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Iron Metabolism in Liver Disease

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I. IRON METABOLISM IN LIVER DISEASE

Robert B. Howard

Certain features of two instances of hemochromatosis, studied recently, have served to stimulate our interest in the problem of the metabolism of iron in liver disease. Because they present features of considerable interest, these cases will be briefly summarized before the broader problem of iron metabolism in other types of liver disease is taken up. They are to be presented in more detail in a future publication[1].

Case No. 1.

, a 62-year old white male, first noted the onset of weakness, tiredness, and loss of weight in 1942. The following year he first noted a mass in the right upper quadrant of his abdomen and shortly thereafter he was first seen at the University Hospitals. Physical examination revealed a slight bronzing of the skin of the entire body. The heart was slightly enlarged and the liver was markedly enlarged, but its surface was neither nodular or tender.

The urine gave a 4 plus reaction for sugar and was otherwise normal. Routine blood studies were normal. Liver function tests on this first admission were essentially normal except that the 24-hour excretion of urobilinogen in the urine was as high as seven milligrams on one occasion. The glucose tolerance curve was of the diabetic type. Liver biopsy confirmed the clinical impression of hemochromatosis.

The patient was placed on a diabetic diet and insulin and was followed in the Out-Patient Department. He was readmitted to the hospital in December, 1944, for reevaluation and repeat laboratory studies were essentially unchanged from those of the previous year. He continued to do well until February, 1946, at which time he was admitted to the University Hospitals for the third and final time. About a week before admission he developed what was thought to be a respiratory infection characterized by weakness and anorexia. He became gradually disoriented and ultimately comatose. Physical examination was essentially unchanged from that on the first admission except that he was comatose. The blood sugar was within normal limits and there was no laboratory evidence of acidosis or azotemia; nor was there anything to suggest adrenal insufficiency. Liver function studies showed an increase in the urobilinogenuria and the cephalin-cholesterol flocculation test was now 3 plus in 48 hours. The serum bilirubin, however, was not elevated. Spinal fluid was normal. Chest x-ray revealed only a slightly enlarged heart, and an electrocardiogram failed to give evidence of any acute myocardial process. Treatment consisted of supportive measures and included parenteral fluids, dextrose and amino acids as well as insulin in amounts sufficient to keep the blood sugar below 200 mgm. per cent. The patient failed to respond and expired four days after admission without having recovered consciousness.

On the day preceding his death, blood was drawn for serum iron determination. This value was found to be 4020 gamma per cent, representing a marked increase over normal. Unfortunately the procedure for the serum iron determination in use at that time required two days for completion; consequently, the patient had died by the time the result was known and the determination could not be repeated. Two simultaneously run control sera were studied, however, and both gave normal results.

Autopsy revealed, in addition to the usual features of hemochromatosis, a cholangioma in the caudate lobe of the liver and an adenocarcinoma of the common hepatic duct. Neither tumor had metastasized and there was nothing to suggest that either was immediately responsible for death. The immediate cause of death was, in fact, not entirely satisfactorily explained. The brain was examined by Dr. A. B. Baker who described focal areas of perivascular de-

myelinization which he felt might be related to liver disease. It is of interest that after the patient's death we discovered that his brother had died in 1941 of generalized peritorutis but that autopsy, in addition, had revealed hemochromatosis.

Comment

The case is that of a 62 year old man with hemochromatosis who died in a comatose state without the reason for the coma being definitely established. Terminally the serum iron was 4020 gamma per cent, a markedly elevated value. The literature contains scattered references to the serum iron level in hemochromatosis. Heilmeyer and Plotner[2] reported a value of 199 gamma per cent in their case while Moore, et al[3] found a value of 101 gamma per cent in theirs. Rath and Finch[4] have studied several cases and have found their serum iron values to be generally in the neighborhood of 200 gamma per cent, that is at or somewhat above the upper limit of normal. These authors also have observed markedly elevated values in terminal patients with the disease. He feels that this represents terminal necrosis of tissue with release of iron.

Case No. 2

,, a 43 year old physician, experienced dyspnea, cough and hemoptysis following a canoeing accident in early July, 1947. About a month later there occurred a transient episode of jaundice accompanied by anorexia, vomiting, diarrhea, and fever. Shortly thereafter the patient discovered that his liver extended to the level of his umbilicus. He was first seen at the University Hospitals on August 22, 1947 at which time his only complaint was epigastric fullness. Physical examination revealed a diffuse rather dark brown pigmentation, definitely more marked in exposed areas. Numerous "spider" nevi were seen over the thorax and upper arms. The heart showed moderate left ventricular enlargement. The liver was massively enlarged and the tip of the spleen was palpable on deep inspiration.

Routine examinations of the urine and the blood were normal. Fasting blood sugar was normal but the glucose tolerance curve was of the diabetic type and glucose was present in three of the five urine samples taken during the course of this test. Liver function tests revealed moderate impairment of function. Liver biopsy revealed hemochromatosis.

