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The Liver in Ulcerative Colitis

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INDEX

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I. THE LIVER IN ULCERATIVE COLITIS

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The material presented in this staff bulletin is in the nature of a preliminary report. We wish to call attention to the association of liver disease in patients with ulcerative colitis. The existence of such an association has been appreciated by the staff of this hospital for a number of years. The occurrence of cirrhosis in such patients, the association of fatty liver in acute and chronic forms of the disease and the results of liver biopsies in a small number of patients with ulcerative colitis form the basis for this report.

The association of chronic ulcerative colitis and hepatic insufficiency received attention from clinicians in Argentina and in France during the thirties. That literature has been reviewed in recent reports[1,2,3,4]. Comfort, Bargen and Marlock[1] in 1938 presented the clinical data of four cases in which hepatic insufficiency was associated with colitis gravis.

Cirrhosis as a complication of chronic ulcerative colitis has been discussed by Tumen, Monaghan and Jobb[2]. In 1947 they described 5 cases of cirrhosis among 151 patients with chronic ulcerative colitis seen on the wards of the Graduate Hospital of the University of Pennsylvania. In four of the five patients the diagnosis of cirrhosis was established by peritoneoscopy.

The occurrence of hepatic insufficiency in ulcerative colitis, based on experiences at the University of Michigan, has been described by Pollard and Block[3]. Their data dealt with 70 cases of nonfatal and 17 cases of fatal ulcerative colitis seen at the University Hospital during a five year period. Four cases of cirrhosis associated with chronic ulcerative colitis were reported; in two instances the cirrhosis had its onset prior to the colitis and was not thought to be etiologically related to the bowel disorder. In the fatal cases, 11 of the 17 exhibited hepatic pathology; a degenerative fatty infiltration was the most common abnormality observed.

This general subject has been recently reviewed by Jones[4] and by Jones, Baggenstoss and Bargen[5] from the Mayo Clinic. The incidence of liver disease and the types of pathologic changes seen in the liver in fatal cases of ulcerative colitis were determined. Their study comprised data from 91 autopsy examinations performed during the period of January 1, 1936 to September 30, 1949. Fatty change of the liver, in moderate to severe degree, was observed in 47 of the 91 cases (52 percent). Frank cirrhosis was found in only 3 of 91 cases of chronic ulcerative colitis. The authors comment that this incidence was no higher than that observed in routine necropsies at the Mayo Clinic.

The occurrence of cirrhosis in young patients with chronic ulcerative colitis has been noted in four case records of the Massachusetts General Hospital as reported in the Weekly Clinicopathological Exercises between 1944 and 1949[6,7,8,9]. In each instance, death was due to cirrhosis. The patients were as follows:

1944 Case: Female; colitis, 9 years; died, cirrhosis - age 19
1948 Case: Male; colitis, 5 years; died, cirrhosis - age 18
1949 Case: Female; colitis, 4 years; died, cirrhosis - age 22
1949 Case: Male; colitis, 15 years; died, cirrhosis - age 29

Material Studied

The data presented in this report has been taken from the case records of 270 patients examined and treated at the University of Minnesota Hospitals during a period of 17 years (Jan. 1, 1936 to Nov. 1, 1951).

The merits of various forms of therapy,

TABLE I

STATUS OF THE LIVER IN 16 FATAL CASES OF IDIOPATHIC ULCERATIVE COLITIS

CASE	YEAR OF DEATH	SEX	AGE AT DEATH	DURATION OF COLITIS	CLINICAL COMMENTS	LIVER AT NECROPSY
A-1	1936	F	49	?	Perforation colon; existence ulcerative colitis unrecognized.	Fatty (severe)
A-2	1937	F	20	30 days	Fulminating course, perforation and peritonitis.	Fatty (severe); central necrosis
A-3	1939	M	63	6 mo.	Severe colitis; ischio rectal abscess	Fatty (moderate)
A-4	1942	F	13	3 years	Mild diarrhea; severe pyoderma; terminal jaundice and coma.	Acute yellow atrophy
A-5	1942	M	16	30 days	Fulminating course	Fatty (extreme; 3120 gm.)
A-6	1944	M	16	8 years	Severe colitis	Fatty (extreme; 2600 gm.)
A-7	1944	F	21	15 years	Moderately severe colitis; recurrent ascites 11 months prior to death.	Cirrhosis, minimal myocarditis, severe
A-8	1944	M	43	2 years	Pulmonary embolism 8 days P.O. (ileostomy)	Fatty (moderate)
A-9	1944	F	55	6 mo.	Coronary thrombosis	Normal
A-10	1946	F	26	3 years	Ileostomy 1943; colectomy and ileo-proctostomy Sept. 1946; small bowel obstruction Dec. 1946.	Fatty (extreme; 2610 gm.)
A-11	1947	F	27	3 mo.	Fulminating course	Fatty (extreme; 2000 gm.)
A-12	1947	F	25	1 year	Ileostomy in March 1947 (unsatisfactory-slough). Recto-vaginal fistula developed; died after attempted revision of ileostomy.	Fatty (severe; 2240 gm.)
A-13	1947	F	35	10 years	Died, pulmonary edema; followed plasma infusion reaction during pre-operative preparation.	Fatty (moderate; 1920 gm.)

