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The Bone Marrow in Pregnancy

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I. THE BONE MARROW IN PREGNANCY

Roy G. Holly, M.D.

Introduction

Bone marrow examination is an essential part of a hematologic investigation. It is surprising that so few studies have been made on the bone marrow in pregnancy when one considers the prevalence of anemia and other hematologic disorders in the pregnant woman. The studies which have been reported have dealt principally with a normal pregnancy or megalobastic anemia in pregnancy. There have been few reports on bone marrow biopsy in iron deficiency anemia or refractory anemias in pregnancy in spite of the fact that these anemias are common.

Examination of the peripheral blood often lacks the specific requirements for accurate diagnosis. Since the erythrocyte as well as the granulocyte and platelet is formed in the red bone marrow, it is logical that much can be learned about erythropoiesis in the bone marrow which may not be so apparent by a study of peripheral blood alone. An accurate diagnosis of megaloblastic anemia in pregnancy can be made only by bone marrow biopsy. Examination of the bone marrow from pregnant patients with an anemia which is not iron deficiency or megaloblastic has disclosed normoblastic hypoplasia. This anemia is being reported as hypoplastic anemia. Evidence for the existence of iron deficiency can be found in the bone marrow. In this regard bone marrow smears and sections can be stained for iron. A future report will deal with this interesting phase of iron metabolism study. It is sufficient here to indicate that iron is absent from the marrow of those patients with iron deficiency while present in various amounts in hemolytic anemias, the anemia of infection and megaloblastic anemia.

Proper interpretation of the abnormal bone marrow in pregnancy demands a knowledge of the normal bone marrow in pregnancy and the puerperium. This report details a quantitative and morphologic study of 96 sternal bone marrow biopsies from pregnant women. Thirty-four of these were normal controls, the remainder were performed on patients with anemia.

Review of the Literature

Normal pregnancy bone marrow studies have been reported by Daniachij,[1] Hansen,[2] Forssell,[3] Pitts and Packham,[4] Markoff,[5] Pignoli,[6] Wolff and Limarzi,[7] Callender,[8] and Leitner[9].

Daniachij[1] studied 50 pregnant and puerperal patients. Serial bone marrow studies were not done but his cases were selected from all months of pregnancy. The post partum examination was performed on the sixth or seventh day. An aspiration technic similar to that described by Arinkin[10] was used. From this study Daniachij described a myeloid and erythroid "reaction" beginning in early pregnancy and most prominent by the sixth month. He felt that the changes were specific and characteristic enough to be called "the bone marrow of pregnancy". A leukoblastic reaction characterized by an increase in neutrophil metamyelocytes was described. The increase in this leukocyte precursor cell in pregnancy has not been confirmed by other authors. Active erythropoiesis was observed in addition to an increase in eosinophil formation. Mitotic figures and basophilic stippling were increased.

Daniachij described megaloblasts as being present in his marrow smears in normal pregnancy but examination of his illustrations indicates that the cells he was describing as megaloblasts were more probably macronormoblasts and not the typical megaloblast as this cell is understood today. Segerdahl[11] and Markoff[5] mention this discrepancy in Daniachij's publication. He also described a greater "reaction" in primiparas than in multiparas. This finding has not been evident to other investigators. The bone marrow on the sixth or seventh post partum day still showed typical pregnancy changes.

Hansen[2] was the first to report an in-

crease in megakaryocytes in the pregnancy marrow. He described increased erythropoiesis with both a relative and absolute increase in normoblasts. Normoblasts in nests or clumps were cited as evidence for increased erythropoiesis. Unfortunately this author did not present detials of his study nor did he indicate the number of marrows examined.

Pitts and Packham[4] studied and reported on 41 pregnancy bone marrows which they compared with bone marrows from 24 non-pregnant females. Increased cellularity was observed with advancing pregnancy. They determined a total cell count per cubic millimeter from approximately 10 cc. of sternal marrow fluid. The mean cell count from the control series was 23,100 per cubic millimeter. At the height of the pregnancy change in the second trimester they found a mean count of 45,510 per cubic millimeter. Wide variations in cell counts were found. Two objections to their conclusions can be mentioned. Aspiration of 10 cc. of marrow fluid for examination introduces a serious error from a variable dilution of the marrow material by sinusoidal blood. Also, several of their patients were anemic with hemoglobins below 10 grams per cent. They represented their bone marrow studies as being taken from patients with normal pregnancy though it is evident that some of this normal group were anemic.

Markoff[5] reported a purely morphologic study of the normal pregnancy bone marrow. It is unfortunate that he made no mention as to the number of cases studied. Erythropoiesis was observed as normal in quality and maturity but increased in absolute number. He described in detail the macronormoblast present in many of his normal pregnancy marrows. Islands or nests of polychromatophilic normoblasts, as well as an increase in mitotic figures, were described as typical of the pregnancy marrow. Myeloid elements were qualitatively normal though increased in number. He briefly commented on seeing large promyelocytes which were similar morphologically to those seen in pernicious anemia. Young eosinophils were increased but he failed to observe an increase in megakaryocytes.

Pignoli[6] found a generalized hyperplasia during pregnancy and in the first day of the puerperium in the pregnancy bone marrows which he studied.

Wolff and Limarzi[7] have reported the largest series of bone marrow biopsies in normal pregnancy. Thirty women were examined serially through pregnancy and re-examined in the puerperium. In addition, 75 individual biopsies were examined. By their standards a normal myeloid-erythroid volume is 6.8 per cent. The mean myeloid-erythroid volume was increased to 14 per cent in normal pregnancy. Though quantitatively increased, no change in the character of erythropoiesis was observed. They described the characteristic cell as the polychromatophilic normoblast. Myelopoiesis was increased. They observed a tendency toward immature forms in this cell series in the third trimester. An increase in marrow platelets was seen but this did not manifest itself by an increase in circulating platelets. Megakaryocytes of the mature type were increased in number late in pregnancy. The pregnancy effect on the bone marrow persisted for as long as three months following delivery.

Callender[8] reported marrow findings from dry smears and section material on 19 healthy pregnant women. She emphasized the wide variation in marrows obtained from non-pregnant subjects. On the basis of the marrow sections, an increase in cellularity indicative of hyperplasia in the late weeks of pregnancy and early puerperium was described. Large "erythroblasts" were described. An increase in plasma cell-like reticulum cells was noted. She did not believe that the changes in the bone marrow in a normal pregnancy were striking enough to justify the description as a "characteristic marrow of pregnancy".

Leitner[9] described 11 bone marrows from normal pregnancy. He noted giant neutrophils similar morphologically to those seen in pernicious anemia. He remarked that the changes in the marrow in

normal pregnancy were not as marked as reported in the earlier literature.

