Carcinoma of the Head of the Pancreas: *
Resection of the Portal Vein and Portacaval Shunt

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Introduction

Since the first pancreatoduodenectomy was performed by Dr. Whipple in 1935,[22] there have been only 15 published cases of survival for five years after operation for cancer of the pancreatic head.[2, 6] As recently as 1954, Stafford *et al.* reviewed 37 consecutive cases with proven cancer of the head of the pancreas operated on at the Johns Hopkins and Union Memorial Hospitals. There were no five year survivors.[19]

Certainly one important reason for such unsatisfactory results is the intimate association of the portal vein and the pancreas. As may be seen in Figure 1, the common bile duct and the portal vein are separated by approximately 2.0 cm. of pancreatic tissue. Any pancreatic neoplasm, unless it is situated very close to the common bile duct, must extend hopelessly close to the portal vein before it grows large enough to cause jaundice; and jaundice is usually the symptom which brings the patient to the surgeon. Could one sacrifice the portal vein and its tributaries which are adjacent to the pancreas, not only could a more satisfactory cancer operation be performed on the lesions which do not grossly involve the vein, but many lesions which are considered unresectable today could be removed. This latter factor, the low resectability rate, is undoubtedly a major reason for the small number of reported five year survivors; and portal vein involvement is probably the most frequent reason for such cancers being deemed unresectable.

Such considerations as these have led a number of men to consider resecting the portal vein with the pancreas en bloc in the excision of cancer of the head of the pancreas. Schafer and Kozy, in 1947, performed pancreatoduodenectomy with resection of the portal vein and portacaval shunt in 22 dogs. Three dogs survived the immediate operation and lived from 34 to 84 days, ultimately dying of stomal ulceration.[17] Child, from 1949 to 1952, published his beautiful work which culminated in ligation and resection of the portal vein in two stages.[4, 13] McDermott, in 1952, reported a case in which the portal vein was resected and the superior mesenteric vein anastomosed end-to-side to the vena cava.[10] Daniel, in 1952, resected a segment of portal vein in the dog and restored continuity with an autogenous iliac vein graft. Thirty-one dogs were operated on, with 13 survivors. Seven of the latter were sacrificed and of these, four grafts were patent at two, four, five, and six months, respectively.[5] Evans and Ochsner, in 1954, based upon a detailed study of the lymphatic drainage of the pancreas, felt that radical resection should include resection of the proximal portions of the superior mesenteric vein with its surrounding lymph nodes.[7]

Like the above men, we have felt dissatisfied with the routine pancreatoduodenec-

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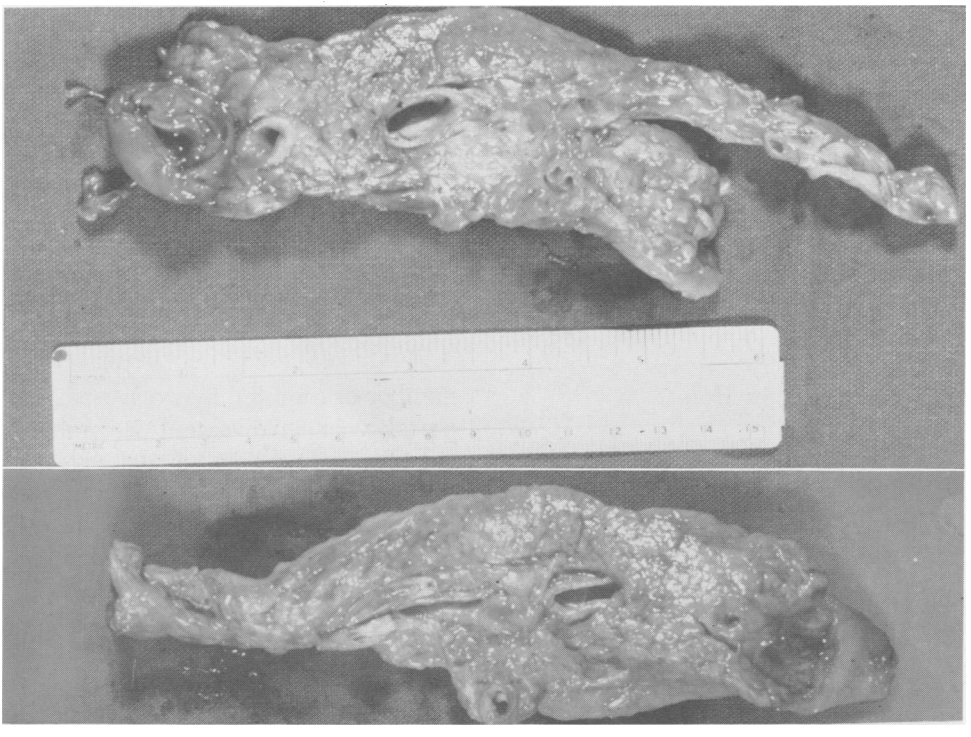

