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Bone Marrow Biopsy

Volume XII Friday, October 11, 1940 Number 2

STAFF MEETING BULLETIN
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Published for the General Staff Meeting each week during the school year, October to May, inclusive.

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William A. O'Brien, M.D.

I. LAST WEEK

Date: October 4, 1940

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:20 p.m.

Program: Movie: "The World of 1960"
"American Saddle Horses"

Biennial Report
R. M. Amberg

Discussion
H. S. Diehl

Present: 114

- - - -

II. MOVIE

Title: "The Riveter"

Released by: A Donald Duck Short.

- - - -

III. ANNOUNCEMENTS

1. CONSCRIPTION REGISTRATION

All those who are not residents of Ramsey and Hennepin Counties may register at the University Registrar's Office or the Armory from 8:00 a.m. until 5:00 p.m. on October 16.

2. STARTING TODAY, Staff Meeting Bulletins will be issued with light weight paper covers and holes punched for covers. All those who receive covers and bulletins today should turn in their card indicating they have done so.

3. CORRECTIONS in First Bulletin, Vol. XII, No. 1:

a. Page 4, line 9 - "McLennan, Charles E."

b. Page 6, line 40 - "Instructor in Psychology, University of Missouri, 1939-40.

c. Page 13 - Surgery Fellow

Frederick B. Mears, Rochester, N. Y.
B.A. '35, M.D. '39, University of Rochester.
Intern, University of Minnesota Hospitals, 1939-40.
Medical Fellow in Surgery, 1940 --

d. Page 14, line 20 -

B.A. '36, University of Utah, M.D. '40, Johns Hopkins University.

4. PROMOTIONS announced by the University of Minnesota are as follows:

From associate professor to full professorship: Halvor O. Halvorson, bacteriology; Cecil J. Watson, medicine; William T. Peyton, surgery; William A. O'Brien, Preventive Medicine and Public Health, Commonwealth Fund Postgraduate Medical Education.

From assistant professor or other rank to associate professor: Starke R. Hathaway, Psychopathic hospital; Wallace D. Armstrong, dentistry; James B. Carey, clinical associate professor of medicine; Della G. Drips, Howard K. Gray, Samuel F. Haines, Howard R. Hartman, Howard L. Mason, Charles W. Mayo, Marschelle H. Power, experimental biochemistry, and Harry L. Smith, all of Mayo Foundation, and Arthur C. Kerkhof, to clinical associate professor, Medical school.

To assistant professor: Phillip Hallock, clinical assistant professor of medicine; Charles J. Hutchinson, clinical assistant professor of medicine; L. Earle Arnow, assistant professor of physiology; Miland E. Knapp, radiology and physical therapy; Donald W. Cowan, students health service; Horatio B. Sweetser, clinical assistant professor of medicine; Claude J. Ehrenberg, clinical assistant professor of obstetrics and gynecology; Everett C. Hartley, clinical assistant professor of obstetrics and gynecology; Herman E. Hilleboe, clinical assistant professor, preventive medicine and public health; Byron E. Hall, H. Corwin Hinshaw, Charles H. Slocumb, Edward B. Tuohy and Marvin M. D. Williams on Mayo Foundation.

IV. BONE MARROW BIOPSY

... Robert Hebbel

Bone marrow biopsy has a place of importance in the diagnosis of diseases of the hematopoietic system. It is, however, a necessary procedure in the minority of cases and in such instances does not always yield a positive diagnosis. In this paper neither an exhaustive review of the literature nor an analysis of our own cases is given. It is intended, rather, to point out the findings in the more common and well known hematologic conditions in which biopsy may be helpful in diagnosis and at the same time indicate the limitations of the procedure.

Examination of the bone marrow during life, although performed earlier by a few investigators (Scott[38] and Schulten[37] - lit.), became a clinically applicable procedure when Seyfarth[41] introduced a method of trephining the sternum in 1923. This method has been used in the studies of Schilling[34], Weiner and Kaznelson[47], Damashek[8,9], Custer[4,6], Barta[2,3] and others. In 1929 Arinkin[1] introduced the method of obtaining marrow by aspiratón biopsy and this simplified procedure has been employed by Nordenson[28], Segerdahl[40], Schulten[37], Scott[38], Henning[14], Markoff[26,27], Tempka and Braun[44], Young and Osgood[49], and many others.