The diagnosis of hemochromatosis having been established, it was decided to treat the patient by repeated venesections in an attempt to remove the stored iron. This form of therapy had been suggested by Dr. Charles Davis and by Dr. William M. Balfour, both of whom had attempted it in patients with the disease. In both cases the bleedings had to be stopped because of failure of hemoglobin regeneration, plasma protein regeneration, or both. Accordingly, blood-letting was begun on September 3, 1947, and has been carried out more or less continuously since. The course of this therapy can be seen in the accompanying Table, No. 1. It will be seen that over this period of 27 months, 68,750 cc. of blood have been removed from the patient's circulation. The iron content of the blood thus removed was approximately 32 Gm.

Coincident with the institution of blood-letting the patient was placed on a low iron diet. Despite the removal of such large amounts of blood and a marked decrease in iron intake, the patient's hemoglobin remained at a level of approximately 13 Gm. per 100 cc. of blood over the entire period.

On this regime the patient has experienced subjective improvement. He has noted an increased feeling of well-being and more energy. There has been definite regression of cutaneous pigmentation. One year after beginning this treatment no measurable decrease in liver size had occurred. Liver function studies remained essentially unchanged within the first five months of treatment except that there was a slight alteration of the serum protein pattern toward more normal values. The latter is of particular interest in view of the large amount of protein re-

moved from the blood over this period. Liver biopsy was repeated one year following the institution of phlebotomy and we feel that the iron content of the liver decreased over that period of time. The patient, at the present time, maintains an active surgical practice.

Also of special interest in this case are the levels of the serum iron at various times during the course of treatment. Representative values are seen in Table No. 1. Prior to the institution of phlebotomy the serum iron was 420 gamma per cent, a high value but a not unexpected one in this disease. Seven repeat observations during the succeeding month ranged from 360 to 415 gamma per cent. No further determinations were made until January, 1948, four and one-half months after blood-letting was begun, when five different blood samples were drawn over a two-day period in connection with a radioactive iron absorption test. The iron content of these sera varied between 7,040 and 8,000 gamma per cent. Inasmuch as each of these samples was analyzed at least twice, and two of them three times, each with similar result, it is felt that this did not represent contamination but that the finding was valid. It is to be emphasized that the time that the serum iron had reached this greatly elevated value, the patient was feeling very well. This marked hyperferremia then was not, in this instance, a terminal event such as it was in Case No. 1 and in Rath and Finch's cases[4]. The exact explanation for this phenomenon is unclear; however, we feel that repeated venesections had mobilized such large amounts of iron from the body stores that hemoglobin regeneration, although sufficient to keep the hemoglobin level constant and relatively normal, was unable to utilize all of the iron thus made available and that iron therefore "overflowed" into the blood serum. It will be further noted that approximately a year after blood-letting was begun, the serum iron had decreased to 44 gamma per cent, a value generally associated with a moderate degree of iron deficiency. This finding suggests that initially mobilization of stored iron took place at a relatively rapid rate but that as the total amount of iron removed from the body increased the ease with which stored iron was mobilized decreased progressively until ultimately mobilization of stored iron lagged behind hemoglobin regeneration resulting in the relatively low value for serum iron. This is not intended to imply that phlebotomy had reduced the body iron stores to a normal, or even a near normal level. There is experimental evidence, however, which indicates that the most recently stored iron is most readily available and that iron stored in the more distant past is less easily mobilized[5]. We may, I think, hypothecate that in our patient we early removed the more recently stored iron leaving behind, perhaps in a more firmly bound state, iron which had been stored much earlier in life.

Comment: The case is that of a 43 year old physician with hemochromatosis who was treated by means of repeated venesections in an attempt to reduce the abnormal iron stores. Over a period of approximately 27 months, 68,750 cc. of blood containing 31.8 Gm. of iron have been removed. The result has been decrease in cutaneous pigmentation and subjective improvement but little or no objective evidence of improvement of liver function although recent studies in the latter regard are lacking.

We do not mean to imply that this should constitute the definitive therapy for hemochromatosis. Obviously it has many disadvantages. Furthermore, it is based on the premise the liver damage in this disease is a result of the deposition of iron in that organ. This viewpoint is accepted by many authors and recent reports on the production of so-called exogenous hemochromatosis in patients receiving multiple transfusions of blood for chronic anemia[6] would seem to bear out this concept. Certain data, however, suggest that such might not be the case. Attempts to produce hemochromatosis in animals, whether by means of repeated whole blood transfusions[7], induced hemolysis[8], or injection of iron compounds[9], have uniformly failed although iron has been deposited in the livers of such animals.

Probably of most significance in this regard are the studies on dietary hemochromatosis by Gillman, Gillman, and Mandelstam[10,11]. In their studies on pellagrinous South African natives they found that some livers contained marked fatty infiltration with or without fibrosis, others contained varying amounts of iron-containing pigment, and still others demonstrated both the cirrhosis and iron. There was, however, no relationship between the amount of iron and the degree of cirrhosis; there were some livers containing large amounts of iron in which no fibrosis was demonstrable. Such findings cast some doubt upon the ability of iron to stimulate connective tissue production.

For these reasons it was felt that studies of iron metabolism in other types of liver disease might be profitable, the thought being that liver disease persons might possibly influence iron absorption and deposition. Hyperferremia in acute hepatitis has been reported by Vahlquist[12] and by Laurell[13] who feel that the rise in serum iron is due to liberation of iron from damaged liver cells. Monasterio and Lattanzi[14] made observations on the serum iron in 57 cases of acute catarrhal jaundice and found values ranging from 166 to 359 gamma per cent. There was rough correlation between the severity of the disease and the height of the serum iron. These authors feel that the hyperferremia occurs as a result of the inability of the damaged liver to handle iron returned to it for storage and utilization by the normal hemolytic processes of the body.