FIG. 1. Sagittal section of a pancreas at two different levels, showing the relationship of the duodenum, common bile duct, portal vein, splenic vein and superior mesenteric artery.

tomy as a cancer operation when dissecting a cancer of the head of the pancreas away from the portal and superior mesenteric veins. Simple ligation of the portal vein after the method of Child did not appear ideal in view of the expected portal hypertension. A vein graft bridging the defect would be the obvious solution, but presented a somewhat more complicated procedure and questionable immediate result. It was felt, therefore, that resection of the vein and portacaval shunt should first be tried before resorting to a vein graft. It is the purpose of this paper to present two such cases and the impressions gained therefrom.

The Eck Fistula

A detailed discussion of the many enigmas that exist regarding the portal circulation is not appropriate here. However, a few facts are known about the effects of diverting the portal blood from the liver, and a brief resumé of such facts is necessary for evaluation of the patients to be reported.

As regards the experimental animal, Eck in his original paper stated that "deprival of the liver of the portal blood flow does not cause any serious disturbance to the body" and "the animal . . . remains in perfect health thereafter." [3] This statement was based, however, on observing one dog for two and a half months after operation. Longer observations have shown that when the portal blood is completely shunted into the vena cava a dog characteristically presents progressive loss of weight, episodic coma, a decrease in total circulating albumin, and fatty infiltration of the liver.[2, 18] Although some long term survivors have been described among Eck fistula dogs,[9, 12] there is evidence that, if the portal diversion is complete, animals, with rare excep-

tions, die within a year.[2] That the typical episodic coma is accompanied by an increased ammonia concentration of the blood as well as an increased amino acid concentration of the cerebrospinal fluid has been demonstrated.[2, 12]

There is considerable evidence that these changes are due to the decrease in hepatic blood supply rather than to some inherent characteristic of portal blood. Thus Bollman *et al.* have shown that if the portal vein is ligated in stages, producing a collateral circulation, a subsequent Eck fistula is not followed by the characteristic symptoms described above.[2] Similarly, Silen *et al.* have shown that when a portacaval transposition is carried out dogs do not develop the hepatic deterioration and decrease in albumin production characteristic of the Eck fistula dog.[18]

The first end-to-side portacaval shunt in a human with a normal liver and patent portal vein was performed by McDermott in 1952.[10] This was a 69-year-old man with a carcinoma of the head of the pancreas. A pancreatoduodenectomy was performed with resection of the portal, splenic, and superior mesenteric veins, and end-to-side anastomosis of the superior mesenteric vein to the vena cava. The immediate course was uneventful, but the patient ultimately died 20 months after operation. His later course was described in McDermott's classic paper on ammonia metabolism in the human. Pertinent points were frequent episodes of stupor, a high blood ammonia, severe hypoalbuminemia, and fatty infiltration of the liver at autopsy. Another similar case has been reported by McDermott. This patient recovered uneventully from the operation, but during the five months in which he had been followed had had one episode of coma, and was kept relatively asymptomatic only when his protein intake was limited to 60 Gm. daily.[11]