Sternal biopsy is advantageous not only because of the accessibility of that bone but because the hematopoietic activity of sternal marrow is sustained throughout life (Custer and Ahlfeldt[7]). Nordenson[29] found the marrow of the sternum, rib and pelvis of a patient to be qualitatively and quantitatively similar. Stasney and Higgins[42], in a group of cases examined postmortem, found a similar condition of the marrow in sternum, rib and vertebra and concluded that the condition of one portion of the marrow reflected that of the whole. Although instances of irregular composition of the sternal marrow have been reported they are uncommon and material removed by biopsy may be considered representative in most instances.

Methods of biopsy

A. Trephine

Trephining of the sternum provides material for both imprints or smears and histologic sections. The topographic relationships of the marrow are preserved in section, but for accurate identification of the various cell types smears or imprints are indispensable. The method provides excellent preparations. The disadvantages are that the technique is more complicated than is that of aspiration biopsy and the necessary cutaneous incision is objectionable particularly if repetition of the biopsy is necessary or advisable.

B. Aspiration biopsy

The chief advantage of this method is its simplicity. Properly executed it causes but little more disturbance to the patient than does a venapuncture, leaves no scar and may be repeated frequently if necessary. Dilution with blood occurs and to eliminate this factor as much as possible most investigators have aspirated small volumes (.1 - .2 cc) of material and from this made direct smears. In most hyperplastic marrows dilution causes little disturbance. However, in hypoplastic marrows so few cells may be obtained that examination of the smears is very tedious and in any instance accidental excess dilution may occasion the same difficulty. In order to more uniformly provide adequate amounts of marrow for examination without resorting to trephine biopsy we have adopted a method of concentrating the cells obtained by aspiration. The technique is based on the method devised by Schleicher and Sharp[35] and further described by Limarzi[23].

The sternal marrow may be approached directly through the cortex of the manubrium or sternal body or through the sternomanubrial junction. All of these avenues of approach have been used by various investigators but the sternal body in the third interspace or at the upper border of the third rib is usually recommended. The structure of the sternum varies and no one site is satisfactory for all cases. The skin, sub-

cutaneous tissues and periosteum are infiltrated with procaine. A shortened 18-gauge spinal puncture needle is then forced into the bone at an angle of about 45° (with the point toward the head of the patient) until the visually experienced sudden "give" indicates that the marrow cavity has been reached. The stilet is removed and, with a tightly fitting, dry syringe, 1 cc. of material (composed of marrow and blood) is aspirated. When the needle is properly placed the flow is prompt, steady and the patient usually experiences a "suction pain." Unless such a flow is encountered the stilet should be replaced and the needle shifted slightly in depth. If there is yet no return a new site should be tried. Prolonged aspiration in the absence of a free flow of fluid does not yield satisfactory material.

The aspirated material is immediately transferred to a paraffined tube containing a minute amount of powdered heparin as an anticoagulent. A hematocrit tube is then filled with this mixture and centrifuged at from 2000-2500 RPM for 5 minutes. Centrifugation separates out the following layers reading from top down: 1. Fat, 2. plasma, 3. myeloid-erythroid cells, 4. erythrocytes. The heights of the several layers are recorded. The fat and plasma are removed and discarded. The myeloid-erythroid layer, together with a very small amount of the erythrocyte layer is removed separately, transferred to a paraffined watch glass and from this mixture smears are made and stained with the May-Grünwald-Giemsa combination.

With this technique we have obtained sufficient material for examination in most attempted biopsies. The procedure causes no significant morphological alteration in the cells and carefully made, well stained smears compare favorably with imprint preparations.

The height of the myeloid-erythroid layer in the hematocrit tube (M-E volume) gives some information concerning the activity of the marrow. Limarzi found the M-E volume to be from 5% - 8% in normal individuals, 1.5% - 3% in aplastic anemias, 20% in microcytic hypochromic anemia, up to 30% in hemolytic anemia, up to 40% in pernicious anemia, and up to 75% in chronic myeloid leukemia. The M-E volume is, however, of limited value in any one instance. It will vary not only with hyperplasia and hypoplasia of the marrow but with the amount of sinusoidal blood which is obtained at aspiration. Consequently elevated M-E volumes are indicative of hyperplasia but reduced values may mean only excess dilution.

Cellular composition of the marrow.

A. Terminology

There is considerable confusion in the literature due to differences in terminology. We employ that used by Downey[11]. For orientation it may be briefly stated that the myeloblast is the stem cell of the marrow under normal conditions and from it are derived:

1. Granular leukocytes through leukoblast, promyelocyte, myelocyte and metamyelocyte stages.

2. Erythrocytes through pronormoblast, basophilic normoblast, polychromatophilic normoblast and orthochromatic normoblast stages.