Reports of serum iron values in cirrhosis of the liver are rather scant, and, in those available, information regarding the etiology of the cirrhosis and the stage of the disease is often lacking. Moore, et al, include one case of portal cirrhosis in a miscellaneous group of patients in whom serum iron determinations were carried out. The value was 66 gamma per cent. Laurell[13] studied six patients with cirrhosis with regard to iron metabolism. The values in these patients ranged between 39 and 184 gamma per cent. From additional data given in his report it is reasonably apparent that two cases were instances of post-infectious cirrhosis and the highest serum iron value 184 gamma per cent occurred in one of these patients. The second patient had a normal serum iron. A third patient had a strong alcoholic history and his serum iron was likewise normal. In the remaining three cases information was insufficient to determine possible etiology. Rath and Finch[4] studied eight cases of cirrhosis and found serum iron values ranging between 65 and 142 gamma per cent. Two of these patients were stated to have "cirrhosis with hepatitis", the remainder "cirrhosis". None of them showed abnormal levels of serum iron.

PRESENT STUDY

Iron metabolism was studied in 31 patients with various types of parenchymal liver disease. Serum iron determinations were carried out according to a modification of the method of Barkan and Walker[15]. Our average normal value in 28 control determinations is 121 gamma per cent, the extremes being 65 and 216 gamma per cent. Multiple laboratory tests of liver function were carried out in all patients and in all revealed evidence of diffuse hepatic disease. Additional confirmation of the diagnosis in the form of liver biopsy or autopsy was obtained in 25 of the 31 cases. Several patients were subjected to the liver biopsy procedure more than once. Many of these sections were specifically stained for iron by means of the Prussian blue reaction.

Results

Pertinent data concerning these patients is presented in Table No. 2. The results of the serum iron determinations are given in graphic form in Chart No. 1. In each instance only the first serum iron determination made is charted on the graph. In certain instances serial determinations were made and these results will be discussed subsequently. Twelve patients were considered to have alcoholic

cirrhosis and these are represented by the open circles. In this group only two initial serum iron determinations were above 65 gamma per cent. These two exceptions were 78 and 316 gamma per cent respectively. These two cases were of special interest and they will be discussed later with the group in which serial determinations were made. One case of cirrhosis in which there was an equivocal history of alcoholism, represented by the cross-hatched circle on the chart, had a serum iron level of 75 gamma per cent. One case of Wilson's disease or hepato-lenticular degeneration had a value of 33 gamma per cent.

The remaining 17 patients represent instances of acute infectious hepatitis, post-infectious cirrhosis, cirrhosis associated with ulcerative colitis, or idiopathic cirrhosis. They are grouped together as non-alcoholic hepaitc disease in the chart and are represented by the letter X on the chart. Only 3 individuals in this group had initial serum iron levels below 100 gamma per cent. One of the latter suffered from severe and prolonged bleeding from esophageal varices and it would be expected that blood loss would ultimately reduce body iron stores and thus produce hypoferremia even in the presence of a condition which might otherwise tend to elevate the serum iron value. Another case in this group of non-alcoholic hepatic disease with serum iron value below 100 gamma per cent was a young woman who had almost completely recovered from a mild episode of infectious hepatitis at the time the test was made.

Of six cases with values between 100 and 160 gamma per cent, two are best classified as "cholangiolitic cirrhosis" with liver function tests indicating relatively good preservation of hepatocellular function. A third case, with a value of 123 gamma per cent, was also one which was thought to have had "cholangiolitic cirrhosis" of long standing stemming from an episode of infectious hepatitis several years previously. A cholecysto-gastrostomy had been performed during the course of this illness and following this the patient was subject to repeated episodes of chills and fever. The patient died in hepatic coma and autopsy revealed cirrhosis of the liver and pigmented common duct stones. Whether or not the latter were primary or secondary to the cirrhosis is controversial. It is possible that in this instance chronic cholangitis may have accounted for the relatively low serum iron value as it is known that chronic infection does reduce the serum iron[16]. The fourth and fifth cases in this group seemed to be clear-cut instances of non-alcoholic cirrhosis. The former had serum iron values of 128 and 141 gamma per cent on different occasions and the latter a value of 135 gamma per cent. The sixth was a patient with so-called Banti's disease who had suffered repeated hematemeses.

The remaining eight cases of non-alcoholic hepatic disease all had serum iron values above 160 gamma per cent. Four patients in this group died in hepatic coma. Their serum iron determinations were 160, 171, 245 and 325 gamma per cent respectively. The highest value, 325 gamma per cent, occurred in a patient with acute hepatitis, presumably infectious which progressed rapidly to acute yellow atrophy of the liver. The highest value observed among the patients in this group who survived was 262 gamma per cent. This occurred in a young man, age 21, who was admitted to the hospital with a diagnosis of brucellosis. The latter diagnosis was confirmed by blood culture and a liver biopsy revealed characteristic granulomata. The patient was started on aureomycin therapy and shortly thereafter he developed chills and fever and still later jaundice. At the height of the jaundice, 6.1 mgm per cent serum bilirubin, the serum iron was 262 gamma per cent. Recovery was uneventful.

