pulp, in acute leukemia of very short duration, were like the normal in amount and arrangement. In all probability these were the reticular fibrils of the organ before the leukemic invasion.

4. With the prolongation of the leukemic disease, the sinuses were not seen in their regular pattern, and the cells of the red pulp were separated by an increased amount of fine and coarse reticular fibrils in a fine-meshed, maze-like arrangement.

5. The reticular fibrils of the red pulp were not separated widely by the infiltrating leukemic cells, but often every cell was encircled by argentophilic fibrils.

6. The arrangement of reticulin fibrils quite often differed from that of the protoplasmic fibrils.

7. The variations in arrangement of the reticular fibrils were the same for the three types of leukemia and could not be used to differentiate between lymphocytic, myelocytic or monocytic leukemia.

8. The reticular fibrillary arrangement of the Malpighian corpuscles appeared to be that of normal corpuscles in lymphosarcoma,

reticulum cell sarcoma and Hodgkin's disease. In the non-tumorous portion of the red pulp the argyrophile fibrils resembled those of a normal spleen. Abundant reticular fibrils coursed through the tumor nodules and had no semblance to the pattern found in the leukemic spleens.

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