PARKLAND MEMORIAL HOSPITAL

MEDICAL GRAND ROUNDS

October 11, 1962

BILIARY CIRRHOSIS

CASE I: [redacted]

The patient, a 54 year old [redacted] female, was first admitted to [redacted] on [redacted] 1959, with the chief complaint of itching. The patient is a domestic and considered herself to be in good general health until [redacted] 1958, when she noted the onset of itching. Pruritis began in the feet and over a period of 2 to 3 weeks, gradually extended over the entire body including the face and palms of her hands. Although the pruritis has been constant since onset, it has fluctuated in intensity. At the time the pruritis started, the patient also noticed that her eyes were yellow, her urine became dark and stools became a light brown color. The degree of scleral icterus, darkness of urine color and stool color has varied intermittently since onset. At no time has the patient had anorexia, nausea, vomiting, change in appetite, nor intolerance to any type of food. She has never had abdominal pain. Prior to onset of her illness, the patient specifically denied ingestion of any drugs. She was not in contact with jaundiced people and had no good history of exposure to hepatotoxins. After her symptoms started, the patient employed a variety of drugs including 666, Pinkham's Compound, mild Nervene, a beef-wine iron tonic, and others, the identity of which are not known. In association with the present illness, the patient lost approximately 30 lbs.

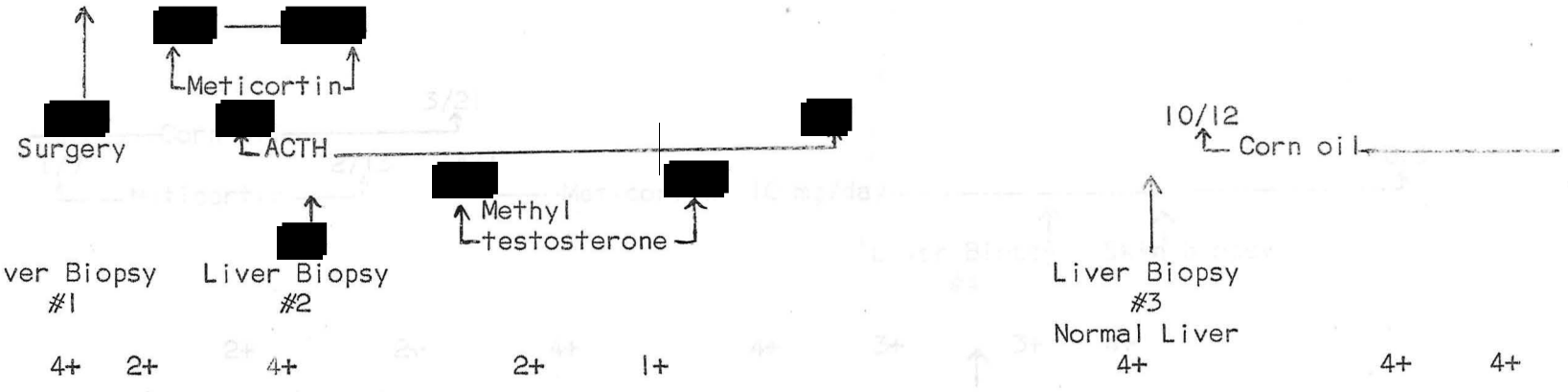
On physical examination, the patient was in no distress. She showed evidence of recent weight loss but did not appear malnourished. Blood pressure was 170/110, pulse 72, temperature 98.6°, respirations 18. Sclerae were icteric; fundi showed arteriolar narrowing, tortuosity and minimal AV nicking; several small nodes were found in the left posterior cervical region, a few in the right supraclavicular region. Skin was dry and darkened; there were scattered excoriations, particularly over the arms. Lungs were clear to percussion and ascultation. Heart: Left border of cardiac dullness percussed 1 cm. outside the left midclavicular line in the 5th intercostal space. Regular sinus rhythm. $A_2 > P_2$. Grade 2 systolic murmur localized to the apex. Abdomen was relaxed with a midline suprapubic scar (hysterectomy 27 years ago). Liver was 2-3 fb. beneath the right costal margin in the midclavicular line; it was firm and slightly tender. The liver edge was sharp. Spleen tip was palpable at the costal margin. No ascites was present. Extremities were normal; specifically, no edema or clubbing was noted. A 4-day oral cholecystogram revealed filling of the gall bladder with diminished opacification. Gall bladder contracted following ingestion of a fatty meal. Cystic and common ducts were demonstrated to be of normal caliber and no signs of cholelithiasis.