Results of serial determinations of serum iron: Repeated determinations of serum iron were carried out in four patients in the alcoholic group at various times in the course of their illnesses. Inasmuch as these findings are of interest in relation to those values in the alcoholic group above 65 gamma per cent

brief resumes of their histories will be given. All had strong histories of alcoholism.

Case No. 28. , a 38 year old female was admitted with intense jaundice, anorexia, and a clinical picture resembling delirium tremens. Liver biopsy revealed a marked fatty cirrhosis. Serum bilirubin was 28.2 mgm % total and serum iron 316 gamma %. One month later after treatment with intravenous fluids and a high carbohydrate, high protein diet, the clinical condition was much improved and the jaundice markedly decreased. Liver biopsy at this time again revealed fatty cirrhosis but with much less fat in the specimen than in the previous one. Serum bilirubin at this time was 2.8 mgm % total and serum iron 36 gamma %. One week after this the serum iron was 58 gamma %.

Case No. 21, ., a 76 year old male was admitted with a 6 month history of weakness, anorexia, and ascites. He was considered to be in impending hepatic coma on admission, although he did respond to questions and to noxious stimuli. The initial serum bilirubin was 1.7 mgm % total and the serum iron 78 gamma %. Five days later he was completely comatose. The serum bilirubin remained unchanged but the serum iron had risen to 160 gamma %. He expired shortly thereafter.

Case No. 26.

. a 72 year old white male was admitted primarily because of roentgenological evidence of a lung tumor. He had had vague abdominal distress and abdominal swelling for an indefinite period. Liver function tests indicated marked liver damage. The initial serum iron, taken at a time when the serum bilirubin was 22.8 mgm %, was 46 gamma %. Five days later he was more somnolent and his condition was generally thought to have deteriorated although he was not comatose. At this time the serum bilirubin was 24.8 mgm % and the serum iron 95 gamma %. He expired about three weeks later but no further serum iron determinations were obtained. Unfortunately autopsy was not permitted. Histological proof of cirrhosis is lacking in this case and it might be argued that the terminal picture was due to a pulmonary carcinoma with metastases. However, the strong alcoholic history plus laboratory evidence suggesting diffuse hepatic disease makes us feel that this was an instance of alcoholic cirrhosis.

Case No. 31

A 46 year old female was admitted because of epigastric fullness and jaundice. Liver function studies indicated marked impairment of function. Initial serum bilirubin was 17.7 mgm % total and the serum iron 30 gamma %. Several days after this the patient lapsed into coma. Unfortunately no serum iron determination was done at this time. She was treated intensively with intravenous fluids and plasma and improved to the extent that she regained consciousness, was eating, and even reading the newspapers. At this time the serum iron was 36 gamma % and the serum bilirubin 26 mgm % total. Within the next week, however, her condition again deteriorated. After she had become comatose for the second time the serum iron was found to have risen to 113 gamma % with no essential change in the level of serum bilirubin. She expired within the next three days and autopsy revealed cirrhosis of the liver. Terminally this patient had hematemeses and it is interesting to note that despite this bleeding her serum iron rose in association with the development of hepatic coma.

It would appear, then, that in this group of patients improvement in liver function was accompanied by a decrease in serum iron levels and deterioration of function by a rise.

Relation of serum iron to blood loss: As has been previously mentioned two patients in the non-alcoholic group suffered chronic blood loss due to bleeding esophageal varices. One patient in the alcoholic group terminally had hematemesis. In the remainder of the patients the stool benzidine test was frequently positive; however, this occurred with

equal frequency in the alcoholic and non-alcoholic groups. A mild degree of anemia occurred in but four of the remaining patients and in three of these it was of the macrocytic type often associated with liver disease. Again these cases were equally distributed between the alcoholic and non-alcoholic groups. In short, we felt that, aside from the three patients with severe bleeding from esophageal varices, the serum iron was not related to hemoglobin level.

Relation of serum iron to serum bilirubin level: The accompanying Chart No. 2 shows the serum bilirubin values plotted against those for serum iron in the alcoholic and non-alcoholic groups. While there may be a slight tendency for high serum iron values to be associated with high serum bilirubin values, the correlation is definitely of a low order. There are, for example, three instances where the serum bilirubin was over 16 mgm. per cent with serum iron levels below 50 gamma per cent and four instances of serum iron values above 160 gamma per cent with serum bilirubin below 6.0 mgm. per cent. We feel that what correlation does exist is due to the fact that, in general, a high level of serum bilirubin is associated with more severe hepatic disease and that the elevation of serum iron is not due to regurgitation of bile per se. Additional evidence in favor of this concept was obtained by the measurement of the serum iron in three instances of jaundice due to extrahepatic biliary obstruction. Two patients had carcinomatous obstruction with intense icterus, the third calculous obstruction with moderate jaundice. Their serum iron values were 100, 97, and 55 gamma per cent respectively.