The above mentioned reviews dealt for the most part with the marrow in normal pregnancy. The bone marrow in iron deficiency anemia in pregnancy has received little attention. Indeed, bone marrow studies of iron deficiency anemia from any cause are rarely reported. Markoff[5] characterized the marrow of iron deficiency anemia in pregnancy as being active. Numerous mitoses were described. Macronormoblasts, giant promyelocytes and increased numbers of reticulum cells were observed. Segerdahl[11] noted normoblastic erythropoiesis with greater or smaller numbers of macronormoblasts in association with iron deficiency anemia in pregnancy. Neither author indicated the number of cases studied. Wolff and Limarzi[7] reported 10 cases of pregnancy iron deficiency anemia in which marrow was examined. They found normoblastic hyperplasia with a moderate to pronounced shift to erythroid immaturity. Scott and Govan[12] have reported the bone marrow findings from 46 patients with anemia in pregnancy. In their patients with iron deficiency anemia they noted normoblastic hyperplasia with a more marked "shift to the left" in those with the more severe anemia. Also they associated the more marked anemia with increases in macronormoblasts and reticulum cells. Although any relation between iron deficiency and megaloblastic anemia seems remote they, nonetheless, described transitions from iron deficiency and normoblastic marrows through marrows with greater numbers of macronormoblasts on to marrows which were typically megaloblastic. In one patient in my own series in whom megaloblastic anemia developed while under observation, no such transition was observed. Also Scott and Govan introduced two cell types which they call "intermediate" and "smear" cells which have not been apparent to other observers.

The morphology of the bone marrow in megaloblastic anemia in pregnancy has received considerable attention. Because there are many differences between Addisonian pernicious anemia and megaloblastic anemia in pregnancy, because nutritional deficiencies and macrocytosis are not always apparent and because the one constant feature of this pregnancy anemia is the megaloblastic bone marrow, the term megaloblastic anemia in pregnancy is now more commonly employed, supplanting such terms as the "pernicious anemia of pregnancy", "nutritional anemia of pregnancy" and "macrocytic anemia of pregnancy". Heilbrun[13] first reported a single case with a description of the bone marrow section obtained by trephining the sternum. Typical megaloblasts were described in a highly cellular marrow. The megaloblasts disappeared after treatment with liver. Abramson,[14] Napier,[15] Wills,[16] Fay and Kondi,[17] Markoff,[5] Hussy,[18] Segerdahl,[11] Guggisberg,[20] Nielson,[21] Daniel and Antis,[22] Davidson,[23] Davidson, Davis and Innes,[24] Miller and Studdert,[25] Fullerton,[26] Thaddea,[27] Callender,[28] Wolff and Limarzi,[7] Leitner,[9] and Ungley and Thompson[29] have all added case reports to the literature with descriptions of the megaloblastic bone marrow. Segerdahl[11] among others has emphasized the regular appearance of the so-called "pernicious anemia neutrophil" in pregnancy megaloblastic anemia. This is manifest in the peripheral blood as a macropolycyte but large hyperpolymorphic neutrophil promyelocytes, myelocytes and metamyelocytes are typical of the bone marrow. It is not clear in some of the earlier articles whether the cell described as a megaloblast was truly the megaloblast as we define it here. This has led to some misleading reports on the incidence and treatment of the anemia. Markoff,[5] Segerdahl,[11] Wolff and Limarzi,[7] Leitner[9] and Ungley and Thompson[29] clearly define the cell they call a megaloblast as a pathologic cell, identical with the cell described in detail by Jones[30]. Although there has been an attempt to establish criteria by which the megaloblastic bone marrow of the pregnancy anemia could be differentiated from the bone marrow of true pernicious anemia, the majority of authors state that such a differentiation is impossible.

Method of Study

Twenty-six normal pregnant subjects

were subjected to bone marrow biopsy at varying times during pregnancy to form the control series. Eight were re-examined in the puerperium, usually at the time of the six weeks post partum examination. Forty patients with iron deficiency anemia in pregnancy had a bone marrow biopsy performed as a part of the initial workup prior to the institution of therapy. Biopsy was carried out again in three patients after treatment and while still undelivered. Megaloblastic anemia in pregnancy has been diagnosed six times on five patients. The anemia reappeared in a second pregnancy in one patient. Hypoplastic anemia in pregnancy is being reported in nine pregnancies in seven patients. Post partum biopsies were made on four of this group.

The procedure for obtaining sternal marrow for study has been described by Sundberg[32]. A University of Illinois sternal biopsy needle was used. About 1 cc. of marrow fluid was aspirated for study. Powdered heparin was used as the anticoagulant. The marrow aspirant was centrifuged in a Wintrobe hematocrit tube. The thickness of the myeloid-erythroid layer was measured and smears were prepared from this layer. The smears were stained with Wright's stain. 500 to 1000 cells were counted to obtain a differential count. The system of nomenclature used in describing the morphology of the bone marrow smears is that of Downey.

In addition to the bone marrow biopsy each of the patients was completely studied by other hematologic procedures. Serum iron, iron binding capacity and erythrocyte protoporphyrin were determined on each patient. The results of these studies were correlated in each case with the bone marrow biopsy. Where appropriate, values for these determinations will be shown in following tables. The changes in serum iron, iron binding capacity and erythrocyte protoporphyrin in normal pregnancy and in pregnancy anemia have been reported.[31]

Bone Marrow in Normal Pregnancy

Sternal marrow biopsies were performed on 26 pregnant patients with hemoglobin values above 10.7 grams per cent. The mean hemoglobin was 11.9 grams per cent with a range from 10.7 to 14.2 grams per cent. Nine of the group were multiparas and 17 were primiparas. The biopsies were obtained at different stages of pregnancy. Two patients were studied in the first, 13 in the second and 11 in the third trimester. Eight of the 26 patients were re-studied in the puerperium.

The myeloid-erythroid volume can be used as a rough index of bone marrow activity. A normal myeloid-erythroid volume is from 6-8 per cent. The mean myeloid-erythroid volume in this series of pregnant patients was 10.1% with some values as high as 22%. This would indicate a slight hyperplasia of the bone marrow in pregnancy. Those patients in whom an increase in myeloid-erythroid volume was noted were those examined late in pregnancy. Section material obtained in a few instances confirmed the impression that there is an increased cellularity in the bone marrow during pregnancy.

The mean post partum myeloid-erythroid volume was 10.2%. Variable amounts of blood loss at delivery make these values hard to interpret. It is significant, however, that slight hyperplasia, as well as other changes to be mentioned, did persist in the bone marrow for two to three months after delivery. These studies confirm the impression that a slight hyperplasia of the bone marrow occurs in most pregnant patients and persists for two to three months after delivery.

Differential counts were made on these 34 marrows. The 26 normal pregnancy differential counts are shown in Table 1, those from the puerperium in Table 2. Scott[33] has assembled normal bone marrow differential counts from 19 different studies. His composite differential count, used for comparison with the counts in normal pregnancy and in anemia, is shown in Table 3.