There is some evidence that in the human, as in the dog, such liver degeneration does not appear if a collateral circulation has been developed before the portacaval shunt is performed. Niedner and Mattes have described a case in which the portal vein was ligated in 1950, during the repair of a common duct stricture. One year later, in 1951, a splenorenal shunt was performed due to portal hypertension. A portogram at this last operation showed the portal vein to be completely occluded, so that the splenorenal shunt apparently effected a complete deviation of portal blood. Five years later, in 1956, the patient was asymptomatic, with an albumin of 4.3 Gm. per cent and essentially normal liver chemistries.[15] Additional evidence is offered by the patient with cirrhosis since, as noted by Blakemore, an end-to-side portacaval shunt is infrequently followed by "ammonia intoxication" when done in the cirrhotic patient who has a relatively complete portal block as evidenced by little or no rise in portal pressure when the portal vein is clamped.[1]

Case Reports

Case 1. E. R., a 68-year-old white woman, was admitted to the hospital on September 24, 1956.

History: The patient complained of jaundice, pruritus, and some nausea of four weeks' duration. There had been no pain and no known weight loss.

Physical Examination: The patient was a well-preserved, rather thin, white female who was markedly jaundiced. The liver was palpable, smooth, and slightly tender, two fingerbreadths below the costal margin. The gallbladder was not definitely palpable. Physical examination was not otherwise remarkable.

Laboratory Data: Pertinent data were an icterus index of 61.5; albumin 3.27 Gm.%; globulin 3.85 Gm.%; prothrombin time 14 seconds (60 per cent); cephalin flocculation 0 in 24 hours; thymol turbidity 18 units.

Operation: Operation was performed on November 16, 1956. There was a tumor mass in the head of the pancreas which measured 3.0 cm. in diameter and which obstructed both the common duct and the cystic duct. There was no evidence of metastatic spread to the rest of the abdomen. However, the tumor was intimately adherent to the portal vein. That the latter was patent was evidenced by the fact that the portal pressure in one of the tributaries of the superior mesenteric vein was 80 mm. of saline and increased to 300 mm.