Relationship of iron staining material in the liver to serum iron: Liver sections, either biopsy or autopsy material, from 11 patients were studied with regard to iron content by means of the iron stain. Seven of these patients were classified as non-alcoholic hepatic disease and four were instances of alcoholic cirrhosis. Two sections, obtained at different times during the patient's course, were available in three of the alcoholic group and in one of the non-alcoholic group. All specimens were stained simultaneously using the same technic. In only three of the 15 sections thus studied was there evidence of iron-containing material. The liver of Case No. 12 who died with the picture of acute yellow atrophy of the liver and who had a serum iron value of 325 gamma per cent showed a moderate amount of rather finely granular iron-containing material throughout the hepatic parenchymal cells. The biopsy specimen of Case No. 8 obtained in February, 1948, showed a similar moderate degree of iron pigment in the hepatic parenchymal cells. The autopsy specimen in the same patient, obtained in May 1949, showed an extremely marked disorganization of liver structure so that identification of the hepatic cells was difficult. However, in the remaining clusters of hepatic cells a similar, but less marked iron pigmentation was apparent. This patient had a severe chronic hepatitis progressing to cirrhosis with death in hepatic coma. The serum iron was 245 gamma per cent. All other sections showed no traces of iron by this histochemical technic. Thus, iron was demonstrable in the liver in the two fatal instances of non-alcoholic liver disease with the highest serum iron levels. Iron-stained sections from the patient with hepatitis associated with brucellosis, whose serum iron was 262 gamma per cent, were not available.

Summary and Conclusions

1. Two instances of hemochromatosis are presented. The first patient exhibited a remarkable hyperferremia terminally. The second was subjected to repeated venesections, 68,750 cc. of blood containing over 31 Gm. of iron being removed over a period of 27 months. Decrease of pigmentation, subjective improvement, and questionable decrease in liver size occurred on this regime. During the course of this therapy, marked hyperferremia was noted associated with no change in the patient's clinical condition.

2. Serum iron determinations were carried out in 12 patients with alcoholic cirrhosis, one patient with questionable alcoholic cirrhosis, and 18 patients with non-alcoholic diffuse liver disease. The serum iron tended to be low, i.e., below 65 gamma per cent in the alcoholic group and higher, generally above 100 gamma per cent and often reaching very high values, in the non-alcoholic group. Except in three patients with massive gastrointestinal bleeding, there was no apparent relationship of serum iron levels to blood loss or to hemoglobin levels. There was only slight correlation of serum iron and serum bilirubin levels.

3. A single determination of serum iron is of no value in assessing liver function because the serum iron level is determined by many varying factors; however, it would appear that in a given individual with diffuse liver disease, a rising value for serum iron is indicative of progressive impairment of hepatic function. Further study of serum iron levels in serial fashion throughout the course of various types of hepatic disease is needed.

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Grateful acknowledgment is made for the technical assistance of Mrs. Evelyn Woltjen who carried out the major portion of the laboratory determinations.

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Table I

Iron Metabolism Studies
Patient B. U.

Date	9-3-47	10-4-47	12-9-47	1-23-48	3-19-48	9-15-48	12-7-48	2-17-49	11-15-49
Hemoglobin in gm/100 cc.	14.9	12.5	15.5	13.7	13.3	13.0	14.0	12.25	14.4
RBC in millions per cu. mm.	4.57	3.52	3.88	3.62	3.36	3.65	4.45	4.02	4.56
Reticulocytes %	0.5	4.0	2.0	3.6	4.4	4.3	2.2	3.0	3.0
Serum iron in gamma/100 cc.	420	362		8000		44			
Blood removed, cum. total in l.	1.05	4.30	9.43	14.93	21.90	47.20	51.60	59.60	68.75
Iron removed, cum. total in GM.	0.52	1.86	4.32	6.85	10.86	21.83	23.80	27.30	31.77