3. Megakaryocytes.

Megaloblasts are never encountered in normal marrow and as seen in pernicious anemia they develop from the stem cell into macrocytes through promegaloblast, basophilic megaloblast, polychromatophilic megaloblast and orthochromatic megaloblast stages.

B. The normal bone marrow

The reported percentages of the various cell types encountered in normal marrow cover wide ranges as indicated in Table I, column 1. Thus, for example, erythroblasts (all stages of the normoblast) are variously reported as making up from 12.1% to 30% of the nucleated cells. Similarly wide ranges are presented in the other categories.

Some authors attach importance to the

proportion of myeloid to erythroid cells--the so-called myeloid-erythroid ratio. Limarzi[23] found the myeloid-erythroid ratio to be from 1.75:1 to 3.75:1. Stasney and Higgins[42] found this ratio to be 1:1. Other hematologists, Scott[38] for example, use a leukoerythrogenic ratio which is the ratio between the percentage of normoblasts and immature myeloid cells. This computation eliminates errors incident to counting mature cells derived from the peripheral blood but has the disadvantage of discounting band forms and mature cells which may be numerous in the marrow itself.

Estimation of the myeloid and erythroid maturity dispersions is also used in analysis. Scott's normal values are as follows:

Myeloid	
Myeloblasts	5.1%
Promyelocytes	12.6%
Myelocytes	37.2%
Young forms	45.0%
Erythroid	
Pronormoblasts	2.5%
Basophilic normoblasts	10.8%
Polychromatophilic and orthochromatic normoblasts	86.6%

Limarzi's[23] normal values are the following (the terminology has here been modified to correspond to the above):

Myeloid	
Myeloblasts and promyelocytes	2.5%
Neutrophilic myelocytes	15-20 %
Neutrophilic metamyelocytes	20-45 %
Mature neutrophiles	10-25 %
Eosinophiles (all stages)	2- 5 %
Basophiles	less than .5%
Erythroid	
Pronormoblasts	Less than 5 %
Basophilic normoblasts	20 %
Polychromatophilic and orthochromatic normoblasts	75 %

Of the other cells encountered in normal marrows lymphocytes predominate. Here again there is a wide range in the reported normal values (3.5% to 24.9%). There are also rare plasma cells and reticulum cells. Megakaryocytes are usually estimated at much less than 1% of the total.

It is evident that the normal variations in the marrow are so great that only extreme deviations from the normal pattern are significant. While differential counts are useful in detailed studies we agree with Schulten[37] that they are in general unnecessary for diagnostic purposes. Significant alterations are apparent from examination of the smears.

Table I. Sternal puncture counts (Scott's[38] tables).

	1 Max-min range 13 authors: normal marrow %	2 Scott's normal %	3* Iron deficiency anemia %	4* Pernicious anemia %	5* Acute aplastic anemia %	6* Acute myeloid leukemia %
Myeloblast	.3 - 5.1	1.8	1.6	2.4	---	75.0
Promyelocyte and myelocyte	5.2 - 21.6	17.6	17.6	6.8	3.6	1.0
Neutrophile (Meta-myelocyte, band, segmented)	38.1 - 66.0	46.5	32.4	24.0	4.2	2.0
Eosinophile (myelo-cyte, segmented)	1.0 - 5.2	3.7	1.2	1.6	.2	---
Basophile (myelo-cyte, segmented)	.07- 1.0	.1	---	.4	---	---
Lymphocytes	3.5 - 24.9	11.3	12.0	11.2	84.8	1.0
Monocytes, reticulum cells, etc.	.25- 9.0	.8	.4	3.6	.2	---
Erythroblasts (all stages)	12.1 - 30.0	17.8	34.8	xN. - 11.6 M. - 38.0	5.6	21.0

* Columns 3, 4, 5 and 6 give the differential counts of sample cases from Scott's series.

x (Column 4) N - normoblast, M - megaloblast.

The bone marrow in disease.

A. The anemias

1. Iron deficiency anemia.

Most investigations of the bone marrow in iron deficiency anemia (Segerdahl[40], Damashek[8], Weiner and Kaznelson[47], Henning[14], von Jagic and Klima[46], and others) have been primarily concerned with the idiopathic hypochromic anemia. Scott points out however that other anemias with iron deficiency as the common denominator such as hypochromic anemia of infants, chlorosis, hypochromic anemia of pregnancy, hypochromic anemia of chronic blood loss, etc., present the same features in the marrow. Erythropoietic activity is elevated while granulopoiesis is not disturbed. Segerdahl[40] and others see nothing characteristic in the marrow in idiopathic hypochromic anemia, Scott considers a preponderance of small, polychromatophilic normoblasts with pyknotic nuclei and ragged, narrow rims of cytoplasm diagnostic of iron deficiency anemia. Stodtmeister[43] by means of serial biopsies in cases of anemia resulting from chronic blood loss demonstrated that under iron therapy the percentage of normoblasts increased to a peak corresponding to the maximum reticulocyte response in the peripheral blood and then fell toward normal as hemoglobin and erythrocyte values returned to normal.