No striking differences were obtained when differential counts in normal preg-

Table 1. Normal Pregnancy Bone Marrow Biopsy

	Age	Mo.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts					Megakaryocytes
								% Normoblast	% Neutrophil	% Eosinophil	% Basophil	% Lymphoid	
.	26	3	0	11.7	35.0	6.9	3.0	17.4	66.8	0.6	0.6	14.8	normal
.	25	3	1	14.2	44.5	7.0	7.0	18.8	65.2	1.4	0.2	14.4	normal
.	20	4	2	12.8	39.0	6.9	5.5	18.8	66.0	2.8	0.6	11.8	normal
.	28	4	1	12.0	36.5	7.0	12.0	17.0	75.8	0.6	0.2	6.4	normal
.	25	4	5	12.0	38.0	7.0	12.0	24.4	62.2	4.0	0.4	9.0	increase
.	23	4	0	12.0	39.0	7.2	9.0	17.2	78.4	0.4	0.4	3.6	sl. increase
.	23	5	2	12.0	36.0	7.1	5.5	20.8	71.8	1.4	0.8	5.2	normal
.	19	5	0	11.6	33.0	6.9	8.0	18.2	69.0	2.6	0.0	10.2	sl. increase
.	21	5	2	12.0	37.0	7.0	6.0	16.0	71.0	2.0	0.2	10.8	normal
.	21	5	0	11.1	35.0	7.0	8.0	19.0	74.0	1.8	0.2	6.0	increase
.	24	6	1	12.7	40.5	7.3	9.5	16.2	73.8	3.8	0.0	6.2	increase
.	20	6	0	12.1	36.5	7.0	---	17.6	73.2	2.0	0.4	6.8	increase
.	27	6	1	12.0	39.0	7.0	19.0	19.8	70.2	2.0	0.8	7.2	increase
.	27	6	0	12.3	38.0	7.0	10.0	15.8	74.8	2.6	0.8	6.0	normal
.	20	6	0	11.1	38.5	7.3	17.0	21.6	69.2	1.4	0.2	7.6	increase
.	19	7	0	11.0	36.5	7.3	20.0	20.5	70.4	1.5	0.3	7.3	increase
.	19	7	0	11.3	36.0	6.8	4.0	14.8	66.4	8.0	0.0	10.8	increase
.	22	7	0	11.5	33.0	7.0	14.0	16.4	71.6	1.6	0.4	10.0	increase
.	24	7	0	11.6	34.5	7.2	11.5	18.4	73.4	1.0	0.4	6.8	increase
.	16	8	0	11.7	38.0	7.0	8.0	18.6	71.2	2.0	0.2	8.0	increase
.	24	8	1	12.7	39.0	7.1	22.0	19.7	69.0	2.9	0.4	8.0	increase
.	15	8	0	10.7	33.0	7.0	6.0	21.4	67.4	2.0	0.4	8.8	increase
.	20	8	0	11.3	33.5	7.1	2.5	15.0	76.4	0.4	0.2	8.0	increase
.	32	9	0	12.2	35.5	7.0	6.0	18.0	65.2	1.2	0.2	15.4	increase
.	17	9	0	11.8	35.0	7.1	8.0	17.4	62.5	2.2	0.8	17.1	increase
.	19	9	0	13.1	38.0	7.2	15.0	18.2	73.2	1.6	0.2	6.8	increase
Mean	22			11.9	37.0	7.0	10.1	18.1	70.4	2.1	0.4	9.0	

Table 2. Normal Pregnancy Post Partum Bone Marrow Biopsy

Age	Days P.P.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts					
							Normoblast %	Neutrophil %	Eosinophil %	Basophil %	Lymphoid %	Megakaryocytes
26	35	0	12.6	36.0	7.1	7.0	15.8	67.6	4.2	0.2	12.2	increase
28	45	1	12.7	38.5	6.9	4.0	19.6	62.6	3.4	0.4	14.0	sl. increase
25	51	5	14.2	41.0	6.9	15.0	21.6	63.0	2.2	0.8	12.2	increase
23	55	2	11.7	36.0	7.0	15.0	21.2	56.6	2.6	0.4	19.2	increase
24	51	1	13.9	43.0	7.2	2.0	23.5	66.5	2.0	0.0	8.0	normal
20	16	0	14.2	41.0	7.1	21.0	25.2	57.0	3.6	0.4	14.0	increase
27	54	1	14.3	43.5	7.0	6.5	19.2	62.4	2.0	0.8	15.6	increase
27	52	0	12.2	35.5	7.1	11.5	10.2	81.6	2.0	0.2	5.9	normal
Mean			13.2	39.5	7.0	10.2	19.5	64.6	2.8	0.5	12.6	

nancy were compared with the normal standard. Normoblast counts ranged from 15.8 to 24.4 per cent. The mean was 18.1 per cent. The mean in the puerperium was 19.5 per cent. The normoblast count did not vary in different stages of pregnancy. One may conclude from these results that the hyperplasia of the bone marrow in pregnancy, if present, is not the result of an increase in any one cell series.

There is one constant morphologic feature of a pregnancy bone marrow, an increase in megakaryocytes, which serves to distinguish this marrow from a normal marrow. The increase in megakaryocytes appears in the second trimester and was observed to be present for at least two months after delivery. The increase was estimated to be of the order of 5 to 20 times normal. The megakaryocytes were of the mature type. Marrow platelets were abundant in all marrows examined though no increase in circulating platelets was observed.

The normoblast series in all the marrows examined was morphologically normal. The characteristic cell was the polychromatophilic normoblast. There did not appear to be a significant shift to more immature or mature cells. Macronormoblasts were seen in a few marrows. The granulocyte series was normal. Eosinophils were increased in a few marrows but this was not a constant finding. The "shift to the left" in the granulocyte series observed by others was not apparent in these marrows, either during pregnancy or after delivery. The lymphoid group of cells were not increased and appeared normal morphologically.

The normal pregnancy effect on the bone marrow can be summarized as follows:

1) A slight generalized hyperplasia in late pregnancy which may persist for 6 to 8 weeks into the puerperium.
2) Normal differential counts.
3) An increase in megakaryocytes.

Bone Marrow in Iron Deficiency Anemia in Pregnancy

As part of the initial workup of those

Table 3. Normal Bone Marrow Differential Cell Count. Mean Values Tabulated by Scott[33] from 19 Investigators.