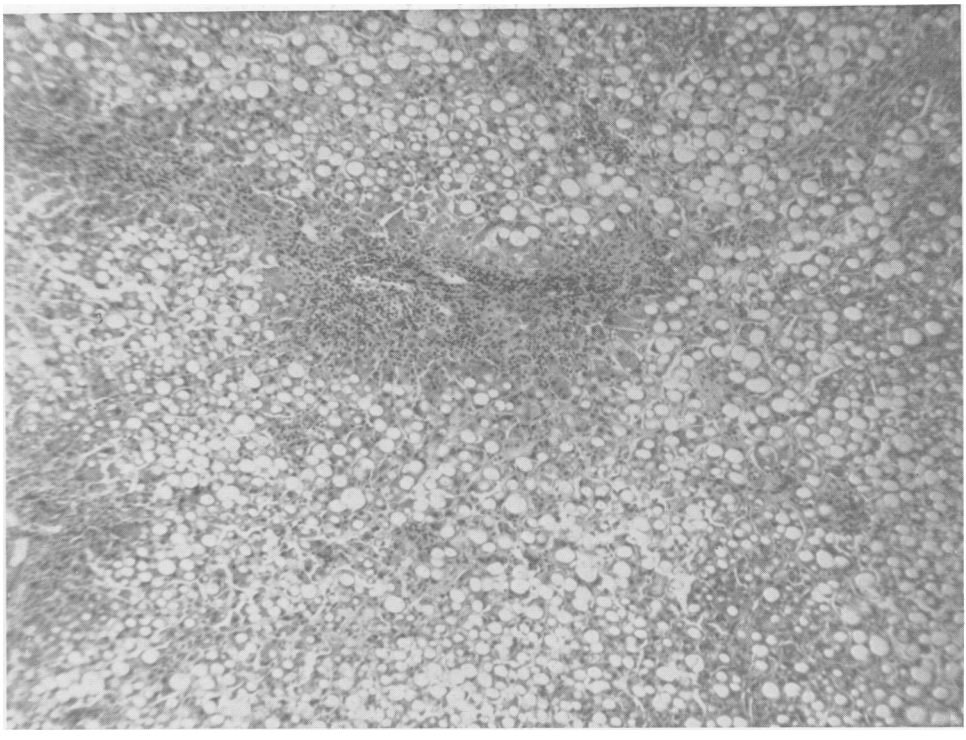

FIGURE 2A

when the portal vein was clamped. A pancreatoduodenectomy was performed, resecting the portal vein, the terminal portion of the splenic vein, and the terminal portion of the superior mesenteric vein en bloc with the pancreas. An end-to-side anastomosis was then performed between the superior mesenteric vein and the vena cava.

Pathologic Report: Adenocarcinoma of the head of the pancreas with obstruction of the pancreatic, common, and cystic ducts, with metastases to the adjacent lymph nodes and to the adventitia of the portal vein.

Postoperative Course: The immediate postoperative course was uneventful, the patient being discharged from the hospital on the 16th postoperative day. She was readmitted to the hospital 2 weeks later, December 18, 1956, semicomatose, with a flapping tremor of both hands and the typical picture of "ammonia intoxication." Recovery from this episode was rapid and dramatic following the administration of 25 Gm. of sodium glutamate intravenously. The patient was discharged on a 40 Gm. protein diet, but returned in one month, January 13, 1957, with a similar episode. Thereafter she was placed on 30 Gm. of sodium glutamate ("Accent") a day orally, but had another more severe episode of coma on March 1, 1957. On March 15, 1957, edema of the fingers and feet became apparent, at which time her serum albumin was 2.21 Gm. per cent. She was placed on a 60 Gm. protein diet and over the next 6 weeks received 25 Gm. of serum albumin a week intravenously. Sulfathalidine 4.0 Gm. a day was also administered. During these 6 weeks, however, she had 2 episodes of severe coma, from one of which she aroused only after receiving 75 Gm. of sodium glutamate and arginine, enemas, et cetera. The albumin administration was therefore discontinued and on May 20, 1957, she was placed on 3.0 Gm. of Mycifradin® (neomycin)* a day and a 100 Gm. protein diet. The sodium glutamate was discontinued. With this regimen her sensorium was excellent with no clinical evidence of ammonia intoxication. However, edema of the extremities and sacral area grew progressively more severe until she was admitted to the hospital for the last time on June 6, 1957. At this time she gave a story of 12 hours of severe left upper quadrant pain. Physical examination revealed a tender, firm, silent abdomen. There was severe anasarca, the legs being so edematous that they were weeping. Serum albumin was 0.65 Gm. per cent and globulin

* Supplied by the Upjohn Company, Kalamazoo, Michigan.