2. Aplastic anemia

The described changes in the marrow vary with the several authors' concepts of the disease. If extreme hypoplasia of the marrow is a part of that concept as expressed by Rosenthal[33] and others then only such a marrow should be encountered. If, on the other hand, the concept of aplastic anemia is based on clinical features a more variable condition of the marrow is found. Thus Rhoads and Miller[30] described marrows ranging from hypoplastic to hyperplastic. The term panmyelophthisis is often used synonymously with aplastic anemia. Schulten[37] objects to this usage without actual demonstration of that change in the marrow and emphasizes the variable cellular composition of marrows in cases presenting the clinical features of aplastic anemia.

In acute aplastic anemia extremely hypocellular marrows are usually found. The M-E volume is very low. The smears reveal only a few normoblasts and myeloid cells. Megakaryocytes are absent. Lymphocytes frequently dominate the picture and there may be a few reticulum cells and plasma cells. A sample differential count from one of Scott's cases is given in Table I, column 5. The marrow is more variable in the chronic forms of the disease. Although hypoplastic the marrow may show but little disturbance of granulopoiesis and erythropoiesis may be active as evidenced by a shift to the left in the maturity dispersion of the normoblasts.

Sternal biopsy is of value in the diagnosis of cases presenting the picture of aplastic anemia. The changes in the marrow in symptomatic aplastic anemia where the disease is the result of known toxic agents such as benzol, x-irradiation, prolonged infections, etc., are like those of the idiopathic form. However, the findings are quite different when the clinical picture of aplastic anemia is produced by an aleukemic leukemia or carcinomatosis of the marrow.

3. Hemolytic anemia.

Congenital hemolytic jaundice has received the most attention. The marrow is hyperplastic and normoblasts make up a large percentage of the cells encountered in the biopsy (Weiner and Kaznelson[47]: 63.8%, Löwinger[25]: 50%, Scott[38]: 42-68%). There is little correlation between the erythropoietic activity of the marrow and the degree of anemia or the reticulocyte percentage of the peripheral blood. Normoblastic development is usually described as normal although Jones[19] has found normoblasts derived directly from the reticulum. Scott finds no disturbance of granulopoiesis and no change in the normoblasts indicative of the spherocytosis of the erythrocytes.

4. Pernicious anemia

The marrow of pernicious anemia has been described by many investigators (Segerdahl[40], Schulten[37], Jones[19], Tempka and Braun[44], Scott[38] and others). In spite of extensive study much controversy revolves about the nature and significance of the megaloblasts which characterize the marrow in this disease. Most European and some American hematologists distinguish sharply between megaloblastic and normoblastic erythropoiesis. Most American hematologists consider the megaloblast as a stage in the development of the normoblast. To the latter group the marrow of pernicious anemia is in a state of maturation arrest and under liver therapy the megaloblasts are "ripened" into normoblasts. The concept is contrary to the demonstrable morphological differences between normoblastic and megaloblastic erythropoiesis (Downey[11], Jones[19]). Jones[19] has reviewed the megaloblast problem in detail.

The marrow in pernicious anemia is very hyperplastic. Normoblastic erythropoiesis is suppressed and megaloblastic erythropoiesis predominates. Normoblasts, chiefly polychromatophilic and orthochromatic forms, are present but their proportionate number is not well established. Megaloblasts at all stages of development are found but the basophilic and polychromatophilic forms are the most numerous. Granulopoiesis is also abnormal and the hyperpolymorphic immature neutrophiles, which are the precursors of the typical pernicious anemia neutrophiles of the peripheral blood, form a characteristic feature of the marrow in this disease (Jones[20]). Abnormal megakaryocytes have also been described. Thus, there is, as first expressed by Tempka and Braun[44], a panmyelopathy in pernicious anemia.