Table 2

Tabulation of Data on Patients with Alcoholic and Non-Alcoholic Hepatic Disease

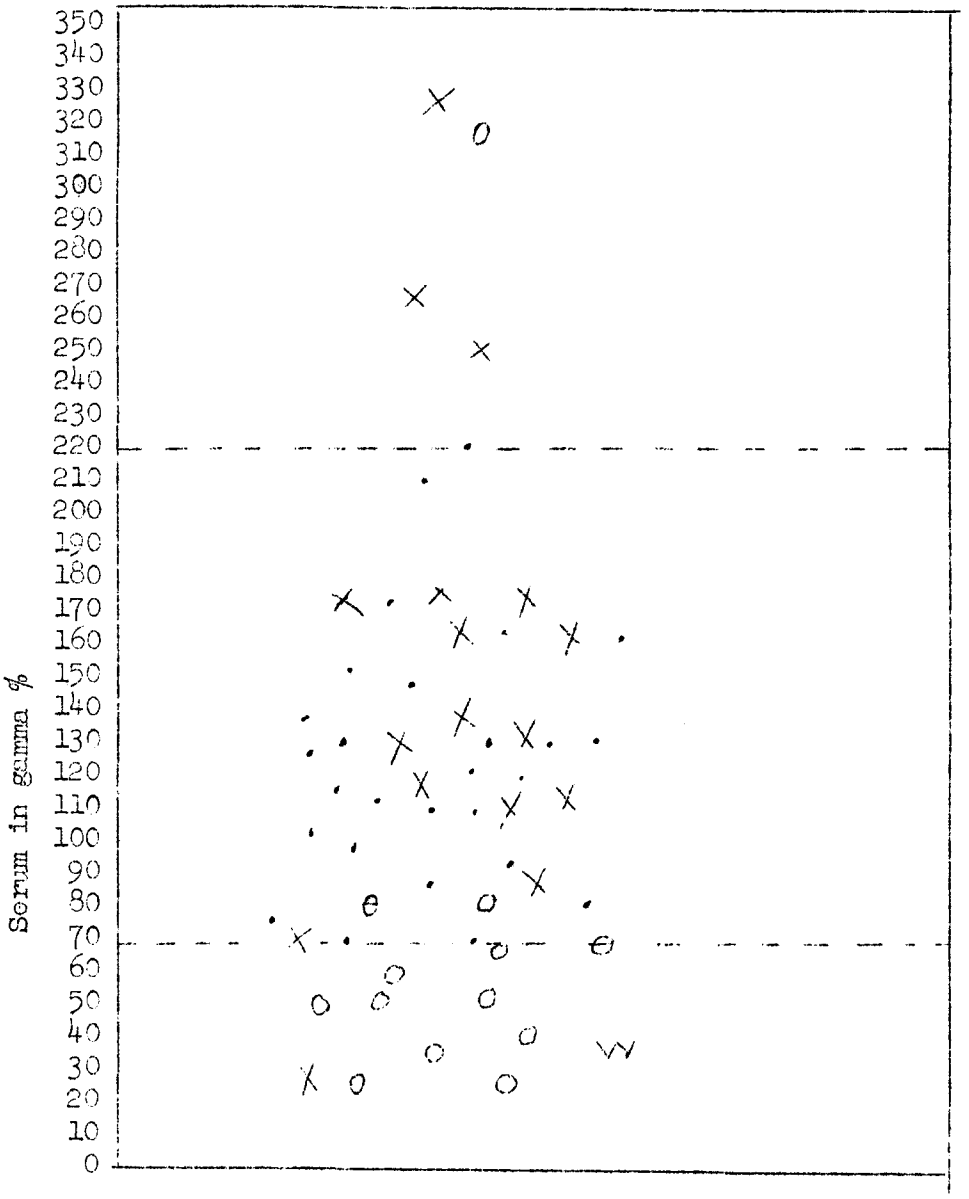
No.	Patient	Sex	Age	Type of Disease	Date	Serum Iron % gamma	Serum bilirubin total -mgm. %	Condition	Bleeding	Iron in Liver
3		M	19	Infectious hepatitis	8-16	160	4.0	Good	0	
4		M	70	Non-alcoholic cirrhosis	9-29 10- 6 10-13	66 66 108	0.8	Fair Fair Fair	0	
5		F	58	Recurrent cholangitis Probable biliary cirrhosis	10-20	123	20.5	Poor	0	
6		M	21	Hepatitis with brucellosis	3- 6	262	6.1	Fair	0	
7		M	26	Infectious hepatitis	4- 5	167		Fair	0	
8		M	44	Post-infectious cirrhosis	4- 5 4-11	245 224		Poor Poor	0	+
9		F	53	"Cholangiolitic" cirrhosis	5-12	108	13.0	Fair	0	0
10		F	26	Idiopathic cirrhosis	4-28	22	4.8	Poor	+	
11		F	18	Non-alcoholic cirrhosis	11-9 5-5	128 141	5.8 7.8	Fair Fair	0	0
12		M	60	Infectious hepatitis with acute atrophy	7-25	325	41.0	Poor	0	+
13		M	58	Hepatitis	7-20	160		Poor	0	
14		F	62	Idiopathic cirrhosis	5-14	170	5.5	Fair	0	0
15		F	47	"Cholangiolitic" cirrhosis	10-27	114	13.6	Fair	0	0
16		M	31	Cirrhosis with ulcerative colitis	11-17	171	45.9	Poor	0	0
17		M	29	"Banti's Syndrome"	8-17	108		Fair	+	
18		F	23	Acute infectious hepatitis, mild	8-17	82		Convalescent	0	
19		M	76	Non-alcoholic cirrhosis	11- 3	135	1.5	Fair	0	
20		M	42	Alcoholic cirrhosis	8-16	20	5.5	Fair	0	0
21		M	76	Alcoholic cirrhosis	10-20 10-25	78 160	1.7 1.7	Impending coma Coma	0	

Table 2 (Cont.)

No.	Patient	Sex	Age	Type of Disease	Date	SI	SB	Condition	Bleeding	Iron in Liver
22		M	49	Alcoholic cirrhosis; heart disease	5- 5	49		Poor	0	
23		M	46	Alcoholic cirrhosis	5-26	55	1.3	Fair	0	
24		M	43	Alcoholic cirrhosis	11- 9	46	0.8	Good	0	0
25		F	51	Alcoholic cirrhosis	11-16	65	6.2	Fair	0	0
26		M	72	Alcoholic cirrhosis; lung tumor	12-22 12-27	46 95	22.8 24.8	Fair Poor	0	
27		M	48	Alcoholic cirrhosis	2- 3	35	0.5	Fair		
28		F	35	Alcoholic cirrhosis	2-16 3-17 3-21	316 36 58	28.2 2.8 1.6	Poor Much improved Same	0	0
29		M	50	Alcoholic cirrhosis	8-17	20		Fair	0	
30		M	56	Alcoholic cirrhosis; porphyria	11- 3	65	0.7	Fair	0	
31		F	46	Alcoholic cirrhosis	10-25 11-3 11-10	30 36 113	17.7 26.0 25.5	Prior to coma Out of coma Again in coma	0 Terminal +	
32		F	56	Questionable alcoholic cirrhosis	8-2	75	0.9	Fair	0	
33		F	17	Wilson's disease	2-11	33	1.0	Fair	0	