	%	%
Myeloblasts	1.0	1.0
Leukoblasts	2.0	2.0
Neutrophils		63.0
Promyelocytes	4.0	
Myelocytes	13.0	
Metamyelocytes	15.0	
Bandforms	16.0	
Mature forms	15.0	
Eosinophils		3.0
Myelocytes	2.0	
Mature forms	1.0	
Basophils		0.5
Normoblasts		18.5
Pronormoblasts	0.5	
Basophilic normoblasts	2.0	
Polychromatophilic normoblast	12.0	
Orthochromatic normoblasts	4.0	
Lymphoid cells		12.0
Lymphocytes	10.0	
Plasma cells	1.0	
Macrocytes	1.0	
	100.0	100.0

patients with iron deficiency anemia in pregnancy, a sternal biopsy was obtained from 40 patients. Three were re-studied after satisfactory responses to oral or intravenous iron. None of the patients had received iron therapy immediately preceding the bone marrow study. Hemoglobin values ranged from 6.0 to 9.8 grams per cent. Twenty-two of the patients were primiparas and 18 were multiparas. Six were studied in the second trimester, 31 in the third trimester and 3 in the immediate puerperium. As evidence for iron deficiency the mean serum iron was 29 gamma per cent, the mean iron binding capacity was 418 gamma per cent and the mean erythrocyte protoporphyrin was 134 gamma per cent for these patients.

Comparison of the bone marrows from patients with iron deficiency anemia in pregnancy with the normal pregnancy bone marrow revealed two important changes. The mean myeloid-erythroid volume was increased to 19.6 per cent, an increase of nearly 100 per cent over the normal pregnancy mean. In addition to this more marked hyperplasia, there was a significant relative increase in normoblasts.

Only 4 of the marrows examined from this group with iron deficiency anemia had a myeloid-erythroid volume under 10 per cent. The greatest increase was in one patient whose myeloid-erythroid layer was 42 per cent. The relative as well as absolute increase in normoblasts probably accounts for the major part of this myeloid-erythroid volume increase. The normoblast count ranged from 20.2 to 52.6 per cent with a mean of 35.4 per cent. There was a rough correlation between the increase in normoblast count and the severity of the anemia. All normoblast counts were above the mean determined for normal pregnancy and the mean for non-pregnant individuals. No significant changes in eosinophil, basophil or lymphoid cell counts were noted. There was a relative decrease in neutrophil precursors. Examination of the fixed and imbedded bone marrow section confirmed the normoblastic hyperplasia. The differential counts are shown in Table 4.

Table 4. Bone Marrow Biopsy in Iron Deficiency Anemia in Pregnancy. These are all pre-treatment biopsies.

							% Differential Cell Counts					
Age	Mo.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Normoblast	% Neutrophil	% Eosinophil	% Basophil	% Lymphoid	Megakaryocytes
20	5	0	7.6	25.0	6.9	14.0	37.2	47.8	4.0	0.4	10.6	increase
26	5	1	7.1	28.0	6.9	15.0	33.4	58.8	0.8	0.4	6.6	increase
19	5	0	9.4	31.0	7.0	26.5	27.6	57.8	2.9	0.8	11.9	increase
19	6	1	7.9	31.5	7.0	14.5	--	--	--	--	--	increase
34	6	0	8.8	30.0	6.9	16.0	35.4	57.0	1.2	0.4	6.0	increase
19	6	0	9.2	29.5	6.8	5.0	28.4	59.6	3.2	0.2	8.6	increase
29	7	5	8.8	31.0	--	35.0	34.0	52.6	0.8	0.2	12.4	increase
36	7	10	6.0	22.0	7.0	--	27.0	57.4	1.6	0.0	14.0	increase
16	7	0	9.0	31.0	6.9	15.0	36.8	51.0	4.2	0.0	8.0	increase
20	8	0	9.7	32.0	6.8	17.0	36.6	53.6	1.2	0.2	8.4	increase
23	8	2	7.0	26.0	7.0	26.0	31.4	56.8	3.2	0.6	8.0	increase
20	8	0	9.8	31.5	7.2	13.0	38.6	53.4	1.8	0.0	6.2	increase
34	8	4	8.8	34.0	6.4	36.0	31.0	55.0	3.2	0.0	10.8	increase
20	8	1	8.3	30.0	--	17.0	32.5	61.5	3.0	0.0	3.0	increase
19	8	0	9.2	32.0	7.0	15.0	52.6	37.2	4.4	0.2	5.6	increase
26	8	2	9.2	32.5	6.8	8.0	39.2	44.9	3.9	0.3	11.7	increase
24	8	0	7.1	27.0	6.6	42.0	20.2	67.8	2.2	0.4	9.4	increase
17	8	0	8.0	28.5	6.8	20.0	35.9	54.4	0.8	0.6	8.3	increase
23	8	2	9.2	29.5	7.1	13.0	31.1	56.4	1.8	0.2	10.5	increase
30	8	2	9.0	32.0	7.0	21.0	33.9	52.6	3.1	0.8	9.6	increase
15	8	0	9.7	32.0	7.1	18.0	40.9	45.0	4.3	0.8	8.8	increase
28	8	0	8.0	27.5	7.1	10.0	26.5	62.4	3.1	0.6	7.4	increase
19	8	0	9.2	30.0	6.9	18.0	35.7	54.4	1.3	0.4	8.2	increase
26	8	2	8.0	25.0	6.9	12.0	42.5	49.7	1.8	0.0	6.0	increase
17	8	0	9.2	26.0	7.0	12.5	35.6	55.6	2.8	0.4	5.6	increase
21	8	0	9.5	33.0	7.1	11.0	44.6	47.5	1.7	0.2	6.1	increase
36	9	6	9.5	33.5	6.4	19.0	33.6	51.6	2.0	0.0	12.8	increase
27	9	0	8.3	31.5	7.0	20.0	23.0	64.5	1.7	0.1	10.8	increase
19	9	0	9.2	29.5	6.7	28.0	33.4	58.2	1.4	0.4	6.6	increase
24	9	4	7.8	28.0	6.9	24.0	44.6	45.8	1.2	0.4	8.0	increase
34	9	8	9.7	32.0	--	24.0	31.4	55.8	2.6	0.0	10.2	increase

20	9	0	9.4	31.0	--	20.0	31.8	61.8	1.4	0.0	5.0	increase
19	9	0	9.4	32.0	7.0	40.0	40.6	51.8	1.3	0.0	6.3	increase
27	9	2	9.5	32.0	7.2	26.0	50.2	41.8	2.0	0.0	6.0	increase
21	9	1	8.8	29.5	7.0	8.5	32.6	55.8	3.8	0.4	7.4	increase
21	9	0	7.2	26.5	7.1	24.0	49.2	37.0	4.8	0.2	8.8	increase
20	9	0	9.1	30.0	7.0	5.5	37.1	56.4	1.9	0.4	4.2	increase
43	P.P.	17	8.4	29.0	--	29.0	37.6	53.0	1.6	0.0	7.8	increase
21	P.P.	1	7.1	24.0	7.0	13.5	25.0	63.5	1.3	0.0	10.0	increase
18	P.P.	0	7.2	31.0	6.4	38.0	44.2	46.2	2.4	0.0	7.2	increase
Mean			8.6	29.5	6.9	19.6	35.4	53.7	2.3	0.3	8.3	

Study of the individual smears revealed a uniform increase in megakaryocytes. Normoblastic development was essentially normal. An occasional smear showed a "shift to the left" with greater numbers of pronormoblasts and basophilic normoblasts but the predominant cell in all marrows was the polychromatophilic normoblast. This cell was small with a scant jagged edge of cytoplasm. Scott[33] has described this type of normoblast as typical of iron deficiency anemia. Mitotic figures were often increased and karyorrhexis was often present, indicating the greater erythropoietic activity. The polychromatophilic normoblasts were characteristically present in small groups or clumps. Macronormoblasts in greater or smaller numbers were present in the majority of the smears studied. The macronormoblast is a large normoblast approaching in diameter the size of a megaloblast. It lacks the specific nucleus of the megaloblast. The finding of large hyperpolymorphic granulocytes, cells similar to those seen in pernicious anemia, was often disturbing especially when seen in marrows which contained a few macronormoblasts. In the absence of the typical megaloblast a diagnosis of megaloblastic bone marrow was not made. Macrophages containing phagocytosed pigment or marrow debris were present in many of the smears examined.