Under the influence of liver extract the marrow rapidly undergoes profound changes which may be demonstrable within 24 hours after the induction of therapy. There is a rapid maturation of the megaloblasts, no new megaloblasts are formed, the proportion of basophilic and polychromatophilic megaloblasts gives way to increased numbers of orthochromatic megaloblasts and by the 12th day only rare orthochromatic and polychromatophilic megaloblasts are found (Jones[19]). Coincident with the rapid maturation of the megaloblasts there is a normoblastic hyperplasia first characterized by the appearance of large numbers of pronormoblasts and basophilic normoblasts This hyperplasia reaches its height prior to the maximum reticulocyte response of the peripheral blood but persists until hemoglobin and erythrocyte values reach normal levels. Pathologic myelopoiesis also disappears and in complete remission the marrow is entirely normal.

B. Agranulocytosis

There is considerable variation in the descriptions of the bone marrow in agranulocytosis. In this disease the granulocytic series alone is involved. Erythropoiesis is not suppressed. The marrow may show almost complete absence of myeloid cells or it may be hyperplastic with an increase of young forms. Custer[5] and Fitz-Hugh and Krumbhaar[12] described a failure of maturation and a proliferation of myeloblasts. Darling, Parker and Jackson[10] described hyperplasia of stem cells and absence of more mature forms in rapidly fatal cases, hypoplasia of myeloid cells coincident with the appearance of many plasma cells and lymphocytes in fatal cases of longer duration, and rapid maturation during the recovery phase of favorable cases. Jaffe[17] described degenerative changes in the leukocytes of the marrow in cases examined postmortem. Rohr[31a] described three types of marrow in agranulocytosis: 1. Severe cases with complete granulopoietic aplasia accompanied by proliferation of reticular cells (Phagocytic, lymphoid, and plasma cell types); 2. Moderately severe cases with marrow hyperplastic at promyelocyte-myelocyte stage; 3. Mild cases with an essentially normal marrow but showing some reduction in metamyelocytes and band forms. Rohr[31b] considered that the reported multiplication of stem cells really represented a proliferation of reticulum cells.

Biopsy of the marrow is of value in this disease for those cases with complete granulocytic aplasia have, in general, a less favorable prognosis than do those with cellular marrows.

C. Infections

Changes in the bone marrow incident to various types of infection have been described by Schilling[34], Barta[3], von Jagic and Klima[45], Henning[14], Markoff[26], and others. These accounts indicate that there is considerable variation in the reactivity of the marrow and, as emphasized by Schulten[37], that for most infections the condition of the marrow has little diagnostic or prognostic significance. Depending on the maturity dispersion of the granulocytes the several authors have made more or less arbitrary classifications of the types of marrow encountered. Thus a marrow might be mature, myelocytic, myelocytic-promyelocytic, etc. It is of interest that Barta[3] found in specific infections accompanied by extreme leukopenia that the marrow presented the features described for idiopathic agranulocytosis, benzol poisoning, etc.

Of particular interest from the standpoint of differential diagnosis is the type of marrow described in certain chronic infections. Here the marrow is predominantly myelocytic-promyelocytic and the picture closely simulates that seen in chronic myeloid leukemia. von Jagic and Klina[45] point out that the toxic changes in the leukocytes and increase of reticulum cells and plasma cells seen in infections are of value in making the distinction.

D. Thrombocytopenic purpura

The marrow is hyperplastic. Myelopoiesis is little disturbed; erythropoietic activity depends on the degree of anemia. Particular attention has been devoted to the megakaryocytes. Pathologic alterations in these cells, particularly lack of granulation, have been described by Frank[13], Schminke[36], Seelinger[39] and others. Rohr[31b] emphasized vacuolization and increased basophilia of the cytoplasm. Jaffe[18] saw no severe degenerative changes but noted increased numbers of agranular, small forms. Markoff[27], on the other hand, found the same morphologic features in this disease as in normal marrows. Schulten[37] was unable to distinguish whether young, old, or degenerate forms were more numerous than normal. There is a notable increase in megakaryocytes according to Jaffe[18], Rohr[31b], Limarzi and Schleicher[24] and others. Limarzi and Schleicher[24] found, in addition to total numerical increase, a greater percentage of young forms. Markoff[27] contended that the normal variation is so great that quantitative estimations are unreliable.

We have had the opportunity to examine the marrow from but two cases. Megakaryocytes were plentiful and while adult forms did not appear to be more numerous than in other marrows, young forms were more readily found. Morphologic changes were not impressive.

The practical value of bone marrow biopsy in this disease is not significantly influenced by the disagreement concerning the morphologic features of the megakaryocyte. It is helpful in separating essential thrombocytopenic purpura from diseases presenting similar clinical features such as acute aplastic anemia, in which megakaryocytes are absent from the marrow, and aleukemic leukemia with its abnormal forms. Wiseman, Doan and Wilson[48] listed biopsy of the marrow as a procedure essential to making a diagnosis of thrombocytopenic purpura.

