THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Examination

This is to certify that we the undersigned, as a committee of the Graduate School, have given Duncan Parham final oral examination for the degree of

Master of Science in Surgery

We recommend that the degree of

Master of Science in Surgery

be conferred upon the candidate.

Chairman

W. J. Gillett

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Date May 16, 1922

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REPORT

OF

COMMITTEE ON THESIS

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by **Duncan Parham**, for the degree of Master of Science in Surgery. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

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THESIS

STUDIES IN OBSTRUCTIVE JAUNDICE

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Submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

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STUDIES IN OBSTRUCTIVE JAUNDICE

Surgery of the patient with obstructive jaundice offers three avenues of danger aside from the so called accidents of surgery: (1) Hemorrhage, (2) Uremia, (3) Hepatic Insufficiency.

The very large danger from hemorrhage in the presence of jaundice is well known to all. In a review of the necropsy findings in twenty-nine cases of obstructive jaundice, by Dr. Waltman Walters of this Clinic, it was shown that in over 50 per cent serious postoperative hemorrhage occurred, and a method of preoperative preparation was described. That such preoperative preparation has met with success is evident from the fact that in the last series of thirty-four patients with obstructive jaundice who received this preparation there was but one case of serious postoperative bleeding. This phase of the subject has been quite fully discussed in the afore mentioned paper.

The second important source of postoperative worry in these patients is uremia. A large percentage of patients with obstructive jaundice shows some albumen and casts in the urine. It is only when albumen and casts are slight, the blood urea not more than moderately elevated and the urine output satisfactory, that an operation is warranted.

That renal insufficiency occurs as a terminal event in patients with obstructive jaundice in which no operation has been performed is illustrated by the following case:

Case I Mr. J. V. Age 68 years, entered the Mayo Clinic October 5th, 1921, with a history typical of gall-stone colic followed by jaundice which became deeper progressively. There was a marked intense jaundice present on examination. His stools were clay colored at all times. A twelve hour specimen of urine contained a large amount of albumen, hyaline, granular and leukocytic casts. The coagulation time of his blood was nineteen minutes. He entered the hospital

October 8th, 1921, complaining of nausea and vomiting. During the next forty-two hours his jaundice deepened. He passed but sixteen ounces of urine in spite of a subcutaneous intake of sixty ounces of normal salt solution. At times he vomited blood. He became restless and noisy, then drowsy and stuperous. October 10th, 1921, the day before his death his blood urea was 294 mgm, per 100 cc and creatinin 5.8 mgm. At autopsy a chronic diffuse nephritis was found with hemorrhage into the gastro-intestinal tract. An impacted stone in the common duct produced a complete obstructive jaundice.

In this series of cases it was noticed that where ether anesthesia was used the blood urea in a large percentage of the cases rose to double the preoperative figure the second or third day after operation. When local infiltration of the abdominal wall was done combined with as little ether as possible (usually one to two and a half ounces) this rise was noted in a smaller proportion of the cases.

As a rule the rise in blood urea forty-eight to seventy-two hours after operation gradually disappears, and without other trouble the patient has a steady normal convalescence. Unfortunately there are some cases which do not do so well. If after operation there is an increase in the cholangitis, or the biliary drainage for any reason becomes insufficient, there may be a greater retention of bile with an increase in the jaundice and in the blood coagulation time and a concomitant increase in the nephritis with rising blood urea. These cases sometimes show an alarming picture of uremia and may terminate in death. One postoperative death from uremia occurred.

Case II. Mr. L. F. 373925, Age 64 years. History: Six weeks ago developed jaundice which was accompanied by generalized pruritus, clay stools and marked constipation. No fever or pain. Urine contained albumen II (on a scale of I, II, III, IV), casts 1. Coagulation time of blood ten minutes. Cholecystogastrostomy for carcinoma of the head of the pancreas was done. On the third day after operation urinary retention developed, necessitating catheteriza-

tion, following which there was marked hematuria. The fourth day after operation the blood urea was 228 mgm. which rose to 360 mgm. and creatinin [illegible]3 mgm. on the eighth day. Transfusion was done twice. He died on the ninth day apparently from uremia. Autopsy revealed marked nephritis. There was blood in the bladder and also some blood in the gall-bladder and gastro-intestinal tract.