Chart No. 1

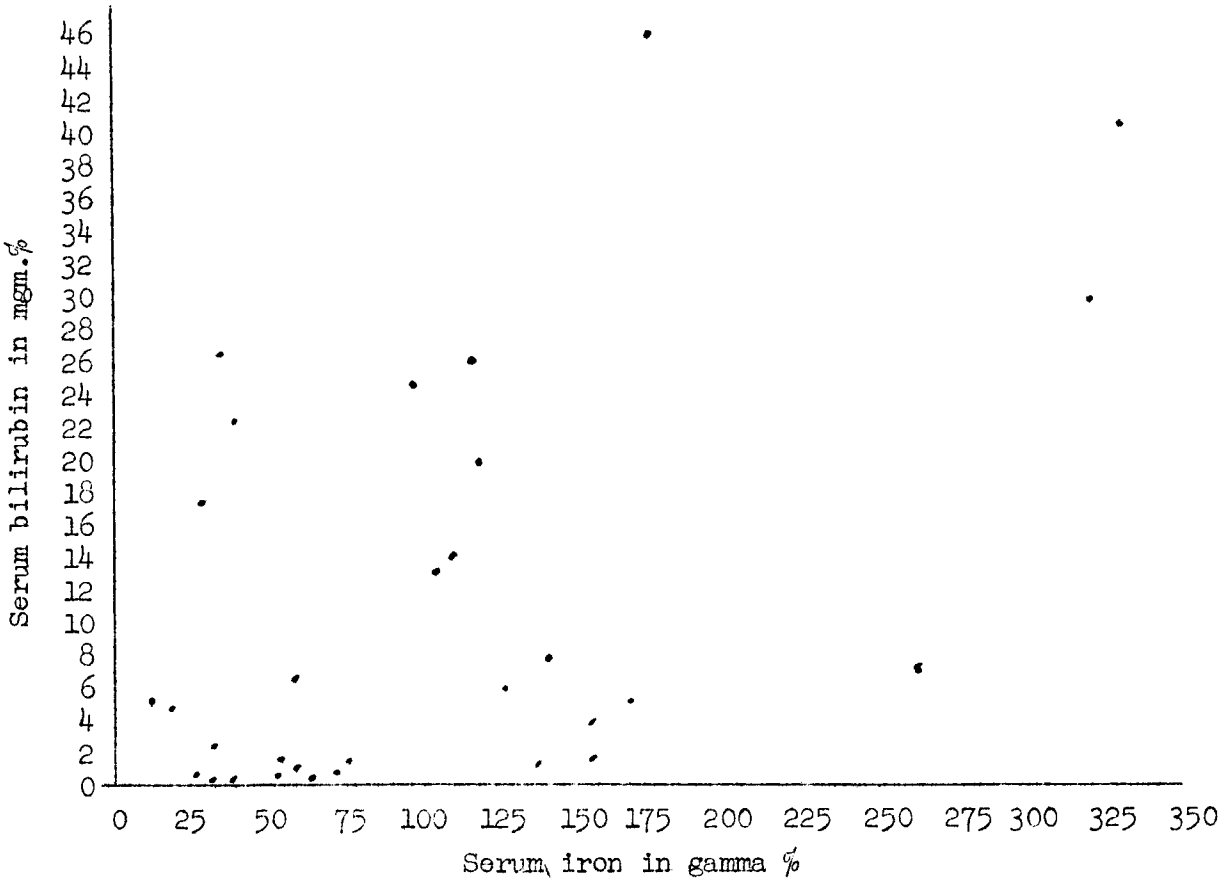
Serum iron in 28 controls and 31 patients with diffuse hepatic disease



. - Control
O - Alcoholic cirrhosis
X - Non-alcoholic hepatic disease
W - Wilson's disease

Chart No. 2

Serum iron values plotted against serum bilirubin values, demonstrating very slight correlation.



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13. Laurell, C. B.
Studies on the Transportation and Metabolism of Iron in the Body.
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14. Monasterio, G. and Lattanzi, A.
Il ricambio del ferro nell'ittero catarrale.
Rassegna di Fisiopatologia Clinica e Terapeutica 15:1, '43.

15. Barkan, G. and Walker, B. S.
Determination of Serum Iron with o-Phenanthroline.
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II. MEDICAL SCHOOL NEWS

Coming Events

January 5-7 - Continuation Course in Cardiovascular Diseases for General Physicians.

January 6 - Clarence M. Jackson Lecture, Tinsley R. Harrison, Southwestern Medical College, Dallas, Texas - "The Evaluation of Cardiac Murmurs" - Medical Science Amphitheater, 8:00 p.m.