E. Leukemia

In those cases of leukemia presenting typical clinical and hematological findings biopsy of the marrow yields no additional information of diagnostic importance. However, cases are not infrequently encountered in which the findings are atypical and the blood picture inconclusive. Here sternal puncture is definitely indicated.

1. Myeloid leukemia

Chronic myeloid leukemia is characterized by hyperplasia of the

meyloid elements of the marrow with maturity dispersions more or less approximating that noted in the peripheral blood in those cases presenting a leukocytosis (Segerdahl[40], von Jagic and Klima[45], Henning[14] and others). It has been pointed out by Schulten[37] and Barta[3] that the character of the marrow is not always specific and may be indistinguishable from that of certain chronic infections. Scott[38] stated, however, that he has not encountered the changes characteristic of leukemia in other conditions.

In acute myeloid leukemia marrows presenting a great preponderance of typical or atypical myeloblasts are considered characteristic by Segerdahl[40], Schulten[37], Damashek[9] and others. That some variation occurs is shown in Klima's[22] description of three types of marrow for such cases: 1. Hyperplasia with about 90% of the cells at myeloblast stage; 2. Hypoplasia but with a similar differential count; 3. May be hyperplastic but with a variable shift to immature forms. Most of Scott's[38] cases fell in Klina's group 1. (The differential count of a sample case is given in Table I, column 6). All of these showed a high percentage of atypical forms--paramyeloblasts, micromyeloblasts, etc. Several cases fell in Klima's group 3. These showed a preponderance of promyelocytes and myelocytes and ran a somewhat longer clinical course.

We have seen no "myeloblastic" marrows in the few cases of acute and subacute myeloid leukemia in which the marrow has been examined. There were three instances in which the shift to immature forms was variable. In all of these maturing granulocytes were present. One showed an increase in promyelocytes and leukoblasts of insufficient degree to be considered diagnostic. The others emphasized the importance of the qualitative changes. In one there were atypical monocytoid forms of myeloblastic origin, and in the other, although the proportion of immature forms was not at all impressive they were so abnormal that a leukemia was the only possible interpretation.

2. Lymphatic leukemia

In cases of chronic lymphatic leukemia presenting the typical peripheral lymphocytosis the marrow shows about 90% lymphocytes (Segerdahl[40], Klima[22] and others). It has been pointed out however that in such cases it is impossible to determine what proportion of the lymphocytes obtained on aspiration came from the marrow and the proportion from the diluting sinusoidal blood. Sternal biopsy has a much greater value in subleukemic and aleukemic cases. In many instances the diagnosis may be clearly confirmed or established by the demonstration of a high proportion of lymphocytes in the marrow. However, the range of reported lymphocyte values for normal marrows is so great that an arbitrary standard cannot be established. Difficulties also arise in situations such as that seen in aplastic anemia where there is at least a great relative increase in lymphocytes. In subleukemic cases (10,000 - 20,000 cell per cu. mm. in the peripheral blood) the marrow shows from 30% - 50% lymphocytes according to Rohr[31], Klima[22] and others. Israels[16] considered a demonstrable lymphocytosis in the marrow to be of diagnostic significance. Henning[15] claimed that absence of lymphocytosis almost negates a diagnosis of lymphatic leukemia. In Scott's series of cases the percentage of lymphocytes in the marrow ranged from 7% - 97%. He concluded that the finding of 40% lymphocytes was sufficient for a positive diagnosis but that a normal count does not exclude the condition. Cases without significant lymphocytosis have also been described by Weiner and Kaznelson[47], Klima[22] and others. Schulten[37] described the case of a patient with an aplastic type of anemia whose bone marrow showed no evidence of leukemia. Splenectomy was performed and that organ revealed no anatomic evidence of leukemia but a subsequent biopsy of the sternal marrow showed typical lymphatic leukemia.

Absence of diffuse involvement of the marrow probably explains the failure to demonstrate the disease in at least

some instances. It may be considered worthwhile in suspected cases where a biopsy gives negative or inconclusive results to repeat the procedure at a different sternal level.

Unless a cellular marrow is encountered an objective diagnosis of lymphatic leukemia must be made with caution. In most of the cases of lymphatic leukemia in which we have studied the marrow the lymphocytosis has been of high degree. There have been, however, notable exceptions. In one case of aleukemic leukemia, proven at autopsy, three biopsies of the sternal marrow failed to reveal evidence of the disease. We have also seen two cases in which one or more negative biopsies were followed by biopsies presenting elevated proportions of lymphocytes. Whether the encountered lymphocytosis in either case is sufficiently high for a positive diagnosis remains problematical and subject to interpretation.