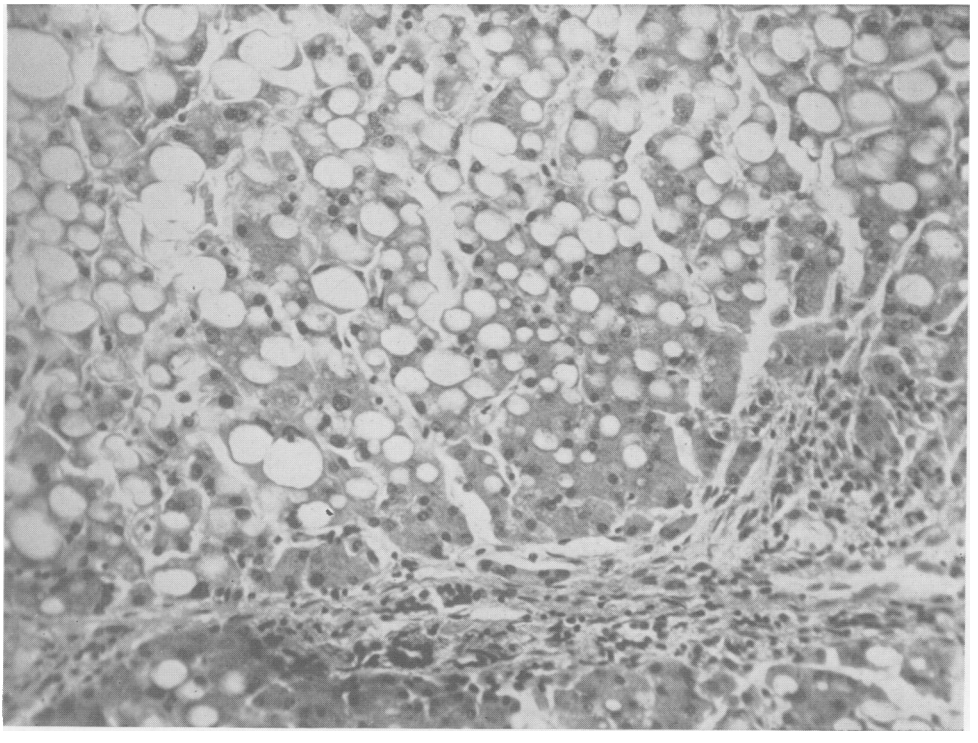

FIGURE 2B

FIG. 2. Microscopic sections of the liver of patient, E. R., Case No. 1. The marked fatty infiltration is apparent. A. Low power. B. High power.

4.35 Gm. per cent. Although it was evident that an abdominal catastrophe had occurred, it was apparent that she would not tolerate surgery at this time. She was therefore treated conservatively over the next 5 days, during which period she received a total of 1,500 cc. of blood and 175 Gm. of concentrated serum albumin. At this point the edema had subsided considerably, but the patient was moribund and presented a generalized peritonitis. An enterostomy and drainage of the abdomen were done, but she expired 24 hours later.

Autopsy: Pertinent findings were generalized peritonitis secondary to a perforated jejunal ulcer just distal to the gastroenterostomy; patency of all anastomoses; no residual cancer in the peri-aortic nodes, pancreatic remnant, or elsewhere; and marked fatty infiltration of the liver with most of the parenchymal cells having a cytoplasm that was markedly vacuolated. There was no actual cirrhosis (Fig. 2).

Case 2. W. W., an 85-year-old white male, was admitted to the hospital on March 16, 1957.

History: He complained of epigastric pain, anorexia, jaundice, and weakness of 3 weeks duration. One year previously he had undergone a mandibulectomy and neck dissection for squamous cell carcinoma of the inferior alveolar ridge with lymph node metastases.

Physical Examination: Pertinent findings were emaciation, jaundice, a tender mass in the right upper quadrant and no evidence of recurrence of the mandibular cancer.

Laboratory Findings: Albumin, 3.3 Gm. per cent; globulin, 2.3 Gm. per cent; cephalin flocculation, 0; thymol turbidity, 2.5 units; prothrombin time, 15 seconds (75.5 per cent).

Operation: The patient was prepared for surgery and operation was performed on April 2, 1957. A carcinoma of the head of the pancreas was found which was intimately adherent to the portal vein and the middle colic artery. Pressure readings were not made, but it was apparent that the portal vein was patent since, when it was clamped, the bowel became cyanotic and the proximal portal vein collapsed. Since pain was a prominent symptom, it was felt that a by-pass procedure would offer little or no palliation. Therefore, a pancreatoduodenectomy was done, resecting the portal, splenic, superior mesenteric veins, and middle colic artery *en bloc* with the pancreas. The supe-