A-14	1948	M	51	15 years	Ileostomy, 1945; colectomy and ileo-proctostomy, 1946 (ca. of descending colon in surgical specimen) Jaundice, June 1947; cholecystectomy aug. 1947 (no calculi); bowel obstruction (carcinoma) 1948.	Hepatitis (mild, 2500 gm. ?-toxic ?-"secondary" type of inflammation)
A-15	1950	F	15	1 year	Onset May 1949; vagotomy, June 1949; diarrhea continued; readmitted July 1950, died, suddenly, Sept. 1, 1950.	Fatty (extreme; 1700 gm.)
A-16	1951	M	17	2 mo.	Died, under anesthesia, when colectomy attempted.	Normal

the incidence of carcinoma, the incidence of complications and the mortality rate in this series will be reported separately by Dennis and Karlson[10].

The diagnosis of idiopathic ulcerative colitis was established in each patient in the series by clinical, x-ray and proctoscopic examinations. The clinical and pathological data of 39 patients with particular reference to the status of the liver is considered in this report. Histologic data (biopsy or autopsy) was available in 38 of the cases.

Results

The appearance of the liver at autopsy in 16 fatal cases of acute and chronic ulcerative colitis is presented in table I. Autopsy findings on 5 additional cases are presented in table II.

The frequent occurrence of fatty infiltration of the liver, often of severe degree, is in accord with the observations of others[3,5]. Most of the patients exhibiting severe fatty change of the liver at necropsy had a severe form of colitis that proved fatal in from one to twelve months (cases A-2, A-3, A-5, A-11 and A-15). The absence of any liver pathology in case A-16 is noteworthy in view of the rapid and progressive form of the colitis and the occurrence of sudden death, the exact cause of which could not be determined on the basis of the autopsy findings.

The occurrence of acute necrosis (acute yellow atrophy) in case A-4 may have been an unrecognized instance of rapidly fatal viral hepatitis. In 1942, the existence of such a disorder as homologous serum hepatitis was not appreciated. This child received a number of blood transfusions during the four months preceeding the onset of jaundice.

The clinical features of case A-7 were strongly suggestive of cirrhosis. The patient was markedly retarded in growth and and development. The continued accumulation of ascitic fluid required frequent paracenteses during the final year of her life. The physical findings did not suggest serious cardiac disease since the only abnormality observed was a harsh

apical systolic murmur. In view of the anemia (Hb 4.4 gm.) and the upward displacement of the diaphragms, the murmur was not considered significant. Although jaundice was absent, bio-chemical evidence suggestive of liver dysfunction was observed during life. At autopsy, a remarkable dilatation of the heart chambers was observed. No hypertrophy existed, the valves were normal and no congenital defects were present. Microscopic examination revealed a diffuse necrosis of the muscle fibers and a marked lymphocytic exudate throughout the myocardium. The pathologic diagnosis was chronic myocarditis of unknown etiology. The liver weighed 800 grams; there was no gross evidence of cirrhosis. Microscopic examination revealed a periportal fibrosis with lymphocytic infiltrate in the portal spaces. A few areas of the liver showed changes suggesting a mild portal cirrhosis but this was not uniform. Although the recorded pathologic diagnosis was chronic hepatitis and portal cirrhosis, this interpretation may be open to question.

The data of 10 cases of cirrhosis associated with chronic ulcerative colitis is given in table II. With the exception of case C-1, the diagnosis of cirrhosis was confirmed by biopsy or autopsy examination. The pertinent clinical data of each case follows:

Case C-1

. - Female - The patient developed ulcerative colitis in 1921 at the age of 40 years. She was admitted to the medical service for treatment of active colitis in 1941; hepatomegaly and diffuse pigmentation of skin were observed. Conservative measures failed to control the colitis and the patient was transferred to the surgical service where an ileostomy was performed. Later in 1941, the patient was readmitted to the medical service because of minor difficulty with the ileostomy. A disgnosis of cirrhosis was considered because of pigmentation and a palpable liver. Liver function evaluation revealed normal results for prothrombin time, hippuric acid excretion and galactose tolerance (I.V. method) but a 15% retention of BSP.

TABLE II

OCCURRENCE OF CIRRHOSIS IN PATIENTS WITH CHRONIC ULCERATIVE COLITIS

CASE NO.	YEAR OF BIRTH	SEX	ONSET OF COLITIS	ONSET, SIGNS OF LIVER DISEASE			COMMENT
				Enlargement	Jaundice	Ascites	
C-1	1881	F	1921	1941	1943	-	Ileostomy 1941; carcinoma colon with metastases and cirrhosis present at exploration (1943); died 1944.
C-2	1891	F	1920	-	-	-	Cirrhosis and cancer of colon discovered at time colectomy, Jan. 1950. Viral hepatitis (?) in April 1950. Liver biopsy Dec. 1950 indicated chronic hepatitis and cirrhosis. Alive 1951.