F. Multiple myeloma

The sternal biopsy findings in multiple myeloma have been described by Zadek[50], Schulten[37] and others. There is as yet no general agreement as to the exact origin of the myeloma cells. Myeloblastic, lymphoblastic and other types have been described in addition to the usual plasma cell type. Since sternal puncture has been used most cases have been found to be of plasma cell type. Klima[21] noted atypical undifferentiated cells in one of six cases of myeloma and pointed out that such instances might be the basis for the various types described. Zadek[50] and others believe that myeloma cells are derived exclusively from the reticulum.

Sternal puncture offers confirmatory evidence in cases presenting the usual clinical and radiologic features. It may establish the diagnosis in obscure cases and aid in differentiating myeloma from multiple carcinomatous metastases. Cases in which there is radiologic or other evidence of a solitary myeloma should have a sternal biopsy.

G. Metastatic carcinoma

The demonstration of tumor cells in sternal biopsies has been rather frequently reported. Rohr and Hegglin[32] studied the marrow in 74 cases of carcinoma and were able to make a positive diagnosis in 10. They reported their findings in detail and pointed out the characteristics of tumor cells as encountered in the marrow. Schulten[37] also describes the findings in metastatic carcinoma.

Sternal puncture is of value in establishing the diagnosis in those cases where a carcinomatosis of the marrow is the cause of an apparent aplastic or leuko-erythroblastic anemia.

Conclusion

The indications for sternal biopsy cannot be arbitrarily defined. In general biopsy is indicated in any case where a disease of the hematopoietic system is present or suspected and the evidence from other sources is insufficient to establish a diagnosis. It is particularly advisable in obscure anemias (aplastic anemia, "splenic" anemia, macrocytic anemias not characteristic of pernicious anemia, leuko-erythroblastic anemia, etc.) as well as suspected leukemia, agranulocytosis and thrombocytopenic purpura. It must be remembered, however, that the biopsy may or may not yield a conclusive diagnosis. It has been noted above, for example, that a myelocytic-promyelocytic marrow may be common to both leukemia and infections, that myeloblastic marrows are described for both agranulocytosis and acute myeloid leukemia, and that in lymphatic leukemia the marrow is not always overrun with lymphocytes. The findings are often subject to interpretation and of value only when interpreted in the light of the clinical and other laboratory data. Appreciation of its limitations increases the value of sternal biopsy.

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V. GOSSIP

John Skinner in an article in "This Week Magazine" of the Minneapolis Tribune, October 5, 1940 entitled "Can You Prove You Were Born" builds up the case for birth registration. In the final paragraph he climaxes his story by showing that Dr. Halbert Dunn, Director of the Vital Statistics Section of the Census Bureau in Washington, formerly director of these hospitals, discovered that his name had been filed incorrectly and that the recorded date of his birth was 18 months in error. This article is part of a campaign to have everyone learn if his birth has been recorded correctly....At the general faculty meeting on October 4 in the junior ballroom of the new Coffman Memorial Union editor-in-chief Morris Fishbein spoke on "Medical Preparedness and Medical Writing." Although he is now a grandfather, this is not the reason he had to sit down between addresses. In the first talk, he outlined the scheme for medical participation in the effort to defend our country and its ideals and philosophy. It resembled in many details the talk made by Dean Diehl at Staff Meeting earlier in the day, except that Dr. Fishbein had spoken to "other" people in Washington. The whole set-up in Washington reminded him of the senegambian who prayed mightily for his country to use him in its hour of peril, and then added as a strong afterthought, "chiefly in an advisory capacity." The editor felt that we could make a good start in medical writing by learning to report a case. The title of the article should be written last, for, after all, what we started out to tell might have been something entirely different. Persons who cloak their thoughts in long runs before they jump can have their excess wordage trimmed to modest proportions by any person trained to look for the "jumps." By way of example, he used something like the following, "In a long experience in both civilian and military hospitals covering a number of years, I am of the opinion in the majority of cases where complications do not exist that the needs of the occasion can best be served by the use of soap as a cleansing agent for wounds! Translated, this means "Soap is a good cleansing agent for the average wound." The boys who build large bibliographies, those who quote extensively from non-medical sources for descriptive flights, those who send in dirty papers, those who write just becaus they think they should be writing, all came in for their share of criticism. The program also included a report by Dr. McQuarrie on his sabbatical stay in China, the method of admission to the Medical School, postgraduate medical education, faculty changes, and the introduction of new faculty members. The room was filled to overflowing, and after the meeting many took the opportunity to see the new Union.....Old graduates who remember the ancient structure on the old campus will find it difficult to realize that Minnesota now has a social center second to none for men and women students. The many restaurants, meeting places, ball rooms, and amusement sections startle everyone by their endless variety and decorations. The Union listening hours now held in the Fine Arts section are presenting recorded programs as part of the general campus stimulation of interest in good music. The loud speaker system has 45 outlets scattered throughout the building. In addition to the 16 pianos there is a fine organ in the grand ball room. Also of interest are the bowling alleys, card, pool, and billiard rooms, and other places where students may learn to effectively use their leisure time after they leave school.....Most unusual is the Campus Club, which occupies the top three floors of the structure. The main lounge and restaurant on the first of the Campus Club floors open out onto a large terrace. This floor also contains the administrative offices, board of directors room, ladies waiting room, the most talked of powder room in the Twin Cities, cigar counter, coat room, and serving kitchens. The next floor houses the reading room and the card, billiard, and pool rooms. It also has individual writing rooms, telephone rooms and quiet rooms for both men and women (nap places!). The top floor has living quarters for the bachelor members of the faculty. To show that they are above mere superstitious beliefs, there are 13 faculty apartments. All of the furnishings were paid for by the Club, which is an organization of faculty members who pay regu-