Despite the demonstration of patent biliary tract by x-ray, the patient was subjected to surgery on [redacted], 1959. Liver was found to be enlarged and not nodular, gall bladder was of normal size, no stones were felt, cystic and common ducts were normal. A cholangiogram performed at the time of surgery following opening of the common duct revealed a normal ductal system. A lymph node measuring 2 x 3 cm. found at the distal end of the common duct was not felt to be compressing the common duct; it was removed and revealed hyperplastic changes. The first liver biopsy was a surgical one taken at the time of this exploration.

Course has been marked by fatigue, pruritis and progressive weight loss. Serum bilirubin increased notably in [redacted] 1961 and has remained elevated since

1959

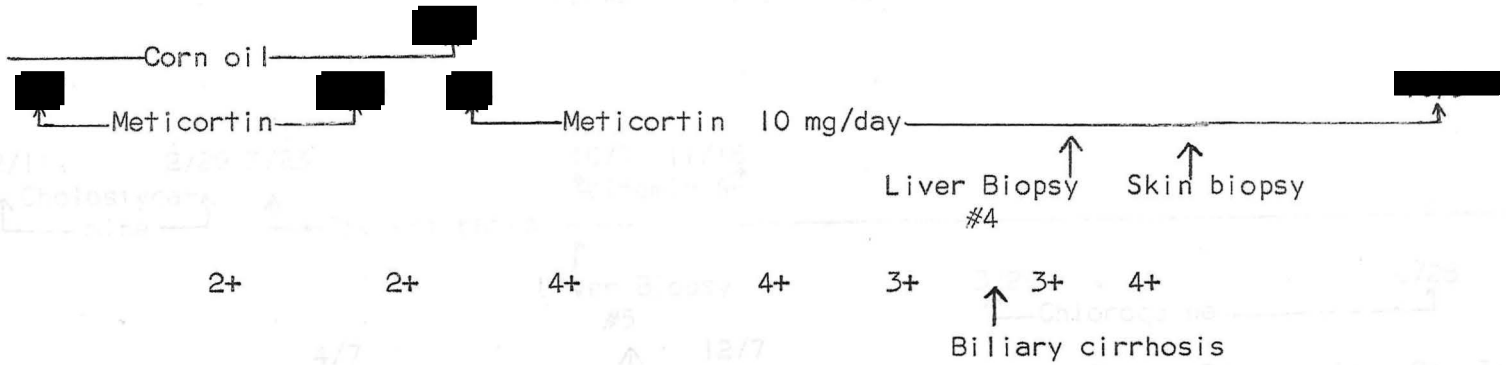
	[redacted]-14													
Bilirubin - I'	5.0-4.6	2.8			2.0	2.7	3.0	1.1		1.8				
Total	7.8-0.6	5.4	3.8	1.0	3.0	5.6	5.4	2.7		5.2,4.8	5.3	6.0	8.2	
Alkaline Phosphatase	50.7-44.	28.0	48.6	34.4	36.3	21.8	33.4	53.9		36.3,48.6	53.6	58.6	45.2	
Thymol Turbidity	6	4.8		0.8	3.5	3.6	3.7			5.7		3.2		
Ceph floc.	0/0	0/2+		0/1+	0/1+	0/1+	0/1+			0/1+				
Cholesterol	373,260	240	710	608	630	491	510	460	410		170	290	125	
Total proteins	7.7	5.4					6.7	6.7						
Albumin	3.5	2.9					4.3	4.0						
Globulin	4.2	2.5					2.4	2.7						
SGOT										196/140				
Prothrombin seconds	10.5				100%					11 sec.				
Ca														



Pruritis	4+	2+	4+		2+	1+				4+		4+	4+	

1960

	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Bilirubin - I'						3.6	1.4	
Total	9.0		5.0	11.2	7.8	6.4	3.8	5.0
Alkaline Phosphatase	48.0	57.9	76.1	31.8	45.7	37.1	88.1	77.1
Thymol Turbidity						2.5		
Ceph floc.				2+/2+	0/0	0/0		
Cholesterol	325	425	497	400	460	404	220	290
Total proteins	7.9					6.8		
Albumin	4.4					4.0		
Globulin	3.5					2.8		
SGOT	156	173	125				90	
Prothrombin seconds								
Ca								