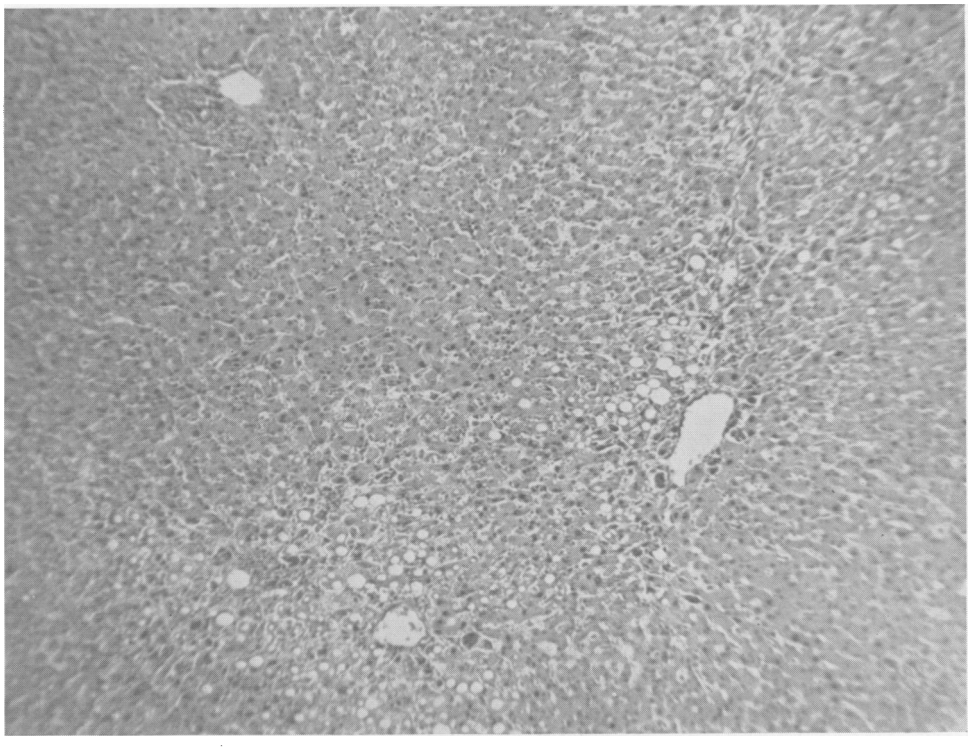

FIGURE 3A

rior mesenteric vein was anastomosed end-to-side to the vena cava. The postoperative course was complicated by considerable serous drainage from a drain which led to the gallbladder fossa. However, at time of discharge from the hospital, on the 28th postoperative day, this had ceased.

Pathologic Report: Adenocarcinoma of the pancreas with involvement of regional lymph nodes and the adventitia of the portal vein and the perineural lymphatics.

Postoperative Course: The patient was maintained from the time of discharge from the hospital on 3.0 Gm. of Mycifradin® a day and 20 Gm. of sodium glutamate ("Accent") a day. At no time did he go into coma, and he showed no gross evidence of ammonia intoxication. He was allowed to eat anything he wanted. Nevertheless, he became progressively more edematous, even though over the next 3 months he received 1,000 cc. of blood and 50 Gm. of concentrated serum albumin in 4 spaced intervals.

On July 10, 1957, he was admitted to the hospital for the last time. He was now having grossly tarry stools. On physical examination the outstanding findings were massive anasarca, including weeping of the skin of the legs as in the previous patient and edema of the scrotum. There was also a severe fungus infection of the mouth and perineum, apparently secondary to the neomycin. Laboratory findings were as follows: hematocrit, 37 per cent; albumin, 0.85 Gm. per cent; globulin, 6.15 Gm. per cent; prothrombin time, 71 per cent; cephalin flocculation, 4 + (24 hours); bromsulphalein retention, 43.5 per cent (45 minutes). The patient was too weak for extensive diagnostic investigation or operation. Treatment consisted of stopping the neomycin, giving mycostatin, a sippy diet, intravenous blood and albumen. Under this regimen he at least held his own, but 10 days later, on July 20, 1957, his temperature rose to 104°, coma ensued, and he died on July 23, 1957.

Austopsy: Pertinent findings were patency of all anastomoses and no evidence of any residual cancer; the gastro-intestinal bleeding apparently arose from diverticula of the left colon; the hepatic segment of the ligated portal vein was occluded by an organized thrombus that extended into the major intrahepatic branches; there was prominent fatty infiltration of the liver (Fig. 3).