The only treatment is that of any impending uremia. Drains should be carefully inspected to see that they are satisfactory.

The third obstacle in the path of recovery in the case with common duct obstruction is hepatic insufficiency. Too little consideration has been given to the incompetent liver by the profession. Because of the remarkable compensatory and regenerative abilities of the liver, it has been very difficult to obtain much exact data as to what liver failure is. It is perhaps safer to speak of these cases as suffering from lack of sufficient liver function rather than of liver insufficiency. The trouble may not be so much an intrinsic lack of vigor on the part of the liver cell as an inability to function sufficiently due to the obstruction in the avenue of excretion.* But no matter how this may be, it is certain that these patients with common duct obstructions show a so called biliary cirrhosis, of various degrees, or more correctly, central atrophy and cholangitis. When this is so marked that the liver is a yellow bile stained organ shrunken to two-thirds its normal size, the prognosis as to the outcome is very serious. An alarming percentage of cases of this type die from lack of hepatic function.

*Note: The term cholemia is sometimes used to signify the train of symptoms accompanying the effect of toxic products retained in the blood which the liver has failed to eliminate. Cholemia means bile in the blood. As a clinical expression it is often used too loosely to mean almost any untoward symtom complex occurring in these jaundiced patients. It is too broad in its scope to encourage a close analysis of the case. Such terms as cholemic uremia, cholemic nephritis, cholemic hepatitis might be used. It would seem better to confine cholemia simply to meaning bile in the blood.

At autopsy the liver is small and yellow, sometimes weighing less than 1000 gm., though in some instances it may be larger than normal. (See history V.) There are many bile thrombi in the canaliculis of the central portion of the lobules. The hepatic cells of the central zone show atrophy although there is considerable fairly good liver tissue present in the periphery of the lobules. However, these latter often show slight hydropic change or a moderate amount of fine fat granules as revealed by Sudan III stain. There is hardly enough definite pathology present to recognize liver inadequacy from a morphological standpoint. On the other hand, the better known syndrome of urinary insufficiency cannot always be diagnosed at autopsy.

The clinical picture is about as follows: Usually the first two to eight days after operation the course is uneventful. Bile drainage and urine output normal. Fluids taken well. Pulse and temperature normal. One of the first things observed at the onset of trouble is a paling and thinning of the bile with a marked increase in the flow. This profuse cholerrhagia does not continue long but the bile remains thin. About the same time the patient begins to grow weaker, the pulse loses volume, the temperature becomes subnormal. Restlessness and irritibility develop with great fatigue and muscular weakness. Soon there is a regurgitant vomiting of liquids taken by mouth. Little is retained by rectum. Jaundice does not deepen markedly but there is an increasing pallor beneath the icteric hue. The face is drawn, the eyes anxious. The patient grows weaker and weaker and finally dies. Urinary output has remained proportional to the fluid intake throughout. Examination of the urine reveals little or no evidence of marked nephritis and the blood urea remains low.

Case III. Mrs. G. B. B. 383124, Age 61, presented herself for examination February 2, 1922. She had complained of attacks of epigastric pain for forty-five years. More severe the past ten years. Four years ago first occurance of jaundice during an attack. July, 1918, cholecystostomy done elsewhere, one large stone removed. Attacks of nausea, vomiting, and jaundice persisted and in

December 1920 cholecystectomy was done elsewhere. Since this last operation jaundice, though fluctuating, persisted. Clay stools, costive bowels, general pruritis, loss forty pounds weight. There was moderate jaundice (II) present on examination. Blood pressure, systolic, 144, diastolic 84; pulse 72, temperature 98.5; weight present 101 pounds. Blood examination; hemoglobin 68 per cent; R. B. C. 4,090,000, leukocytes, 8,9000. Urine; specific gravity, 1021, albumen 0. sugar 0. casts 0., R. B. C. 0., pus 1-6. Bile present, urobilin and urobilinogen present.