C-3	1890	M	1921	1941	1942	1941	Died March 1942; ascites present 8 months; terminally, hepatic coma followed upper G. I. hemorrhage. Autopsy: Cirrhosis and chronic ulcerative colitis.
C-4	1904	F	1933	1944	1946	-	Cirrhosis suspected 1944 (hepatomegaly and skin pigmentation): diagnosis proven 1946 (biopsy) at time of colectomy (ca. colon discovered). Patient died 1948 - Metastatic Ca.
C-5	1910	M	1930	1938	1938	-	Cirrhosis suspected on basis of hepatosplenomegaly and jaundice; confirmed by needle biopsy (1944). Alive when last seen, in 1947.
C-6	1917	M	1941	1947	1947	1948	Patient expired in hepatic coma 8 months after onset of ascites. Autopsy revealed portal cirrhosis and evidence of "healed" ulcerative colitis.
C-7	1923	M	1944	1948	1948	1951	Diagnosis of cirrhosis 1949 (biopsy); control of ascites and rectal bleeding constitute current (1951) problem.
C-8	1926	F	1930	1941	1936	1941	Ileostomy (1941) resulted in marked improvement. In 1945 patient exhibited signs of metastatic carcinoma. Autopsy revealed chronic ulcerative colitis, cancer of colon with metastases and cirrhosis.
C-9	1930	F	1942	-	1951	1951	Died Sept. 1951. Jaundice appeared in Jan. and ascites in May of 1951. Autopsy revealed cirrhosis and chronic ulcerative colitis.
C-10	1933	F	1939	1946	1946	1947	Died Oct. 1947 in hepatic coma. Autopsy revealed cirrhosis and chronic ulcerative colitis.

In 1943, the patient was admitted to the surgical service for a colectomy. A diagnosis of cirrhosis was entertained on the basis of the physical findings and mild jaundice (serum bilirubin 4 mg. per 100 cc.). Operation revealed cirrhosis of liver and carcinoma of colon with widespread metastases. The patient was considered inoperable. She expired at home in 1944. No autopsy was performed.

Conclusion: Carcinoma of colon and cirrhosis of liver; duration of idiopathic ulcerative colitis 23 years.

Case C-2

- Female - The patient developed ulcerative colitis in 1920 at the age of 29. In 1939 patient underwent a radical mastectomy for carcinoma of the breast. Her colonic disease remained intermittently active until Jan. 1950 when the patient was admitted to the surgical service where a colectomy and ileostomy was performed. Preoperatively, liver function tests revealed normal values for the bilirubin, BSP, cephalin flocculation and prothrombin tests. The serum albumin was 2.3 grams, globulin 4.7 grams; the serum cholesterol was 126 (63% esterified). At operation the liver appeared abnormal and a biopsy disclosed cirrhosis (mild). An adenocarcinoma of the colon was present in the resected specimen. The postoperative course was marked by a persistent tachycardia and a failure to gain weight and strength. The clinical impression of possible hyperthyroidism appeared to be confirmed by a satisfactory response to propylthiouracil and iodine.

In April 1950 the patient developed malaise, anorexia and jaundice. This was interpreted as probable homologous serum hepatitis since she had received blood transfusions in January. After a stormy course in her local hospital the patient recovered.

In June of 1950 the patient returned to the University Hospital for evaluation and consideration of an abdominal exploratory operation (i.e. "second look", cancer case). Because of certain abnormalities (17% BSP, 2 + cephalin-cholesterol and a thymol turbidity of 8 units) it was felt that recovery from viral hepatitis was incomplete. Operation was postponed.

The patient returned in December 1950 for operation. An enlarged left supraclavicular node was noted. Biopsy revealed carcinoma; this was judged, on the basis of histology, to be from the breast cancer (1939) rather than the cancer of the colon (1950). Liver function evaluation at this time revealed a negative cephalin-cholesterol test, a thymol turbidity of 7 units and 16% BSP retention. The abdomen was explored. No evidence of abdominal metastases was observed. Biopsy of the liver revealed active inflammation and cirrhosis. The interpretation was chronic hepatitis.

The patient received a course of deep x-ray therapy to the neck and axilla because of the late recurrence of the breast cancer. She is alive and well in 1951.

Conclusion: Idiopathic ulcerative colitis, 30 years; cirrhosis and cancer of colon noted at colectomy; probable viral hepatitis with recovery during convalescence from colectomy; carcinoma of the breast (1939) with late metastases (1950).

Case C-3

- Male - This patient died at University Hospitals in March 1942. The immediate cause of death was hepatic coma following a massive gastrointestinal hemorrhage (ruptured esophageal varix). Ulcerative colitis occurred at the age of 32. The colonic disease was never incapacitating and was controlled by conservative measures. In August 1941 the patient developed ascites; repeated paracenteses were required. In October 1941 the patient was admitted to this hospital. A diagnosis of cirrhosis was established by clinical and laboratory evidence; the presence of chronic ulcerative colitis (quiescent) was confirmed by x-ray and proctoscopic examinations. Despite various measures the patient's condition gradually deteriorated. Au-

topsy disclosed a finely hobnailed liver (portal cirrhosis), esophageal varices, splenomegaly and chronic ulcerative colitis.

Conclusion: Cirrhosis of liver in 52 year old male; chronic idiopathic ulcerative colitis of 31 years duration.

Case C-4

- Female - The patient died in 1948 at the age of 44 of widespread metastases from carcinoma of the colon. A diagnosis of idiopathic ulcerative colitis was established at the Mayo Clinic in 1933 when the patient was 29 years of age. She was admitted to the medical service of the University Hospital in 1941 because of symptoms of active colitis. Anemia and skin pigmentation were noted.

In 1944, studies on the medical service revealed a palpable liver; liver function studies were within normal limits save for a 2 plus cephalin flocculation test. The patient was subsequently transferred to the surgical service where an ileostomy was performed.

