HEPATIC WEDGE PRESSURE, BLOOD FLOW, VASCULAR RESISTANCE AND OXYGEN CONSUMPTION IN CIRRHOSIS BEFORE AND AFTER END-TO-SIDE PORTACAVAL SHUNT

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Research Article

HEPATIC WEDGE PRESSURE, BLOOD FLOW, VASCULAR RESISTANCE AND OXYGEN CONSUMPTION IN CIRRHOSIS BEFORE AND AFTER END–TO–SIDE PORTACAVAL SHUNT [1,2]

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Surgical decompression of the portal system by construction of an anastomosis between the splenic and left renal veins or between the portal vein and inferior vena cava is an effective treatment for portal hypertension in cirrhosis. Shunts of this type have been shown to be remarkably effective in the prevention of recurrent variceal bleeding (1, 2). In view of the known high incidence of repeated and eventually fatal hemorrhages in those cirrhotics who have already had one episode of variceal bleeding, there is little question concerning the indication for a shunt in such patients, providing they have sufficient hepatic reserve to withstand the immediate trauma of surgery.

With improvement in surgical technique and patient selection, the previously formidable mortality from these operations has been greatly reduced. Consideration can now be given to extending the indication for shunt surgery to patients with demonstrable varices which have not yet ruptured (3). In debating the merits of "prophylactic shunts," we need both statistics concerning the life expectancy and probability of variceal rupture in these patients under conservative therapy, and information concerning the changes in hepatic hemodynamics and metabolism that might result from the various shunting procedures.

The available data bearing on the latter problem are limited and are concerned largely with the changes after splenorenal shunt. Bradley, Smythe, Fitzpatrick, and Blakemore, using the standard bromsulfthalein method to measure liver blood flow, found an average fall of 22 per cent in five patients after this operation (4). Hepatic oxygen consumption did not appear to be decreased. Nardi, using a less widely accepted technique for liver blood flow determination (the disappearance rate of radioactive colloidal chromic phosphate), noted a fall in six of nine patients after splenorenal shunt (5). The mean change in the nine patients was a fall of 24 per cent.

In the end-to-side portacaval shunt, the portal vein is ligated and divided, and its distal end is implanted into the vena cava. Diversion of portal blood from the liver is therefore complete, and hepatic hemodynamic changes would be expected to be even greater than after a splenorenal shunt. Published studies on hemodynamic changes are limited to three cases included in the report of Bradley, Smythe, Fitzpatrick, and Blakemore (4), and in these three, hepatic blood flow fell an average of 36 per cent. In the clinic from which our patients are drawn, end-to-side portacaval shunt is the procedure of choice for the relief of portal hypertension in cirrhosis (6). In 10 such patients, we have made pre- and postoperative comparisons of the standard liver function tests, and the data obtainable from hepatic vein catheterization, namely, hepatic blood flow and oxygen consumption, wedged hepatic venous pressure, and postsinusoidal hepatic vascular resistance. This communication details our findings and discusses their implications on the therapy and pathologic physiology of portal hypertension.

MATERIALS AND METHODS

Ten patients with end-to-side portacaval anastomoses were the subjects of the study. All were chronic alcoholics and in each, a surgical liver biopsy confirmed the diagnosis of cirrhosis. Esophageal varices were visualized by X-ray in seven cases and by esophagoscopy in

three. Bleeding from ruptured varices had occurred in all patients except one (J. J.). He had splenomegaly, leukopenia and large esophageal varices demonstrable by X-ray and esophagoscopy. The patients were studied prior to and again following the shunting procedure, as soon as the clinical condition permitted. In two subjects (J. J. and T. S.), the preoperative studies were made on the day of surgery, just prior to the operation. The postoperative studies were made within two months of surgery in eight subjects, three and one-half months after surgery in one (C. M.) and nine months after surgery in another (J. R.).

Hepatic vein catheterization was performed by the usual technique (7). All patients were fasting at the time of the study. Wedged hepatic vein pressure (WHVP) was recorded with the catheter tip wedged into and occluding a small hepatic venous radical (8). The pressure levels reported are net pressures computed by subtracting the measured inferior vena caval pressures from the measured wedged pressure. The use of vena caval pressure as a reference point eliminates errors due to elevation of right atrial pressure, or to inaccurate positioning of the zero point of the pressure recorder (9). Whenever possible, WHVP was recorded from more than one site in the liver to guard against inaccuracy occasioned by incomplete wedging of the catheter. If different levels of WHVP were encountered at different sites, the highest pressure was utilized. In all the preoperative and in nine of the postoperative studies, WHVP, hepatic blood flow, and oxygen uptake data were obtained with the catheter in the right hepatic lobe. However, in Patient R. R., the postsurgical data were obtained with the catheter in the left lobe, since it was impossible to enter a right hepatic vein sufficiently deep to preclude mixing of vena caval and hepatic venous blood during sampling.