February 5th, she was sent in to the hospital and preoperative preparation was begun. Coagulation time was normal (four and one-half minutes) but 10 cc. of 10 per cent calcium chloride was given intravenously. Blood urea was 20 mgm. per 100 cc.

February 7th, choledochostomy was done for choledocholithiasis. The common duct was 2½ cm. in diameter. Two stones removed. Local anesthesia was used with only whiffs of ether. After operation convalescence was satisfactory until the fifth day. Bile drainage and urinary output good. Jaundice clearing slightly. On the fifth day bile drainage through tube ceased, only a slight drainage around tube. Aspiration and manipulation next day of tube loosened obstruction with restoration of drainage. The following day (seventh day postoperatively) the bile became thin and pale but excessive in amount (1260 plus cc. in 24 hours); urine output 1590 cc. Bile drainage continued thin but gradually reduced in amount. The urinary output on the ninth day became less in amount and remained so until death. Blood urea on eighth day 34 mgm. per 100 cc. Urine showed moderate albumen and many hyaline casts. The patient grew restless and drowsy. The pulse and strength growing steadily weaker until death on the fifteenth day. Leukocytes on the tenth day were 34,000. There was slight sanguineous discharge from wound the last seven days. Autopsy revealed a sinus passing down to the region of the common duct from which exuded a thick purulent material. No generalized peritonitis. Very little gross hemorrhage in region of

wound and none elsewhere. Heart and lungs practically normal. The liver small weighing 985 gm. The cut surface presented a brownish green mottling. The lobule markings not distinct. Common duct and hepatic ducts dilated. Microscopic examination shows cells around the central veins shrunken in size, their shape irregular. This condition in some lobules extended out to the periphery. In the sinuses around the central vein is a moderate amount of brownish black pigment.

The kidneys were atrophic, weighing together 185 gm. Microscopic examination showed moderate cloudy swelling, areas of rather marked interstitial fibrosis, many hyalinized glomeruli and atrophied tubules. Considerable bile pigment present. Death here was due to nephritis complicated by lack of hepatic function.

Case IV. Mrs. C. Z. W. 381682, Age 40 years presented herself for examination January 13, 1922. There was a history of recurring attacks of right upper abdominal pain without jaundice. September 6, 1921 cholecystectomy was done elsewhere. Shortly after jaundice developed at first with a fluctuating intensity but the six weeks prior to examination had been intense constantly. She had lost considerable weight. On examination there was a deep generalized jaundice. Blood pressure 110-80, pulse 90; blood hemoglobin 69 per cent, red blood cells 4,490,000. Coagulation time was eight minutes. Urine showed moderate albumen and casts. Preoperative preparation begun January 15th; 31 cc's of $CaCl_2$ was given intravenously in four doses, the coagulation time of the blood being reduced to three minutes. January 19th hepaticoduodenostomy was done for absent common duct. Marked biliary cirrhosis noticed with atrophic liver. She did badly after operation. The jaundice seemed to deepen the third day and weakness became progressively worse. On the second day the pulse rose to 120 and on the morning of the fourth day the pulse became increasingly weak and rapid and there was a syncope for three minutes. Frequent coffee ground

vomiting occurred. There was moderate oozing from wound the third night. At noon the fourth day she died. The temperature was ninety-nine degrees the second and third days, falling shortly before death. Outside of marked cardiovascular asthenia the heart and lungs were negative. Urine output was eight ounces first day, seventeen ounces second day, scanty third day and anuria fourth day after operation. There was moderate albumin without casts in the urine. The blood urea before operation was 26 mgm. per 100 cc's and on the third day after operation 68 mgm. Death seemed due to a general asthenia with insufficient liver function and complicated by moderate internal hemorrhage.