The important bone marrow changes attributable to iron deficiency anemia in pregnancy may be listed. (1) A normoblastic hyperplasia characterized by an increase in the myeloid-erythroid volume and by a relative as well as an absolute increase in normoblasts. The characteristic cell is the polychromatophilic normoblast. These cells are often small with a jagged rim of cytoplasm. They frequently occur in nests or clumps. (2) An increase in the number of macronormoblasts. Occasionally hyperpolymorphic neutrophil precursors are seen. This latter cell is similar to that seen in pernicious anemia. (3) An increase in megakaryocytes as in normal pregnancy

Biopsy was carried out again in three patients of the iron deficiency anemia group before delivery but after correction of the anemia. The findings are shown in Table 5. A decrease in the myeloid-erythroid volume and in the relative normoblast count was observed. Megakaryocytes were increased as is

Table 5. Bone Marrow Biopsy in Iron Deficiency Anemia in Pregnancy. These are biopsies taken after iron treatment before delivery.

Age	Days of Iron Rx.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts					Megakaryocytes
							Normoblast %	Neutrophil %	Eosinophil %	Basophil %	Lymphoid %	
36	39	10	10.5	34.5	--	3.0	20.0	63.4	1.8	0.2	14.6	increase
26	78	1	13.1	42.0	7.0	8.5	23.5	62.0	6.2	0.4	7.9	increase
19	70	0	11.3	36.0	7.0	--	24.3	61.5	1.8	0.7	11.7	increase
Mean			11.6	37.5	7.0	5.7	23.9	62.3	3.3	0.4	11.4	

typical of a pregnancy bone marrow. The polychromatophilic normoblast resumed its normal appearance as might have been anticipated.

Bone Marrow in Megaloblastic Anemia in Pregnancy

Six patients had severe anemia in pregnancy which was diagnosed by means of sternal biopsy as megaloblastic anemia. The characteristic finding was the presence of the typical megaloblast. This cell has been described in detail by Jones[30]. The megaloblast is a large cell with a fine mesh-like nucleus with distinct chromatin-parachromatin differentiation. With greater numbers of megaloblasts present in the marrow, normoblastic development is depressed. Characteristic hyperpolymorphic neutrophils were always present. All of the marrows were hyperplastic. Following therapy there was a rapid disappearance of megaloblasts from the marrows with a marked relative increase in normoblastic activity. Differential counts from the bone marrow study in megaloblastic anemia in pregnancy are shown in Table 6. In our experience the finding of the megaloblast in the marrow has been associated with a high serum iron and normal erythrocyte protoporphyrin. Remission has followed Vitamin B_{12} plus Vitamin C therapy or folic acid.[36]

Bone Marrow in Hypoplastic Anemia in Pregnancy

Factors other than iron deficiency and an antipernicious anemia factor deficiency have been shown to influence bone marrow function. Chemicals, heavy metals, steroids, and other hormones and antibiotics are just a few of the substances which are known to alter bone marrow function in animals and some humans. It is entirely possible that a factor or factors produced during pregnancy or metabolic changes coincident to pregnancy could well alter bone marrow function by depressing it. Aplastic anemia has been described in association with pregnancy.[34,35] The majority of the cases which have been reported have been fatal to the pregnant patient. One would anticipate that a fatal case would be of sufficient interest and unusual enough to warrant publication. Might there be a level of bone marrow de-

Table 6. Bone Marrow Biopsy in Megaloblastic Anemia in Pregnancy.

Age	Mo.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts						Megakaryocytes
							Normoblast %	Neutrophil %	Eosinophil %	Basophil %	Lymphoid %	Megaloblast %	
40	P.P.	9	8.4	27.5	--	18.0	14.4	42.0	2.6	0.8	13.2	27.0	increase
23	9	2	8.0	21.0	7.0	17.5	13.0	38.0	3.4	1.0	6.0	38.6	normal
24	9	3	8.1	23.0	7.0	24.0	17.0	47.2	1.8	0.6	9.6	23.8	increase
34	9	1	6.9	15.0	7.3	51.5	7.0	36.4	3.0	0.6	7.3	45.7	increase
18	8	0	9.2	25.0	8.0	40.0	14.6	35.0	1.4	0.2	13.0	35.8	increase
20	7	0	7.3	21.0	7.2	19.2	8.2	31.4	1.0	0.0	11.2	48.2	increase
Mean			7.9	22.1	7.3	28.4	12.4	38.3	2.2	0.5	10.0	36.6	

pression with anemia, and perhaps leukopenia and thrombocytopenia, not severe enough to cause death?

In the course of the routine examination of all pregnant patients with anemia it became apparent that some patients did not manifest evidence of iron deficiency and were not megaloblastic. These patients were refractory to usual forms of therapy other than the transfusion of whole blood. Evidence for hemolysis did not exist. The anemia was moderate to severe in degree. None exhibited leukopenia, yet they did not manifest the usual pregnancy leukocytosis. Two of the patients have been determined to have lowered platelet counts. The significant finding in each of these patients has been normoblastic hypoplasia. There are other features of interest. In the non-pregnant state each of these patients has normal hematologic values. Four patients were reexamined following delivery and in each the bone marrow showed normoblastic hyperplasia. So far as can be determined by searching hospital and physician records every pregnancy of these 7 patients has been associated with an anemia which has proved refractory to treatment. Two patients were seen and examined at the University Hospitals during two pregnancies. Each time they were found to have hypoplastic anemia.

The myeloid-erythroid volume in the nine cases which have been studied has been low, normal or only slightly increased. The significant feature in the bone marrow is the normoblastic hypoplasia. The mean normoblast count was 11.4 per cent with a range from 5.4 to 14.6 per cent. The differential counts are shown in Table 7. These were all satisfactory biopsies. The fat layer averaged about 1 per cent and megakaryocytes were increased in all. No significant changes in the developing red cells were observed. Myeloid and lymphoid elements were relatively increased. Hemoglobin values were found to range from 6.7 to 9.9 grams per cent. The serum iron has been found to be normal or elevated. The erythrocyte protoporphyrin is normal.