	1961							1962					
[redacted]													
Bilirubin - I'		5.4	5.4	12.8	15.5	11.4	10.0	18.0	9.6	12.0	12.6	13.6	8.0
Total	9.6	10	10.6	21.2	25.0	19.6	17.2	22.0	20.0	18.8	30.4	22.8	14.5
Alkaline Phosphatase	67.6	75.6	71.2	48.4	62.3	66.4	60.4	60.1	39.2		55.1	51.1	45.3
Thymol Turbidity	6.5					25.5	15.4	25.7	14.0	12.5	14.0		17.0
Ceph floc.	2+/2+			0/1+	0	1+/2+	0/2+	1+/2+		1+/3+	1+/3+	2+/4+	0/2+
Cholesterol	338	430	365	355	350	372			380	370	355	308	174
Total proteins													
Albumin													
Globulin													
SGOT				90				115	210	120	216	150	105
Prothrombin seconds						11.5							

Stool fat normal 2+ edema
1+ ascites

[redacted] [redacted] [redacted] [redacted] [redacted]

Cholestyra-mine Cholestyramine Vitamin A

Liver Biopsy #5

[redacted] Chloroquine

Pruritis 3+ 4+ 2+ 2+ 2+ [redacted] 0 2+ 3+ 4+ 4+ [redacted] 0 0 0 2+ 2+ 4+ 2+ 2+ 1+ 2+ 3+

Biliary Cirrhosis

CASE 2: [redacted]

This 40-year-old WF was admitted to [redacted] for the 3rd and final admission on [redacted]/62 because of fever and nausea, of 2 days' duration. She expired on [redacted]/62.

The pertinent medical history dates to 1955. At that time the patient developed increased nervousness, weakness and intermittent nausea without vomiting. This was attributed to a contemplated change in residence from a small town to [redacted], a change which was unhappily anticipated by the patient. Because of these symptoms, she visited a [redacted] who prescribed Thorazine, dosage unknown. She took this medication regularly for 3 to 4 weeks. After one week the patient noted the appearance of itching, jaundice, pale stools and dark urine. Nevertheless, she continued to take the Thorazine. Three weeks later she became violently nauseated, vomited repeatedly, had 4 prolonged shaking chills and was hospitalized at [redacted] Texas. Her attending physician diagnosed obstructive jaundice secondary to Thorazine. The pertinent laboratory findings at that time are listed on the last page of the protocol. A gall bladder series did not visualize the gall bladder. The patient remained jaundiced and continued to have pruritis. Also, she rather persistently had 5-6 stools/day, often foamy, light-colored and foul smelling. In March 1956, a short course of steroids was given without effect. Approximately one year after the onset of her illness, the patient developed a generalized nodular eruption which waxed and waned, occasionally nodules breaking open and discharging a yellow substance. Her skin gradually became rough and thickened, especially in areas exposed to sunlight. The patient over the ensuing years received numerous drugs including vitamin D, vitamin K and estrogens. In 1958, the patient fell, fracturing her pelvis, right hip and left tibia. She was hospitalized at St. Joseph's Hospital in Fort Worth, where many xanthomata were noted, as well as hepatosplenomegaly. As a result of the laboratory data (shown on the last page) plus the clinical picture, a diagnosis of xanthomatous biliary cirrhosis was made. X-rays revealed diffuse rarefaction of bone. Late in 1958 the patient fractured her left radius and ulna. Poor healing of all fractures was observed. Since 1958 the patient was confined to a wheel chair.

The patient took no medications from 1958 to 1960 because of previous disappointing results. In September 1960, she was referred to Dr. Jean Wilson for evaluation.

1st [redacted] Admission, [redacted]/60: Hx as above plus the following points: Skin eruption had subsided considerably. Pruritis remained as did diarrhea. Initial weight loss of 25 lbs. had not progressed. Abdomen had gradually enlarged for 4 years. No history of previous episodes of jaundice or allergies. No family history of liver disease or jaundice. Patient did not drink alcohol. No history of abdominal pain. PE: VS WNL; skin roughened and thickened over exposed areas. Numerous 1/2 to 3/4 cm. subcutaneous nodules, primarily over the face, back and arms; sclerae icteric. Liver and spleen both down 4-5 fb. below respective costal margins, non-tender; no ascites; diffuse decreased muscle mass and limitation of movement of both hips and left knee. Lab data: Hemoglobin 11.7, WBC 5,900 with 75 polys, 2 bands, 23 lymphs. UA: Occ. RBCs and WBCs, BUN 18, FBS 75, Ca 8.7, P 3.1. Liver biopsy was interpreted as compatible with post- necrotic cirrhosis. The patient was placed on calcium balance studies and eventually discharged on vitamin D 50,000 u, Ca lactate 3.6 gm. and NH_4Cl 0.6 gm. per day.