lar initiation fees and annual dues. Impartial observers believe it to be the best example of modern furnishings of any club in the northwest. There were so many substantial savings on the building as a whole that more money was spent on furnishings than usual. The entire building was done by an interior architectural firm, who bid on it after the University had made an estimate on furnishing it in the usual way. There was only $1,000 difference in the two bids. The building is so new and so different that there are the usual objections by those who resist change of any sort. Other critics believe it is too good for us. It is hoped that it may become the great social center which was envisaged by the late President Coffman, when he learned that most of our students did not enjoy many social advantages while at the University.....This week in Missoula, Montana, graduates of the University of Minnesota will gather for their first fall meeting. They will discuss their plans for the year which will include a weekly review of our staff meetings. Each member is assigned one bulletin for report. In addition, all subscribe for the bulletin, and, according to reports, find them of value. There are 14 regular attendants including a graduate of Harvard and one from Cornell who have become ex-officio members. At the last meeting of the Montana State Medical Association in Bozeman a state medical alumni association was formed, and it was suggested that they too should study with us. It was at this meeting that visiting speakers Hammes, Fansler, Leven, Watson, and O'Brien were met at the train by the committee-in-charge plus a wheezy band. The only thing that was missing were the horses to take us down the main street. They would have been there had not Mickey Hanley of Billings rented them to the Shriners for a special celebration.....Pathologist Lawrence Berman was the winner of the fourth prize in the Abbott Camera Competition. His subject was "Hilltop". Dr. Berman was formerly connected with the Department of Photography at the Farm School, and is considered by local photographers to be one of the best amateurs in the Twin Cities. Others who received honorable mention were Bacteriologist Charles Heilman of the Mayo Clinic, Pathologist A. J. Hertog of Eau Claire, Wisconsin, formerly of our staff; and Ernest J. Losli of Minneapolis....When Radiologist Lee G. Rigler was in Boston, he saw Drs. Sosman and Dyke, who taught at the Center for Continuation Study last year in the course in Neurologic Roentgenology. Dr. Sosman was President of the American Roentgen Ray Society this year and arranged an attractive program. He had an "Information Please" session in which some of the radiologic leaders in this country were asked to make diagnoses on radiographs taken of animals sick from various causes. At the banquet a slight-of-hand performer showed radiologists how to more effectively remove articles from the wearing apparel of those who come to their offices by doing it so cleverly that they did not even realize it was being done. President Sosman, who guarded himself against having his pockets picked by emptying them, finally wound up by having his suspenders taken off without his knowledge...Base Hospital #26 has been formed. Pathologist James S. McCartney is in command. The medical services will be directed by Dr. James B. Carey, the surgical service by L. Haynes Fowler, orthopedics by Ed. Evans, ophthalmology and otolaryngology by Colonel Edwards, laboratories - Dr. Gerald Evans, radiology by Dr. Ude.....The first two weeks of school were hectic as usual -- the first for the freshmen, the second for the upper classmen. It seems that we have had more than our usual amount of extra-curricular activity what with the New Union, the dedication of the Museum of Natural History and the dedication of Ada B. Comstock Hall for Women. Two very good football games enlivened the opening sessions, but now things are down to normal, as we await the first step to combat the menace which hangs over the land in the form of our conscription registration on October 16... .....