A colectomy was performed in January 1946. Liver function tests at this time revealed a total serum bilirubin of 3.9 mg., a 2 plus cephalin cholesterol test and 20% BSP retention. At operation a hobnailed liver was observed and the diagnosis of cirrhosis was confirmed by biopsy. A small adenocarcinoma was found in the sigmoid portion of the resected colon; the adjacent lymph nodes contained cancer cells.

In June 1948 the patient showed obvious signs of intra-abdominal carcinomatosis; she expired shortly thereafter. No autopsy examination was conducted.

Conclusion: Cirrhosis of the liver; adenocarcinoma of colon with metastases; chronic ulcerative colitis of 13 years duration (at time of colectomy).

Case C-5

- Male - The patient developed ulcerative colitis in 1930 at the age of 21 years. The disease was controlled by conservative measures. In 1938, the patient experienced an exacerbation of his colonic disease. This was associated with the appearance of jaundice and hepatomegaly. In 1940 a diagnosis of cirrhosis was considered because of the presence of liver enlargement and abnormal liver function tests. During his seventh admission to the medical service in 1944, hepatosplenomegaly was demonstrated. X-ray examination suggested the presence of esophageal varices. The serum bilirubin was elevated (3.9 mg. per 100 cc.) but the cephalin-cholesterol test and the serum albumin level were normal. Needle biopsy of the liver disclosed cirrhosis (termed mild or early by the pathologist). Barium enema study revealed evidence of chronic ulcerative colitis (termed quiescent).

The patient was seen again in 1947 in the out-patient clinic. The physical findings remained unchanged. The patient failed to complete the recommended studies and has been lost to subsequent follow-up.

Conclusion: Chronic ulcerative colitis (mild) of 14 years duration; cirrhosis of the liver (biopsy diagnosis).

Case C-6

- Male - This patient died of hepatic coma in December 1948. He was 31 years of age.

The patient was first seen at the Mayo Clinic in 1941 where a diagnosis of idiopathic ulcerative colitis was established. The onset was acute and the initial illness severe being marked by fever, arthritis and the frequent passage of bloody stools. Supportive treatment and blood transfusions succeeded in arresting the disease. The colonic disorder remained quiescent and the patient enjoyed fair health until 1947 when jaundice appeared.

The patient was first seen at the University Hospital in April 1948. A clinical diagnosis of cirrhosis was made on the basis of hepatomegaly, jaundice, ascites and marked impairment of liver function. Proctoscopic examination dis-

closed a "healing" ulcerative colitis. After careful diliberation by the staff, ileostomy and an eventual colectomy were proposed. It was hoped that the apparent relentless progress of the liver disease might be arrested by extirpation of the diseased colon. In May 1948, an ileostomy was performed under local anesthesia.

The patient recovered from the operation uneventfully but failed to show improvement in liver function. In November 1948 the patient was readmitted because of continued jaundice and the recent development of mental confusion. The final month of life was marked by intermittent episodes of unconsciousness; terminally, characteristic features of hepatic coma were apparent.

Autopsy disclosed a 1280 gram finely nodular liver; microscopically a severe active portal cirrhosis was in evidence. The colon was slightly thickened and the mucosa was atrophic; no ulcerations were present.

Conclusions: Cirrhosis, portal type; chronic ulcerative colitis (inactive or healed) of 7 years duration.

Case C-7

- Male - The patient developed diarrhea at the age of 21 while serving in the United States Navy (1944). Jaundice was first observed in 1948 and has continued to the present time.

In 1949 the patient was studied at the Mayo Clinic. A diagnosis of chronic ulcerative colitis was established by x-ray and proctoscopic examination. Jaundice was present; BSP retention was 40%. A liver biopsy revealed cirrhosis, grade 3.

In April of 1951 the patient was admitted to the medical service of the University Hospital. Jaundice and ascites were present. Marked impairment of liver function was noted; hypoprothrombinemia unresponsive to vitamin K and thrombocytopenia were observed. Rectal bleeding was a prominent feature initially but eventually subsided. Sufficient improvement resulted from dietary and other measures to permit the patient to return to his home.

Conclusion: Chronic ulcerative colitis, duration 7 years; cirrhosis and ascites.

Case C-8

- Female - This patient died in 1945 at the age of 19. She was first admitted to the medical service in July of 1941 because of a recent hematemesis. The initial examination revealed a pale emaciated 16 year old girl; hepatosplenomegaly and ascites were apparent. The superficial veins over the abdomen were prominent. The clinical history revealed that the patient first exhibited diarrhea at the age of 4 years. The diarrhea persisted and was marked by passage of blood and mucus at intervals. The girl was chronically ill throughout her childhood. Jaundice was first noted at the age of 10.

The presence of chronic ulcerative colitis was established by x-ray and protoscopic examination. A diagnosis of cirrhosis was entertained and although esophageal varices were not demonstrated, their presence was suspected as a cause of the recent hematemesis. As a result of transfusions, dietary measures and sulfonamide therapy, the patient improved and was discharged after two months.

The patient's improvement was short-lived and she was readmitted in November 1941 with an exacerbation of the bloody diarrhea. Physical findings were similar to those noted on the initial admission although the ascites had decreased. Jaundice (serum bilirubin 2.9 mg./100 cc.) and liver functional impairment was again demonstrated. It proved impossible to control the diarrhea by conservative means. In December 1941, the patient was transferred to the surgical service where an ileostomy was performed. Following this operation the patient exhibited remarkable improvement. The rectal discharge was reduced to a minimum and she gradually lost her ascites. Within one year her body weight more than doubled.