Four patients were studied after delivery. In each there was a relative in-

Table 7. Bone Marrow Biopsy in Hypoplastic Anemia in Pregnancy

Age	Mo.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts					
							Normoblast	Neutrophil	Eosinophil	Basophil	Lymphoid	Megakaryocytes
24	9	0	8.6	27.0	--	11.0	5.4	84.4	1.8	0.6	7.8	increase
27	8	1	9.4	29.0	7.0	1.5	13.7	70.0	0.4	0.6	15.3	increase
21	6	0	8.9	30.0	7.2	11.0	14.6	75.0	2.0	0.6	7.8	increase
23	6	0	9.0	31.0	7.2	--	14.0	71.4	2.2	1.0	12.4	increase
21	7	0	9.9	32.0	7.3	5.5	10.2	79.2	0.6	0.4	9.2	increase
27	8	1	9.0	28.0	--	--	13.8	77.6	1.0	0.2	7.4	increase
29	8	3	9.9	31.0	--	11.0	10.2	77.4	2.4	0.4	9.6	increase
28	7	2	6.7	20.0	7.7	11.0	9.0	71.0	5.7	2.0	12.3	increase
30	9	3	9.7	33.0	7.0	4.0	11.2	76.8	4.2	0.8	7.0	increase
Mean 25			9.0	28.5	7.2	7.9	11.3	75.8	2.2	0.7	10.0	

crease in normoblasts. The post partum differential counts are shown in Table 8. Patient E.S. exhibited the most marked change following delivery. Whereas prior to delivery the normoblast count was 5.4 per cent, after delivery it was 56.2 per cent. The mean post partum normoblast count was 35.1 per cent, a significant increase when compared with antepartum values.

Thus far no cause for this anemia in pregnancy has been ascertained. It is being called hypoplastic anemia[37] because this term most clearly defines the underlying pathology, namely a normoblastic hypoplasia of the bone marrow. It appears to be specific for pregnancy. To date none of these patients have gone on to exhibit features of aplastic anemia in the non-pregnant state.

Summary and Conclusions

1. Normal Pregnancy: There is a generalized hyperplasia of the bone marrow in most pregnant patients. Differential counts are normal. No morphologic changes have been noted in the red and white cell series. Megakaryocytes are increased in a pregnancy bone marrow.

2. Iron Deficiency Anemia: There is a marked normoblastic hyperplasia of the bone marrow. Macronormoblasts may be present. Normoblasts with scant jagged cytoplasmic rims are frequently found in clusters. Megakaryocytes are increased.

3. Megaloblastic Anemia: There is a marked hyperplasia of the bone marrow. Typical megaloblasts are present in variable percentages depending on the severity of the anemia. The pernicious anemia leukocyte is found in this pregnancy anemia.

4. Hypoplastic Anemia: This anemia is characterized by normoblastic hypoplasia. Following delivery and associated with remission of the anemia there is a normoblastic hyperplasia in the bone marrow. Leukocyte and lymphoid elements are relatively increased. Megakaryocytes are increased.

Indications for bone marrow study on

Table 8. Bone Marrow Biopsy in Hypoplastic Anemia in Pregnancy.
These 4 biopsies were obtained after delivery.

Age	Days P.P.	Para	Gms.% Hgb.	% H'crit	Micra MCD	% M-E Volume	% Differential Cell Counts					
							Normoblast %	Neutrophil %	Eosinophil %	Basophil %	Lymphoid %	Megakaryocytes
24	40	0	10.8	34.0	--	8.0	56.2	30.6	3.6	0.0	9.6	increase
27	8	1	13.6	42.0	7.0	6.5	22.8	67.0	1.2	0.4	8.6	increase
21	43	0	12.9	38.5	7.8	4.0	33.2	52.4	1.2	0.0	13.2	increase
28	6	2	7.8	24.0	--	18.0	28.3	64.0	1.7	1.0	5.0	increase
Mean			11.3	34.6	7.4	9.1	35.1	53.5	1.9	0.4	9.1	

pregnant patients can be defined as follows:

1. Any patient with possible leukemia, lupus erythematosus or with other conditions which would warrant bone marrow biopsy in the non-pregnant state.

2. Any patient with a rapidly developing anemia near term or in the puerperium without blood loss to account for the anemia.

3. Any patient with an anemia which is refractory to oral or intravenous iron treatment.

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II. MEDICAL SCHOOL NEWS

Coming Events

December 8	Special Lecture; "Studies on Experimental Diabetes;" Dr. Arnold Lazarow, Associate Professor of Anatomy, Western Reserve University, Cleveland, Ohio; 15 Owre Hall; 4:00 p.m.
January 7	Phi Delta Epsilon Lecture; "Present Concepts in the Management of Intussusception;" Dr. Mark R. Ravitch, Director of Surgery, Mt. Sinai Hospital, New York City; Owre Amphitheater; 8:00 p.m.
January 7 - 9	Continuation Course in Pediatrics for General Physicians.
January 25 - 30	Continuation Course in Neurology for General Physicians and Specialists.
January 27	J. B. Johnston Lecture; "Recent Advances in the Morphology and Significance of the Cerebral Cortex;" Dr. Andrew T. Rasmussen, Professor Emeritus of Anatomy, University of Minnesota; Museum of Natural History Auditorium; 8:00 p.m.

* * *

Faculty News

The Medical School was recently host to Dr. R.J.G. Sinclaire, a well-known authority on rheumatoid arthritis, who is associated with the Department of Medicine, University New Buildings, Edinburgh, Scotland. Dr. Sinclaire took part in several informal discussions and seminars.

Dr. Donald W. Cowan, Assistant Director, Students' Health Service, and Mr. Richard Bond, Public Health Engineer, attended the meeting of the American Public Health Association in New York from November 9 to 13. Dr. Phillip D. Kernan, Assistant Professor of Public Health, attended the recent meeting of the North Central Section of the American College Health Association at Grand Forks, North Dakota, where he presented a paper entitled, "Productivity of a Survey of Chest X-Rays on the Faculty, Students, and Employees of the University of Minnesota."

Dr. Donn G. Mosser, Instructor, Department of Radiology, attended the meeting of the American Cancer Society in New York during the first week in November.

* * *

Publications of the Medical School Faculty

Frick, P. G. and Hagen, P. S.: Congenital Familial Deficiency of the Stable Prothrombin Conversion Factor; Restudy of Case Originally Reported as "Idiopathic Hypoprothrombinemia". J. Lab. & Clin. Med., 42: 212, 1953.

Glick, David, Alpert, M., and Stecklein, H. R.: Studies in Histochemistry: XXVII. The Determination of L-Ascorbic Acid, and Dehydro-L-Ascorbic Acid Plus Diketo-L-Gulonic Acid in Microgram Quantities of Tissue. J. Histochem. & Cytochem., 1: 326, 1953.