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Cardiovascular Diseases

A course in Cardiovascular Diseases for general physicians will be presented at the Center for Continuation Study January 5-7, 1950. The course will bring to our campus Dr. Tinsley R. Harrison, Professor of Medicine of Southwestern Medical College. During his visit to our campus, Dr. Harrison will also deliver the annual Clarence M. Jackson lecture on the evening of Friday, January 6, at 8:00 p.m. Dr. Harrison's subject for the Jackson lecture will be "The Evaluation of Cardiac Murmurs."

The continuation course is sponsored by the Minnesota Heart Association, the Minnesota State Medical Association, and the Minnesota Department of Health.

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Minnesota Medical Foundation Meets

The annual meeting of the Minnesota Medical Foundation was held Friday, December 9, in the Campus Club, Coffman Memorial Union. Dr. Donald J. Cowling was the principal speaker and delivered an address on the subject, "Our Universities and Colleges." Dr. Erling S. Platou, past President and one of the founders of the Foundation, described the events which lead to the creation of the Foundation 10 years ago.

Drs. Karl Anderson and E. T. Bell of Minneapolis and Dr. Vernon Smith of St. Paul were elected for 4-year terms to the Board of Trustees. Dr. G. N. Aagaard was elected to serve the unexpired term left vacant by the resignation of Dr. Maurice B. Visscher.

Dr. Owen H. Wangensteen, President of the Foundation, reported that Mrs. Grace B. Dayton, Mrs. Ida B. Williams, Mr. John C. Benson, Mr. Charles A. Ward, and Mr. I. A. O'Shaughnessy had been named patron members of the Foundation. Amendments to the by-laws of the Foundation, which were adopted, permit the expansion of the Board of Trusteee to 24 members from its present number of 12.

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E. T. Bell Fund

Mr. Stanley Wenberg, Director of the Greater University Fund, reported on the progress of the E. T. Bell Fund at the recent annual meeting of the Minnesota Medical Foundation. A total of $27,015 has now been received or pledged since the fund honoring Dr. Bell was announced. The E. T. Bell Fund, sponsored by the Minnesota Medical Foundation and a special project of the Greater University Fund, was created to honor Dr. E. T. Bell, Professor Emeritus of Pathology. The purpose of the Fund is to equip and maintain a pathological museum in the new Mayo Memorial building. The museum, to be called the E. T. Bell Pathology Museum, will serve an important function in undergraduate, graduate, and postgraduate medical education.

Mr. Wenberg's report indicated that the 3-year goal of $100,000 appears to be possible with continued effort on the part of all Foundation members and medical school alumni. There has been a good response to a suggestion by Dr. Owen H. Wangensteen that all medical alumni pledge $100 or more to this project honoring one of Minnesota's most beloved teachers. Many contributors have taken advantage of the opportunity to give a portion, approximately 1/3, of their gift at this time and pledge the remainder in a 2-year period. Students and friends of Dr. Bell are reminded that gifts sent prior to December 31 may be deducted from 1949 income tax.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

December 18 - December 24, 1949

No. 269

Sunday, December 18

9:00 - 10:00 Surgery Grand Rounds; Station 22, U. H.

10:30 - 11:00 Surgical Conference; Cholinesterose in the Differential Diagnosis of Jaundice; Jose Orellana; M-109, U. H.

Monday, December 19

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

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; M-109, U. H.

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

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

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

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Classroom, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

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

4:00 - Public Health Seminar; Subject to be announced; 113 Medical Science.

4:00 - Pediatric Seminar; Disorders of Sleep; A. Jensen; 6th Flr.W., Child Psychiatry, U. H.

5:00 - 5:50 Clinical-Medical-Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy, O. J. Baggenstoss and Staffs; M-109, U. H.

Tuesday, December 20

8:15 - 9:00 Roentgenology-Surgical-Pathological Conference; Craig Freeman and L. G. Rigler; M-109, U. H.

8:30 - 10:20 Surgery Conference; Small Conference Room, Bldg. I, Veterans Hospital.

Tuesday, December 20 (Cont.)

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

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell; Veterans Hospital.

12:30 - Pediatric-Surgery Rounds; Drs. Stoesser, Wyatt, Chisholm, McNelson and Dennis; Sta. I, Minneapolis General Hospital.

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

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

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

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

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

8:00 - Minnesota Pathological Society; Anoxia and Convulsion. A Contribution to Hypothalamic Cortical Relations; Ernst Gellhorn; Medical Science Amphitheater.

Wednesday, December 21

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans Hospital.

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

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

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; E-101, U. H.

Thursday, December 22

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink & Lyle Hay; Veterans Hospital.

Thursday, December 22 (Cont.)

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

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Classroom, Minneapolis General Hospital.

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

Friday, December 23

8:30 - 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.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Veterans Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser and Staffs; Minneapolis General Hospital.

12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.

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

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

4:00 - 5:00 Clinical Pathological Conference; A. B. Baker; Todd Amphitheater, U. H.

4:00 - 5:00 Electrocardiographic Conference; George N. Aagaard; 106 Temp. Bldg., Hospital Court, U. H.

Saturday, December 24

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; M-109, U. H.

8:00 - 9:00 Pediatric Psychiatric Rounds; Reynold Jensen; 6th Floor, West Wing, U. H.

Saturday, December 24 (Cont.)

8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Small Classroom, Minneapolis General Hospital.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 11:30 Surgery-Roentgenology Conference; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

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