Discussion

Although "ammonia intoxication" was controlled clinically in the second case with

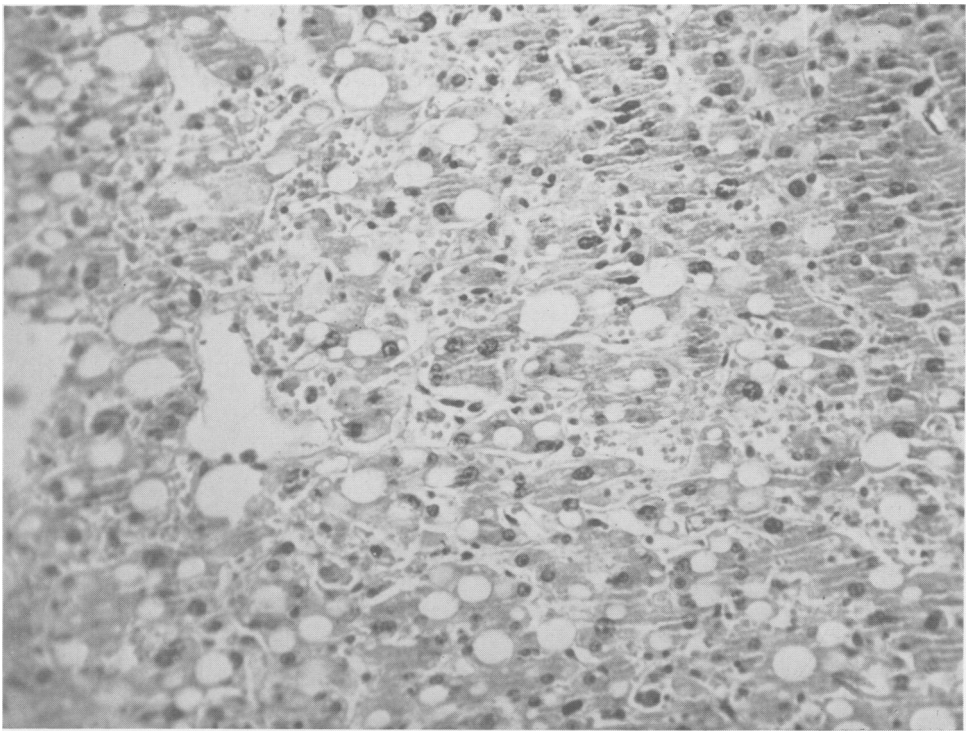

FIGURE 3B

FIG. 3. Microscopic sections of the liver of patient, W. W., Case No. 2. The fatty infiltration is evident. A. Low power. B. High power.

neomycin and sodium glutamate by mouth, both of these patients presented a distressingly similar picture of progressive hepatic deterioration and almost complete cessation of albumin production, with massive edema. This phenomenon was the ultimate indirect cause for their death. One other Eck fistula formed in the human with a normal liver and patent portal vein has been reported in the literature with prolonged follow up. This patient died with a similar picture of hypoalbuminemia.[11] The close correlation of the course of these three patients with the known fate of the Eck fistula dog is sufficient evidence, we believe, to conclude that a portacaval shunt is not a satisfactory method of reconstruction after resection of the patent portal vein in the presence of a normal liver.

There is a possibility that such a shunt would be satisfactory if the portal vein has been occluded by the tumor and a collateral circulation has developed. However, it has been our experience that if a pancreatic cancer has extended so far as to occlude the portal vein, it has usually extended too far in relation to other structures for complete excision.

Certain positive impressions have been gained, however, in performing these two operations. First, resection of the portal, superior mesenteric, and splenic veins dramatically opens a wide field for dissection of the lymphatic tissues about the aorta and superior mesenteric artery. Our two cases as well as the case of McDermott had lymph node involvement and involvement of the adventitia of the portal vein. No cancer was found at autopsy, three and one-half, seven, and 20 months after operation, respectively. Although minute cancer foci may still have been present, these autopsy

findings demonstrate that there is at least a possibility that these patients were cured of an otherwise unresectable cancer.