Only an incomplete autopsy could be obtained. There was less than a pint of blood in the abdomen. Microscopic examination of the liver revealed bile thrombi and atrophy of liver cells about the central veins, and five granules of fat in the cells of the peripheral zone. Moderate fibrosis and lymphocytic infiltration occurred in the portal areas. The kidneys showed an occasional sclerosed glomerulus and atrophic tubules with moderate swelling and granular change in the tubular epithelial cells. There was much bile pigment present, and also many bile casts.

This is the only case that received preoperative preparation with calcium that had serious postoperative bleeding which, in this case, seemed only contributory to the fatal outcome. The morning that death occurred the coagulation time was twenty-one minutes and the calcium time twelve minutes.

Case V. E. G. 377643, Age 57 presented himself for examination November 18th, 1921. He had been perfectly well until an attack of influenza in February 1919, followed by increased thirst and polyuria. Urine at this time showed sugar. No treatment given. He began to lose weight and strength. May 1921, he developed pain and tenderness in upper abdomen and in June a mass in the epigastrium was discovered. This disappeared with relief of symptoms except

that slight pain and jaundice persisted. Six weeks ago jaundice became more intense.

Examination revealed marked jaundice (II) pallor (I) and emaciation (I-II). Blood pressure 130-80, pulse seventy-six. Normal weight 250 pounds, present weight 147 pounds. Urine; specific gravity 1022, albumin I, sugar trace and pus I. Blood hemoglobin 78 per cent, red blood cells 3,980,00 and white blood cells 5,000. Stools clay and stercobilin absent. Blood urea [illegible] 17 [illegible] mg. per 100 cc. Blood sugar 210 mgm. Coagulation time eight minutes.

Patient was sent to hospital and received antidiabetic diet and forced fluids. The urine output varied from 500-1600 cc a day. The sugar disappeared in the urine. He received a transfusion of 500 cc citrated blood November 29, 1921 and the coagulation time the next day was six minutes and fifty seconds. December 1, 1921 cholecystostomy was done. There was a pancreatitis IV, and a biliary cirrhosis III was present. Carcinoma of the head of the pancreas was questionable. White bile exuded from the dilated common duct. After operation there was a profuse drainage of thin, pale bile. After the fourth day his condition grew progressively worse. The pulse and heart sounds became more feeble. There was increasing muscular weakness, drowsiness and indifference and irritable restlessness. Urinary output was satisfactory throughout. On the seventh day the patient complained of pain under the right ribs radiating to the right shoulder. Leukocytes were 25,000. "Coffee ground" vomiting appeared and death occurred two days later from asthenia. (See Table 1)

DATE 1921	BILE DRAINAGE CC	URINE OUTPUT	SPEC. GRAV.	ALB.	SUG.	CASTS	PUS	BILE	BLOOD HG	WBC	UREA	CREAT.	
11-22			1022	1	Tr.		1-3		78%	5,000	17mg.		
12-1	980	880	1016	11	o	1	1-4	+			28		operation
12-2	1600	970											
12-3	1650	900											
12-4	1780	770											
12-5	960	800									76	2.1	
12-6	1015	380	1018	11	o			+					
12-7	280	980											
12-8	15	600	1017	11	Tr.			+					
12-9	Died 9:15 A.M.												

At autopsy the liver was enlarged 2550 gm. but showed marked central atrophy and hydropic change in the cells of the peripheral zones. The kidneys weighed together 413 gm. and showed only moderate signs of nephritis. There was carcinoma of the head of the pancreas, miliary gastric ulcers, right adhesive pleuritis, and old endocarditis; coronary sclerosis and purulent seminal vesiculitis were the only other important pathological changes.

The liver seemed responsible for death in this case. Many surgeons have called attention to the seriousness of finding white bile at operation. (5) (21) (32). The drainage after operation contained some bile but it was chiefly seromucous.

It is certain that in a large percentage of the cases doing badly there is a combination of insufficient renal and hepatic function. Either may dominate the picture and their relative importance may change. The following case is very interesting in this regard.