The patient was seen at intervals at the out-patient clinic. In April of 1943 the serum bilirubin was 1.5 mg. per 100 cc. and the BSP dye retention had dropped to 3%. Satisfactory progress continued until June 1945 when crampy abdominal pain with radiation to the back occurred. This was associated with rectal bleeding. A barium enema revealed a constricted area in the descending colon interpreted as evidence of active colitis. Colectomy was advised and the patient was admitted to the surgical service.

Investigation at this time revealed anemia, leucopenia and evidence of liver functional impairment. Shortly after admission, a thrombophlebitis involving the right femoral vein developed. Colectomy was postponed and treatment with anticoagulants and antibiotics was instituted. During this period, examination disclosed the appearance of enlarging supraclavicular lymph nodes on the left side. Lymph node biopsy revealed a gelatinous carcinoma. The proposed colectomy was therefore deferred. The patient's condition rapidly deteriorated. Terminally the patient had several hematemeses. The principal necropsy findings were gelatinous carcinoma of the descending colon, generalized abdominal carcinomatosis, cirrhosis of the liver, splenic vein thrombosis, esophageal varices and chronic ulcerative colitis.

Conclusion: Chronic ulcerative colitis, duration 15 years; carcinoma of the colon; cirrhosis of the liver.

Case C-9

..... - Female - This 20 year old patient died in September 1951 of progressive liver failure. Ulcerative colitis developed in 1942 when the patient was 11 years of age. Migratory polyarthritis was a prominent early feature of her illness. The diagnosis of ulcerative colitis was established at the Mayo Clinic in 1942. A medical regimen was adequate to control the diarrhea; in 1945 the proctoscopic appearance of the colon suggested a healing process. A prominent feature of this girl's illness from 1945 to 1948 was the occurrence of deep necrotic ulcers of the left leg. These proved very resistant to treatment and eventually required skin grafting.

The first clinical evidence of hepatic disease was the appearance of bilirubinuria in January 1951. In May 1951 definite jaundice was apparent and ascites developed. The patient was admitted to the medical service in September 1951. The patient was anemic (Hb. 4.5 grams), icteric (serum bilirubin 6.7 mg. per 100 cc.) and markedly emaciated. The abdomen was markedly distended with free fluid; the spleen was palpable; enlargement of the liver could not be demonstrated. Liver functional impairment was marked as judged by the results of customary tests. The serum cholesterol value was 60 mg. per 100 cc. and the albumin level was 0.8 grams per 100 cc. Febrile reactions occurred following attempted blood transfusions; the patient's condition deteriorated rapidly and she expired after a brief period of hospitalization.

Autopsy examination revealed chronic ulcerative colitis with pseudopolypi, a coarsely nodular cirrhotic liver, (1100 grams), splenomegaly (850 grams) and esophageal varicosities. Microscopic sections revealed a post necrotic cirrhosis.

Conclusion: Chronic ulcerative colitis (duration 9 years); cirrhosis of the liver.

Case C-10

- Female - This patient expired at the University Hospitals in October 1947. She was 14 years of age. The immediate cause of death was hepatic coma following severe hemorrhage from esophageal varices.

Ulcerative colitis developed at the age of 6 years; intermittent bloody diarrhea continued until an ileostomy was performed in March 1947. The first evidence of liver disease was noted in November 1946. Examination at the Willmar Clinic revealed jaundice, hepato-splenomegaly and spider nevi. The diagnosis

of ulcerative colitis was established by x-ray examination.

The patient was admitted to the Pediatric Service of this hospital in February 1947. The physical findings were similar to those noted on the previous examination. Impairment of liver function was demonstrated by laboratory studies. Proctoscopic examination revealed characteristic lesions of an advanced ulcerative colitis. An ileostomy was performed; needle biopsy of the liver revealed an active hepatitis with evidences of cirrhosis.

Following the ileostomy the patient exhibited some temporary improvement although her jaundice remained. She was readmitted to the hospital in August 1947. Ascites was now present but in other respects the physical findings remained unchanged. Colectomy was considered but the impairment of liver function appeared to constitute too great a hazard. Despite various forms of therapy the patient gradually failed; she died, in coma, following a massive hematemesis.

Autopsy revealed a coarsely nodular cirrhotic liver, splenomegaly and esophageal varices and chronic ulcerative colitis.

Conclusion: Chronic ulcerative colitis (duration 8 years); cirrhosis of the liver.

Since 1947, a number of the patients with ulcerative colitis seen on the Medical and Surgical Services of this hospital have been studied for the presence of liver disease by means of liver function tests. The tests have included some or all of the following: serum bilirubin, cephalin-cholesterol flocculation, thymol turbidity, zinc turbidity, bromsulfthalein excretion, urine urobilinogen, total and fractional proteins, total and esterified cholesterol, alkaline phosphatase and prothrombin time determination. In 13 such patients, needle biopsy of the liver was secured at the time of operation. The results obtained are presented in table III. In only one instance was a severe fatty infiltration encountered (case B-13).