Secondly, when the superior mesenteric artery was clamped temporarily together with the vein, the small intestine did not become discolored and the patients showed no systemic reaction during the 20 to 30 minutes of occlusion necessary to complete the resection and perform the portacaval shunt. These vessels were clamped by Moore *et al.* for 95 minutes without apparent damage to the bowel.[14] Such facts suggest that adequate time would be available for the interposition of a well-planned vein graft. We have observed on these two cases, as well as on other cases with normal portal systems and normal livers, that when the portal vein is clamped the hepatic end of the vein collapses completely while the distal vein becomes engorged. This suggests a pressure differential large enough to prevent clotting in a graft. As a matter of fact, a report of one such attempt has been found in the Japanese literature. Kikuchi of Tohoku University has described a case in which, after pancreatoduodenectomy, the continuity of the portal vein was restored by a homologous, alcohol-treated vein graft, inserted by a non-suture technic with a polyethylene splint. The patient died 27 hours later of unrelated causes and at autopsy the vein graft was patent.[8]

There is a natural reluctance on the part of surgeons to perform vascular anastomoses in the presence of a divided pancreas, intestine, and bile duct. However, a number of such cases have been described whose immediate uneventful recovery belies this reluctance. A total of 11 cases have been reported, including the two described in this paper, in which a segment of the portal vein has been successfully resected during pancreatoduodenectomy, and either re-anastomosis or portacaval shunt performed (Moore *et al.*[14] Waugh and Giberson,[21] Parsons,[16] Dennis and Varco,[6] Sweet,[20] McDermott,[11] Zimmerman[28]). Obviously the really constructive advances in the surgical cure of cancer will depend upon methods of earlier diagnosis. However, until we are able to diagnose cancer of the pancreatic head before jaundice appears, resection of the portal vein and its tributaries offers the most likely means of increasing the cure-rate. It is the writer's opinion that a vein graft after such a resection is feasible.

Summary

Two cases are reported in which pancreatoduodenectomy, resection of the portal vein, and portacaval shunt were performed for cancer of the head of the pancreas. These patients died in a few months with fatty infiltration of the liver and severe hypoalbuminemia.

Resection of the portal vein is feasible and should increase the curability of cancer of the pancreatic head. However, a portacaval shunt should not be performed in the presence of a patent portal system. A vein graft is probably feasible and should be tried.

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Discussion

Dr. Champ Lyons: It has been my privilege to follow some of the developments in these cases as Dr. Hubbell lives 100 miles from Birmingham and comes up regularly to assist us in the teaching program. I have also had the privilege of reviewing his paper.

To me it is extremely significant that hypoalbuminemia has resulted in these cases. I think perhaps the emphasis that has been given on the hypoalbuminemia by this paper is the most significant finding. Dr. Hubbard has stated that he would rather not do a fistula into an open portal vein because of this. I am sure he is probably right, but I would like to suggest that there may perhaps be another mechanism involved. The Scandinavian literature reported the development of hypoalbuminemia as the result of the Bilroth II anastomosis and its correction by the conversion of that anastomosis to a Bilroth I. I think Dr. Hawkins in some of his papers, I can't quite recall the exact ones, mentioned that as one reason for preferring the Bilroth I. Dr. Ravdin told me this morning that he had on two occasions found patients with Bilroth II's and hypoalbuminemia who had been cured by converting to a Bilroth I. The mechanism of a hypoalbuminemia produced in these patients may prove to be a very fertile field for investigation. I think it also raises a very obvious obligation on the part of those who are doing various end-to-side or side-to-side anastomoses for relief of portal hypertension to follow and study the albumin levels.

We happen to have followed with Dr. Longmire in a preference for side-to-side, and I was quite pleased to see that in a certain percentage of his patients there has been an actual rise in albumin. Perhaps careful attention to both eualbuminemia and hypoalbuminemia will afford a basis for the long-term comparison of end-to-side and side-to-side shunts.

Dr. William P. Longmire, Jr.: I would like to compliment Dr. Hubbard on his interesting presentation. We have been interested in this general subject and have reviewed the literature recently in an effort to evaluate cases of this type.

The problem of ammonia intoxication occurs under three conditions. In the first place, it occurs