Case VI. Mr. T. S. 379535, Age 64 years, presented himself for examination December 13, 1921. He enjoyed excellent health until March 1921 when he was taken ill with an attack of dizziness, weakness, and general malaise. In April jaundice developed with clay stools. Loss of weight 235 pounds to 165 pounds April to July. Only pain was a dull ache posterior thoracic region and both shoulders. Gradual improvement July to November, jaundice remaining only faint.

November 24th jaundice became deep again, accompanied by malaise, loss of strength and weight. Frothy white stools five to six times daily. On examination intense jaundice (III-IV) was present. Weight was 157 pounds. Emaciation II. Blood pressure 118-66, pulse seventy-six. Urine showed moderate albumin, a few hyalin and granular casts. Blood hemoglobin 66 per cent, white blood cells 10,900. He was sent to the hospital for preoperative preparation. The coagulation time of the blood was reduced from seven minutes to three minutes by intravenous injection of 25 cc of 10 per cent calcium chloride solution given in three doses. The blood urea before operation was 24 mgm. December 20, 1921 choledochostomy for choledocholithiasis was done. There was marked biliary cirrhosis and subacute pancreatitis present. The gall-bladder was contracted and contained no stones. Drained.

Postoperative course was satisfactory until the fifth day when he experienced a sharp pain in abdomen radiating to right shoulder. This was followed by slight deepening of the jaundice and slight decrease in the bile flow. The blood urea on this day was 60 mgm. For the next six days he showed increasing signs of uremia. On the eleventh day the blood urea had risen to 208 mg. The urine was loaded with hyalin and granular casts. The leukocyte count was 20,000. At the same time the blood showed a great quantity of bile macroscopically and the coagulation time was sixteen minutes. During the next few days the nephritic picture improved markedly. There was an excessive flow of very thin bile the twelfth and thirteenth days and though large in quantity the total quantity of bile pigment present seemed decreased in amount. On the sixteenth day the blood urea was only 128 mgm. and there were only a few casts in the urine. The blood contained less bile and the coagulation time was eight minutes. Though the kidneys seemed to be getting better he had a change for the worse about the twelfth day. Weakness increased so that he could hardly raise his arms. The pulse and respiration grew more feeble progressively. He became restless, and

indifferent. The bile drainage remained very thin though it became less in quantity. On the nineteenth day after operation he died. Urinary output had remained satisfactory throughout.

Autopsy revealed a liver weighing 1500 gm. giving a firm shrunken appearance. There was a purulent discharge from the bile ducts. On microscopic examination there were many bile thrombi in the capillaries of the central region. The hepatic cells here are shrunken and distorted. There was moderate fibrosis of the portal areas with lymphocytic infiltration and a few polymorphonuclears.

The combined weight of the kidneys was 325 gm. There were definite macroscopic and microscopic signs of marked nephritis present.

Cumston in a review of the conclusions of many French observers, Helouin, Lamond, Gerandee, Sacquepee, Merklen, Lioust and others, points out the fact that icterus may accompany acute nephritis with little or no pathology. The azotemia is thought due to the renal insufficiency and also to hyperfunction of the liver. In this case the general picture is one of clearing nephritis. The lowering of the blood urea is probably due to two factors, better elimination by the kidneys and also to diminished formation of urea due to lowered hepatic function.

What can be done for these patients? Unfortunately little. Crile suggests intermittent drainage of the bile; application of heat over the liver may be of aid. It has been suggested that morphia is contraindicated as an hepatic depressant. As these patients show marked loss in body weight and depletion in body fluids, it is imperative to force fluids and nourishment for several days prior to operation. As Mann, Opie and others have shown the importance of carbohydrates in hepatic insufficiency, glucose proctoclysis should be employed both before and after operation.

Enough has been said by others of it to be unnecessary to repeat the importance of conservative operative procedures in the presence of jaundice.

The outcome of the cases in this series has given much encouragement. On account of the type of patients the mortality was necessarily high, but was lower than occurred previously in a review of a group of similar cases.

I wish to express my thanks to Dr. Waltman Walters for the assistance he has given me in his constant collaboration in the observation of patients and discussion of the problems arising.

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