Summary

The frequent occurrence of fatty infiltration of the liver noted in the fatal cases in this series (table I) is consistent with the findings of others. Mallory[11] has commented "Four out of five patients dying of ulcerative colitis show at autopsy a massive fatty infiltration of the liver, and an occasional case will show diffuse fatty cirrhosis, essentially similar to that seen in chronic alcoholism".

The results of the biopsy study in patients undergoing elective surgery (table III) revealed only one instance of fatty infiltration. However, it is current practice to carefully prepare such patients for major operations by high protein feedings and by preoperative blood and plasma transfusions. Perhaps fatty infiltration of the liver in ulcerative colitis is, in part at least, an expression of a deficiency in lipotropic factors. If so, the surgical biopsy specimen may fail to reveal fat since mobilization and disappearance of such liver fat can occur quite rapidly when nutrition is improved. Information relative to this question might be obtained by securing needle biopsy of the liver prior to the institution of the pre-operative nutritional program. Ten patients in this series have exhibited the association of cirrhosis and ulcerative colitis. Four patients, 2 males and 2 females, have died as a result of cirrhosis (C-3, C-6, C-9 and C-10) at the ages of 52, 31, 20 and 14 years. Four patients, all females, had ulcerative colitis, cirrhosis and cancer of the colon. Three have died as a result of widespread cancer (C-1, C-4, C-8) at the ages of 40, 44 and 19 years and one (C-2) survives at present. Two male patients were living when last seen (1951 and 1947). One of the two (C-7) is an invalid as a result of the two diseases.

TABLE III

RESULTS OF NEEDLE BIOPSY OF LIVER SECURED AT OPERATION IN THIRTEEN PATIENTS WITH CHRONIC ULCERATIVE COLITIS

CASE	SEX	AGE	DURATION OF COLITIS	EVIDENCE OF LIVER DISEASE (CLINICAL)	LABORATORY EVIDENCE OF LIVER DYSFUNCTION *	OPERATION PERFORMED	MICROSCOPIC APPEARANCE OF LIVER
B-1	F	45	11 years	None (1947)	Not determined	Colectomy	Normal
B-2	F	44	1 year	None (1950) None (1951)	Serum albumin 2.5, prothrombin 17"/12" Serum albumin 3.3	Ileostomy Colectomy	Minimal fat Minimal fat
B-3	F	45	12 years	None (1951)	Normal	Colectomy Ileo-proctostomy	Normal
B-4	M	45	15 years	None (1950)	Serum albumin 2.2, prothrombin 17"/12"	Colectomy	Minimal fat
B-5	M	41	10 years	None (1951)	Normal	Colectomy	Minimal fat
B-6	F	36	12 years	None (1950)	Normal	Colectomy	Normal
B-7	F	34	13 years	Hepato-splenomegaly (1948)	BSP - 24%	Colectomy	Normal
B-8	M	22	10 years	Hepatitis(I.H.) 1945 Hepatomegaly 1946 None 1947	 BSP - 13% BSP - 6%; thymol turbidity 9 units	Colectomy	Normal
B-9	F	34	13 years	Peritonitis and Jaundice (Jan. 1946) None (Oct. 1946)	Results consistent with "toxic" hepatitis. Normal	Colectomy	Normal
B-10	M	23	16 years	None (1947) Hepatitis (Feb. 1948) None (Dec. 1948) None (Mar. 1949)	Not determined Results consistent with viral hepatitis BSP - 19% BSP - 17%	Colectomy	Normal
B-11	M	24	6 years	None (1947) None (1949)	Total protein 4.2 Prothrombin 19"/12"	Vagotomy Colectomy	Normal Normal
B-12	F	23	2 years	Hepatomegaly 11-3-50 11-13-50	Serum albumin 0.9; cholesterol 100 Serum albumin 2.7 (transfusions)	Colectomy	Minimal fat
B-13	F	9	2 years	Hepatitis(I.H.)Feb.'47 None (May 1947)	Thymol turbidity 6 units	Colectomy	Severe fatty infiltration

* In most instances, laboratory tests included serum bilirubin, thymol turbidity, cephalin-cholesterol, total and fractional proteins, prothrombin time, total and esterified cholesterol and bromsulfthalein excretion.

Conclusions

1. The records of 270 cases of ulcerative colitis seen at the University Hospital since 1934 have been reviewed to determine the occurrence of associated liver disease.

2. Cirrhosis of the liver has been observed in ten patients with chronic ulcerative colitis. Four of the patients have died as a result of cirrhosis. Carcinoma of the colon occurred in four of the ten patients and caused death in three.

3. Fatty infiltration of the liver, often of an extreme degree, has been observed in 11 of 16 cases of acute or chronic ulcerative colitis.

4. Fatty infiltration of the liver was observed in one instance among 13 patients in whom liver biopsy was secured at the time of operation (colectomy).

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Chronic ulcerative colitis, with pseudopolyposis and adenocarcinoma, portal cirrhosis, post-atrophy type,
N. Eng. J. Med. 240:388-390 (Mar. 10) 1949.