Hilding, A. C.: The Tectorial Membrane in the Theory of Hearing. Ann. Otol., Rhin., & Laryng., 62: 757, 1953.

** Dedication of the Lyon Laboratories -- February 11, 1954
Dedication of the Mayo Memorial Medical Center -- October 21, 1954.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Physicians Welcome

December 7 - 12, 1953

Monday, December 7

Medical School and University Hospitals

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; W-612, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:30 - Tumor Conference; Doctors Kremen, Moore, and Stenstrom; Todd Amphitheater, U. H.

11:30 - 12:30 Physical Medicine Seminar; Bandaging Techniques; Lloyd Stein; Heart Hospital Auditorium.

12:15 - Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:30 Physiology Seminar 201; Evidence for New Pathway in Heme Synthesis; Samuel Schwartz; 214 Millard Hall.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

1:30 - 3:30 Dermatology Hospital Rounds; H. E. Michelson and Staff; Dermatology Histopathology Room, M-434, U. H.

4:00 - 5:00 Residents Conference; Presentation of Cases from Minneapolis General Hospital; Heart Hospital Theater.

4:30 - ECG Reading Conference; Staff Room, Heart Hospital.

4:30 - Infectious Disease Rounds; Sta. 43, U. H.

4:30 - Public Health Seminar; Epidemiology of Brucellosis; Wesley W. Spink; 15 Owre Hall.

5:00 - 6:00 Physiology-Surgery Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staff; Eustis Amphitheater.

Ancker Hospital

8:30 - 10:00 Tuberculosis and Chest Conference; Auditorium.

2:00 - 3:00 Surgery Journal Club; Classroom.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Eldon Berglund; Newborn Nursery, Station C.

10:30 - 12:00 Medicine Rounds; Thomas Lowry; Sta. F.

11:00 - Orthopedic and Fracture Rounds; Drs. John Moe and Arthur Zierold; Sta. A.

11:00 - Pediatric Rounds; Erling Platou; Station K.

12:30 - Surgery Grand Rounds; Dr. Zierold; Sta. E.

1:30 - 2:30 Tuberculosis Conference; J. A. Myers; Sta. M.

2:00 - Pediatric Rounds; Robert A. Ulstrom; Stations I and J.

Monday, December 7 (Cont.)

Veterans Administration Hospital

1:30 - Cardiac Conference; Drs. Berman, Weisbart, and Smith; Rounds Immediately following conference.

Tuesday, December 8

Medical School and University Hospitals

9:00 - 9:50 Roentgenology-Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 12:00 Cardiovascular Rounds; Station 30, U. H.

12:30 - 1:30 Physiology 114C -- Respiration; E. B. Brown; 129 Millard Hall.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

12:30 - 1:30 Bacteriology Seminar; Chemotherapeusis of Viral Infections; George Clifford; 214 Millard Hall.

3:30 - Pediatric Seminar; Sarcoidosis; Mildred Schaffhausen; Sixth Floor, U.H.

3:30 - General Physiology-Biophysics Seminar; 323 Zoology Building.

* 4:00 p.m. Special Lecture; "Studies on Experimental Diabetes"; Dr. Arnold Lazarow, Associate Professor of Anatomy, Western Reserve University, Cleveland, Ohio; 15 Owre Hall.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

4:30 - 5:30 Clinical-Medical-Pathological Conference; Todd Amphitheater, U. H.

4:30 - ECG Reading Conference; James C. Dahl, et al; Staff Room, Heart Hospital.

5:00 - 6:00 X-ray Conference; Presentation of Cases from St. Cloud Hospital; Drs. Nessa and Anderson; Eustis Amphitheater, U. H.

Ancker Hospital

8:00 - 9:00 Fracture Conference; Auditorium.

9:00 - 10:00 Medical X-ray Conference; Auditorium.

Minneapolis General Hospital

10:00 - Cardiac Rounds; Paul F. Dwan; Classroom, Sta. I.

10:00 - Pediatric Rounds; Spencer F. Brown; Stations I and J.

11:00 - 12:00 Medicine-Surgery Conference; Classroom, Sta. M.

12:30 - 2:30 Dermatology Rounds and Clinic; Carl W. Laymon and Staff.

12:30 - ECG Conference; Boyd Thomes and Staff; 302 Harrington Hall.

1:00 - Tumor Clinic; Drs. Eder, Coe, and Lipschultz; Classroom.

1:00 - Psychiatry Grand Rounds; J. C. Michael and Staff.

Veterans Administration Hospital

7:30 - Anesthesiology Conference; Conference Room, Bldg. I.

8:30 - Surgery Staff Seminar; Medical Conference Room, Bldg. I.

9:30 - Infectious Disease Rounds; Drs. Hall, Zinneman, and Brown.

9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.

Tuesday, December 8 (Cont.)

Veterans Administration Hospital

10:30 - Surgery-Tumor Conference; L. J. Hay, J. Jorgens and Donn Mosser; Conference Room, Bldg. I.

1:00 - Review of Pathology, Pulmonary Tuberculosis; Conference Room, Bldg. I.

1:30 - Combined Medical-Surgical Chest Conference; Conference Room, Bldg. I.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III

3:00 - Psychosomatic Conference; C. K. Aldrich; Surgical Conference Room, Bldg. 43.

4:00 - Thoracic Surgery Problems; Conference Room, Bldg. I.

Wednesday, December 9

Medical School and University Hospitals

8:00 - 9:00 Roentgenology Surgical-Pathological Conference; Paul Lober and L. G. Rigler; Todd Amphitheater, U. H.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Surgery Case; O. H. Wangensteen, C. J. Watson, and Staffs; Todd Amphitheater, U. H.

12:30 - 1:30 Physiology 114B -- Transport Seminar; Nathan Lifson and M. B. Visscher; 214 Millard Hall.

12:30 - 1:30 Radioisotope Seminar; Underground Cobalt Unit, Hospital.

1:00 - 2:00 Dermatology Clinical Seminar; 300 North Clinic.

1:30 - 3:00 Pediatric Allergy Clinic; Albert V. Stoesser and Lloyd Nelson; W-211, U. H.

3:30 - 4:30 Dermatology Pharmacology Seminar; J. D. Krafchuk; 3rd Floor Conference Room, Heart Hospital.

4:30 - 5:50 Dermatology Infectious Disease Seminar; J. D. Krafchuk; 3rd Floor Conference Room, Heart Hospital.

4:30 - ECG Reading Conference; Staff Room, Heart Hospital.

5:00 - 6:00 Residents Lecture; Intestinal Obstruction; Grafton Smith; Todd Amphitheater, U. H.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Eustis Amphitheater, U. H.

5:30 - 7:30 Dermatology Journal Club and Discussion Group; Hospital Dining Room.

7:30 - 9:30 Dermatology Pathology Seminar; Review of Interesting Slides of the Week; Robert W. Goltz; Todd Amphitheater, U. H.