After initiation of therapy, the patient's strength improved, steatorrhea subsided. However, because of failure to note significant improvement in the bone disorder, she was readmitted for further Ca studies on [redacted], 1961. She was discharged on 250,000 u Vitamin D/day in [redacted], 1961.

3rd [redacted] Admission, [redacted]/62: The patient's condition remained unchanged until 2 days pta. At that time she was started on chloroquin 250 mg. bid; the 1st day on this drug, the patient had 3 loose BM's. The day pta the patient developed fever to 101°, recurrent chilliness and nausea. With the onset of fever, the patient noted swelling of the face, hands, abdomen and feet. Soreness in the right upper arm appeared 2 days pta. Only other symptoms were a chronic non-productive cough, recent onset of sleepiness, change in color of urine to amber and decreased urine volume the day pta.

PE: T 102.8°, BP 130/70, P 108, R 20. General: Mildly agitated and hyperkinetic. Fluid: Generalized 1+ edema, including the face. Skin: Coarse, dry, warm. HEENT: Fundi WNL. Sclerae modestly icteric. Pharynx clear. Neck: Thyroid not felt. Chest: Scattered rales at both bases. Heart: PMI in 5th ICS at LMCL. Grade 2 precordial systolic murmur. Harsh systolic "scratch" heard at pulmonic area. No gallop or diastolic sounds. Abdomen: Distended; liver and spleen down 405 fb. ? ascites. Ext.: Tenderness of right biceps with no objective findings. Neurol.: No asterixis. DTR's symmetrically 3+.

Course: Examination of a catheterized urine on admission revealed it to be loaded with bacteria. However, there were no GU symptoms and it was not thought to be the cause of fever. The chest film was suggestive of an early pneumonia and the patient was started on penicillin on [redacted]. 3 of 4 blood cultures grew coagulase-positive staphylococci resistant to penicillin and staphcillin was started on [redacted]/62. Sputum culture grew coagulase-positive staph. Urine culture grew E. coli, >500,000/cc. sensitive to achromycin which was started on [redacted]62. The patient became afebrile after 10 days. Stool guaiac was positive, first noted on [redacted]/62, not bloody or tarry. Transfusions were given. On [redacted] the stools became tarry. On [redacted], bloody stools and vomitus were observed. A Blakemore tube was passed and bleeding subsided, but not immediately. The Blakemore tube was removed after 30 hours. 24 hours later bloody stools recurred and the hemoglobin fell further. It was elected to do a portacaval shunt on [redacted]/62. Operative findings included 2 liters of ascites, varices in the porta hepatis, portal pressure of 385 mm. before the shunt, 270 mm. afterward. The gall bladder and common duct were normal. The liver was dark green and finely nodular. Blood loss was 4 liters. Post-op, the patient's condition did not improve. She gradually became somnolent starting on [redacted]/62 and expired after becoming comatose and hypotensive on [redacted]/62. At no time was a clear liver flap observed.

Ward Diagnoses:

1) Xanthomatous biliary cirrhosis presumably secondary to Thorazine toxicity, with progressive liver failure
2) Staphylococcal pneumonia and septicemia
3) Gastrointestinal hemorrhage due to bleeding varices

	[redacted]/55	[redacted]3/56	[redacted]/58	[redacted]/60	[redacted]/60	[redacted]/60	[redacted]/61	[redacted]/62	[redacted]62	[redacted]162
Bilirubin - I'			6.4		1.4				6.4	
Total			14.9	5.4	4.8	2.3	6.5	13.8	11.4	32.
Icterus Index	39.3;45	30-50	53.							
Alkaline Phosphatase Bodansky units	26.6			27.1	19.7	19.5			13.	5.8
Thymol Turbidity					3.5	3.1			4.8	3.5
Ceph Floc.					0/1+	0/1+			2+/3+	2+/3+
Cholesterol			1800	279 (60% free) Total lipids normal.	325					
Total proteins			9.3	8.1	6.7				4.2	
Albumin			2.8	3.5	3.3				1.8	
Globulin			6.5	4.6	3.4				2.4	
SGOT					160				142	
Ca			5.3	8.9	8.7	10.2		8.5	7.8	

Xanthomata appear

fractures

Xanthomata disappear

Stool fat 13.1 gm/day

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