10. Dennis, C. and Karlson, K.:
Unpublished data.

11. Mallory, T. B.:
In discussion,
Reference number 8.

II. MEDICAL SCHOOL NEWS

Coming Events

Nov. 26 - Dec. 1	Continuation Course in Child Psychiatry for Pediatricians and General Physicians
November 27	Special Lecture; "Facts and Theories of Comparative Psychiatry," Dr. E. Eduardo Krapf, Professor of Medical Psychology, University of Buenos Aires, and Consultant in Psychiatry, World Health Organization; Owre Amphitheater; 8:15 p.m.
November 28	Special Lecture; "Mental Health Problems of Aging," Dr. E. Eduardo Krapf; Museum of Natural History Auditorium; 8:15 p.m.
Nov. 29 - Dec. 1	Rheumatic Fever Symposium; Museum of Natural History Auditorium.
January 3 - 5	Continuation Course in Gynecology for General Physicians
January 7 - 9	Continuation Course in Pediatrics for General Physicians

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Faculty News

Dr. Ralph Knight, Head of the Division of Anesthesiology, was recently named President Elect of the American Society of Anesthesiologists. The election took place at the Society's meeting at Washington, D.C. Dr. Knight presented two papers before the Society: "Pentothal - Curare Mixture" and "The Care of the Patient with Poliomyelitis."

Dr. Henry E. Michelson will present a paper on the subject, "Inflammatory Nodose Lesions of the Lower Leg," at the meeting of the American Academy of Dermatology on December 7. The meeting of the Academy will be held in Chicago.

Dr. Gaylord W. Anderson, Mayo Professor and Director, School of Public Health, recently took over his duties as President of the American Public Health Association. Dr. Anderson's inauguration took place at the recent annual meeting of the A.P.H.S. at San Francisco, California, October 29 to November 2. The retiring president of the association was Dr. William P. Shepard, Medical School alumnus who was recently honored by the University of Minnesota as recipient of the Outstanding Achievement Award.

Dr. Walter A. Fansler, Clinical Professor of the Department of Surgery, and Head of the Division of Proctology, was one of the guest speakers at the recent meeting of the Southwestern Medical Association in Dallas, Texas, November 5 through 8. Dr. Fansler spoke on the subject, "The Repair of Anorectal Incontinence Following Operations for Fistulae."

Dr. Howard M. Frykman and Dr. Walter A. Fansler attended the meeting of the American Board of Proctology in Philadelphia November 17 to 20. Dr. Frykman presented a paper on, "Pruritus Ani."

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New Minnesota Medical Foundation Members

D. K. Rizer, M.D., Minneapolis
Leonard O. Titrud, M.D., Minneapolis
Katherine A. Nye, M.D., St. Paul
George M. Tangen, M.D., Minneapolis
M. H. Nathanson, M.D., Los Angeles, Cal.
Louis A. Fried, M.D., Minneapolis
Norman P. Johnson, M.D., Minneapolis
Wm. S. Terry, M.D., Minneapolis
John R. Earl, M.D., St. Paul

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There will be no Bulletin published on Friday, November 30. The next issue of the Bulletin will appear on December 7.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Physicians Welcome

November 26 - December 1, 1951

Monday, November 26

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; M-109, U. H.

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

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 - Physiology Seminar; The Influence of Anesthesia and Nociceptive Stimuli on the Centers of the Autonomic System; E. S. Redgate; 214 Millard Hall.

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

4:00 - Pediatric Seminar; Some Observations on Sepsis in the Newborn; Richard T. Smith; Sixth Floor West, U. H.

4:30 - 5:30 Dermatological Seminar; M-346, U. H.

4:30 - Public Health Seminar; 15 Owre Hall.

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

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

Minneapolis General Hospital

7:30 a.m. Fracture Grand Rounds; Dr. Zierold, Station A.

11:00 - Pediatric Rounds; Dr. Top; 7th Floor.

12:30 p.m. Surgery Grand Rounds; Dr. Zierold; Station E.

1:00 - 2:00 X-ray Conference; Classroom, 4th Floor.

1:30 - Pediatric Rounds; Dr. Ulstrom; 4th Floor.

Veterans Administration Hospital

9:00 - G. I. Rounds; R. V. Ebert, J. A. Wilson, Norman Shrifter; Bldg. I.

Monday, November 26 (Cont.)

Veterans Administration Hospital (Cont.)

11:30 - X-ray Conference; Conference Room; Bldg. I.

2:00 - Psychosomatic Rounds; Building 5.

3:30 - Psychosomatic Rounds; Building 1, Dr. Aldrich.

Tuesday, November 27

Medical School and University Hospitals

8:30 - Conference on Diet Endocrines and Cancer; M. B. Visscher; Physiology Library.

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

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

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

12:30 - Selected Topics, Permeability and Metabolism; Nathan Lifson; Physiology Library.

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

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

4:00 - 5:00 Physiology-Surgery Conference; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; Presentation of Cases by Ancker Hospital Staff; Doctors Aurelius, D. Peterson, and Traub; Eustis Amphitheater, U. H.

*8:15 p.m. Special Lecture; Facts and Theories of Comparative Psychiatry; Dr. E. Eduardo Krapf, Professor of Medical Psychology, University of Buenos Aires, and Consultant in Psychiatry, World Health Organization; 15 Owre Hall.

Ancker Hospital

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

Minneapolis General Hospital

8:00 - Pediatric Rounds; Dr. Gibbs; 5th Floor Annex.

10:00 - Psychiatric Grand Rounds; J. C. Michael and Staff; 3rd Floor Annex.

11:00 - Pediatric Rounds; Dr. Platou; 7th Floor.

Veterans Administration Hospital

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

Tuesday, November 27 (Cont.)

Veterans Administration Hospital (Cont.)