Ancker Hospital

8:30 - 9:30 Clinico-Pathological Conference; Auditorium.

12:30 - 1:30 Medical Journal Club; Library.

Minneapolis General Hospital

8:30 - 9:30 Obstetrical and Gynecological Grand Rounds; William P. Sadler and Staff; Station C.

9:30 - Pediatric Rounds; Max Seham; Stations I and J.

10:30 - 12:00 Medicine Rounds; Thomas Lowry and Staff; Station D.

Wednesday, December 9 (Cont.)

Minneapolis General Hospital (Cont.)

11:00 - Pediatric Seminar; Arnold Anderson; Classroom, Station I.

11:00 - Pediatric Rounds; Erling S. Platou; Station K.

12:15 - Pediatric Staff Meeting; Classroom, Station I.

1:30 - Visiting Pediatric Staff Case Presentation; Classroom, Station I.

2:00 - 4:00 Infectious Disease Rounds; Station D.

4:00 - 5:00 Infectious Disease Conference; Wesley W. Spink; Classroom.

Veterans Administration Hospital

8:30 - 10:00 Orthopedic X-ray Conference; E. T. Evans and Staff; Conference Room; Bldg. I.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker

9:00 - Gastro-Intestinal Rounds; Drs. Wilson, Zieve, Hay, Brakel and Nesbitt.

12:30 - X-ray Conference; J. Jorgens; Conference Room, Bldg. I.

4:00 - Combined Medical-Surgical Conference; Drs. Flink and Hay; Conference Room, Bldg. I.

5:00 - Medical Journal Club; Conference Room, Bldg. I.

7:00 p.m. Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, December 10

Medical School and University Hospitals

9:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

12:00 - 1:00 Medical Journal Club; Spontaneous Abortion; Jim Schlichting; 116 Millard Hall.

1:30 - 4:00 Cardiology X-ray Conference; Heart Hospital Theatre.

4:30 - ECG Reading Conference; James C. Dahl, et al; Staff Room, Heart Hospital.

5:00 - 6:00 Radiology Seminar; Radiation Therapy of Testicular Tumors; Robert J. Kurth; Eustis Amphitheater, U. H.

7:30 - 9:30 Pediatric Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hour; 206 Temporary West Hospital.

Ancker Hospital

8:00 - 10:00 Medical Grand Rounds; Auditorium.

Minneapolis General Hospital

9:30 - Neurology Rounds; Heinz Bruhl; Station I.

10:00 - Pediatric Rounds; Spencer F. Brown; Station K.

10:00 - Psychiatry Grand Rounds; J. C. Michael and Staff; Sta. H.

11:30 - 12:30 Clinical Pathological Conference; John I Coe; Classroom.

12:30 - 2:30 Dermatology Rounds and Clinic; Carl W. Laymon and Staff.

Thursday, December 10 (Cont.)

Minneapolis General Hospital (Cont.)

1:00 - Fracture - X-ray Conference; Dr. Zierold; Classroom.

1:00 - House Staff Conference; Station I.

Veterans Administration Hospital

8:00 - Surgery Grand Rounds; Conference Room, Bldg. I.

8:00 - Surgery Ward Rounds; Lyle Hay and Staff; Ward 11.

11:00 - Surgery-Roentgen Conference; J. Jorgens; Conference Room, Bldg. I.

1:00 - 3:00 Metabolic Disease Conference; Drs. Flink, Heller and Hoseth.

Friday, December 11

Medical School and University Hospitals

8:00 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Medicine Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:30 - 1:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Vascular Rounds; Davitt Felder and Staff Members from the Departments of Medicine, Surgery, Physical Medicine, and Dermatology; Out-Patient Department, Heart Hospital.

11:45 - 12:50 University of Minnesota Hospitals Staff Meeting; The Nutritional Role of Intestinal Micro-Organisms; K. R. Johansson; Powell Hall Amphitheater.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

1:30 - 2:30 Dermatology Grand Rounds; Presentation of Cases from Grouped Hospitals (University, Ancker, General and Veterans) and Private Offices; H. E. Michelson and Staff; Skin Clinic; W-312, U. H.

2:30 - 4:00 Dermatology Hospital Rounds; H. E. Michelson and Staff; Begin at Dermatology Histopathology Room, M-434, U. H.

3:00 - 4:00 Neuropathological Conference; F. Tichy; Todd Amphitheater, U. H.

4:00 - 5:00 124 Advanced Neurophysiology Lecture; Werner Koella and Ernst Gellhorn; 111 Owre Hall.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

4:30 - ECG Reading Conference; James C. Dahl, et al; Staff Room, Heart Hospital.

5:00 - Urology Seminar and X-ray Conference; Eustis Amphitheater, U. H.

Ancker Hospital

1:00 - 3:00 Pathology-Surgery Conference; Auditorium.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Wallace Lueck; Station J.

10:30 - Pediatric Surgery Conference; Oswald Wyatt; Tague Chisholm; Station I, Classroom.

Friday, December 11 (Cont.)

Minneapolis General Hospital (Cont.)

12:00 - Surgery-Pathology Conference; Dr. Zierold, Dr. Coe; Classroom.

1:00 - 3:00 Clinical Medical Conference; Thomas Lowry; Classroom, Station M.

1:15 - Pediatric X-ray Conference; Oscar Lipschultz; Classroom, Main Bldg.

2:00 - Pediatric Rounds; Robert Ulstrom; Stations I and J.

Veterans Administration Hospital

10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.

1:00 - Pathology Slide Conference; E. T. Bell; Conference Room, Bldg. I.

2:00 - Autopsy Conference; E. T. Bell and Donald Gleason, Conference Room, Bldg. I.

Saturday, December 12

Medical School and University Hospitals

7:45 - 8:50 Orthopedic X-ray Conference; W. H. Cole and Staff; M-109, U. H.

9:00 - 10:00 Infertility Conference; Louis L. Friedman, David I. Seibel, and Obstetrics Staff; Eustis Amphitheater, U. H.

9:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; Heart Hospital Amphitheater.

9:15 - 10:00 Surgery-Roentgenology Conference; L. G. Rigler, J. Friedman, Owen H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; Todd Amphitheater, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium.

Minneapolis General Hospital

8:00 - Urology Staff Conference; T. H. Sweetser; Main Classroom.

11:00 - 12:00 Medical - X-ray Conference; O. Lipschultz, Thomas Lowry and Staff; Main Classroom.

Veterans Administration Hospital

8:00 - Proctology Rounds; W. C. Bernstein and Staff; Bldg. III.

8:30 - 11:15 Hematology Rounds; Drs. Hagen and Fifer.

11:15 - 12:00 Morphology . . . . Dr. Aufderheide; Conference Room.

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* Indicates special meeting. All other meetings occur regularly each week at the same time on the same day. Meeting place may vary from week to week for some conferences.