8:30 - Infectious Disease Rounds; Dr. Hall

8:45 - Surgery Journal Club, Conference Room, Bldg. I.

9:00 - Liver Rounds; Samuel Nesbitt.

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

10:30 - Surgery Tumor Conference, Conference Room, Bldg. I.

1:00 - Surgery Chest Conference; T. Kinsella and Wm. Tucker; Conference Room, Bldg. I.

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

3:30 - 4:20 Clinical Pathological Conference; Conference Room, Bldg. I.

Wednesday, November 28

Medical School and University Hospitals

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

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; Allen Judd 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 - 1:20 Radio-Isotope Seminar; Subject to be announced; Leon Singer; 12 Owre Hall.

1:30 - Conference on Circulatory and Renal Systems Problems; M. B. Visscher; 116 Millard Hall.

4:00 - 5:00 Vascular Rounds; Davitt Felder and Staff Members from the Departments of Medicine, Surgery, Physical Medicine, and Dermatology; Sta. 42,U.H.

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

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

5:00 - 7:00 Dermatology Clinical Seminar; Dining Room, U. H.

7:00 - 8:00 Dermatology Journal Club; Dining Room, U. H.

8:00 - 10:00 Dermatological-Pathology Conference; Review of Histopathology Section; Robert Goltz; Todd Amphitheater, U. H.

Wednesday, November 28 (Cont.)

Ancker Hospital

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

3:30 - 4:30 Journal Club; Surgery Office.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Dr. Platou; 7th Floor Annex.

11:00 - Pediatric Rounds; Dr. Top, 7th Floor.

12:00 - Surgery Seminar; Dr. Zierold; Classroom.

12:15 - Pediatric Conference; 4th Floor Annex.

1:30 - Pediatric Rounds; Dr. Huenekens and Dr. Ulstrom; 4th Floor Annex.

2:00 - Infectious Disease Rounds; 8th Floor.

4:00 - Infectious Disease Conference; Classroom, 8th Floor.

Veterans Administration Hospital

8:30 - 10:00 Orthopedic X-ray Conference; Conference Room, Bldg. I.

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

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

*8:15 p.m. Special Lecture; Mental Health Problems of Aging; Dr. E. Eduardo Krapf; Professor of Medical Psychology, University of Buenos Aires, and Consultant in Psychiatry, World Health Organization; Museum of Natural History Auditorium.

Thursday, November 29

Medical School and University Hospitals

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.

12:30 - Physiological Chemistry Seminar; Metabolic Effects of Cortisone; S. Nayyar; 214 Millard Hall.

11.00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

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

4:00 - 5:00 Physiology-Surgery Conference; Todd Amphitheater, U. H.

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

Thursday, November 29 (Cont.)

Medical School and University Hospitals (Cont.)

5:00 - 6:00 X-ray Seminar; Angiocardiography in Congenital Heart Disease; Robert G. Bronson; 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.

Minneapolis General Hospital

8:00 - Pediatric Rounds; Dr. Gibbs; 5th Floor.

8:30 - Neurology Rounds; Dr. Heilig, 4th Floor Annex.

9:00 - Neurology Grand Rounds; J. C. Michael and Staff; Station A.

11:00 - Pediatric Rounds; Dr. Platou; 7th Floor.

11:30 - Pathology Conference; Main Classroom.

1:00 - 2:00 Fracture - X-ray Conference; Dr. Zierold; Classroom, 4th Floor Annex.

2:00 - Psychiatry Rounds; Dr. Benton; 4th Floor Annex.

Veterans Administration Hospital

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

9:15 - Surgery Grand Rounds; Conference Room, Bldg. I.

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

Friday, November 30

Medical School and University Hospitals

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

11:45 - 12:50 University of Minnesota Hospitals Staff Meeting; Football Pictures; Powell Hall Amphitheater.

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

2:00 - 3:00 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

Friday, November 30 (Cont.)

Medical School and University Hospitals (Cont.)

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

4:00 - 5:00 Dermatology Seminar; W-312, U. H.

4:00 - Neurophysiology Seminar; 113 Owre Hall.

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

8:00 - Pediatric Allergy Rounds; Dr. Nelson; 4th Floor.

11:00 - Pediatric Rounds; Dr. Top; 7th Floor.

11:00 - Pediatric-Surgery Conference; Drs. Wyatt and F. Adams; Classroom, Sta. I.

12:00 - Surgery-Pathology Conference; Drs. Zierold and Coe; Classroom.

1:30 - Pediatric Rounds; Dr. Ulstrom, 4th Floor.

Veterans Administration Hospital

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

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

1:30 - Chest Conference; Wm. Tucker and J. A. Meyers; Ward 62, Day Room.

3:00 - Renal Pathology; E. T. Bell; Conference Room, Bldg. I.

Saturday, December 1

Medical School and University Hospitals

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

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.

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

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

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

Saturday, December 1 (Cont.)

Medical School and University Hospitals (Cont.)

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

11:30 - Anatomy Seminar; Myoglobin; Frances E. Schaar; 226 Institute of Anatomy.

Minneapolis General Hospital

8:00 - Pediatric Rounds; Dr. Gibbs; 5th Floor.

11:00 - 12:00 Pediatric Clinic; Dr. Thomas and Dr. May; Classroom, 4th Floor Annex.

Veterans Administration Hospital

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

8:30 - Hematology Rounds; P. Hagen and E. F. Englund.

* 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.