With the catheter deep in a hepatic vein, the estimated hepatic blood flow (EHBF) was determined by the bromsulfthalein (BSP) method (7). After a primer dose of from 40 to 60 mg. of BSP was given intravenously, a dilute BSP solution was infused at a given rate by a constant infusion pump. An amount of BSP primer necessary to produce a plasma concentration of approximately 1.5 mg. per cent was estimated from a previously performed 30 minute BSP test (5 mg. per Kg.), and from the patients' body size. An infusion rate was then chosen (usually from 2.0 to 2.5 mg. per minute) which, it was anticipated, would not exceed the liver's ability to keep the plasma BSP levels constant. Simultaneous samples of femoral arterial and hepatic venous blood were taken at approximately 5 minute intervals beginning 20 minutes after injection of the BSP primer. BSP concentrations in the serum were determined colorimetrically after the method of Gaebler (10). The hepatic plasma flow was computed from the hepatic removal rate of BSP and the peripheral arterial-hepatic venous BSP concentration difference. EHBF was calculated from this value and the arterial hematocrit. The rate of BSP infusion (mg. per minute) was corrected for the rate of change of BSP concentration (ΔBSP) in

the arterial plasma by the formula of Bradley, Ingelfinger, Bradley, and Curry (7), and the resultant value was taken to be the hepatic removal rate of BSP (^{R}BSP). The validity of the values for hepatic blood flow obtained in this study was determined by the relationship of the rate of change of the arterial BSP concentration to the hepatic removal rate of BSP. It is felt that the correction applied for the rate of change of the arterial plasma BSP levels is, at best, an approximation, since the plasma volume is estimated from a nomogram. Therefore, as this correction factor becomes large in proportion to the value for hepatic BSP removal, the calculation of EHBF becomes progressively less reliable. Thus, values for ^{R}BSP of less than 1.5 mg. per minute were not considered acceptable in this study unless the rate of change of the arterial BSP concentration was less than 0.00026 mg. per ml. per minute. In the postoperative study of Patient C. W., for example, the ^{R}BSP was small, 1.44 mg. per minute. However, ΔBSP was only 0.00020 mg. per ml. per minute and the EHBF was therefore considered valid. We do not feel that the use of BSP extraction percentage, ^{E}BSP (arterial-hepatic venous BSP difference divided by the arterial BSP concentration), as the criterion for the validity of the hepatic blood flow determination is satisfactory, since this technique automatically eliminates the calculation of high hepatic blood flows if they do exist. As an example of this, in Patient C. M.'s preoperative study, the BSP extraction was only 10 per cent at a plasma BSP level of 2.20 mg. per cent, yet the rate of rise of BSP concentration in the arterial blood was relatively small (0.00016 mg. per ml. per minute), and the ^{R}BSP fairly large (3.28 mg. per minute). By our criteria, this would be a valid estimation of EHBF, whereas it would be unacceptable by the criteria suggested by Bradley, Ingelfinger, Bradley, and Curry (7).

The values for hepatic resistance (HR) were determined by dividing WHVP by EHBF and multiplying the quotient by a factor of 100 to bring the values near unity. If WHVP equals hepatic "sinusoidal" pressure, then HR represents the postsinusoidal vascular resistance.

Simultaneous samples of femoral arterial and hepatic venous blood were obtained anaerobically in heparinized syringes immediately following each BSP sample. Arterial and hepatic venous blood oxygen content was determined by the method of Van Slyke and Neill (11) in Patients R. R., C. M., T. S., J. R., M. L., and J. J., preoperatively, and in R. R., C. M., T. S., C H, and J J., postoperatively. In all other instances, the oxygen content was computed from the blood oxygen saturation (determined with a Waters-Conley oximeter) and blood hemoglobin values.

In the preoperative studies splanchnic oxygen consumption (SOC) was computed from the arterial-hepatic venous oxygen difference and the hepatic blood flow. SOC includes both hepatic oxygen consumption (HOC) and the oxygen uptake of the viscera drained by the portal vein. This latter component of the total SOC is relatively small (see below). Postoperatively HOC was
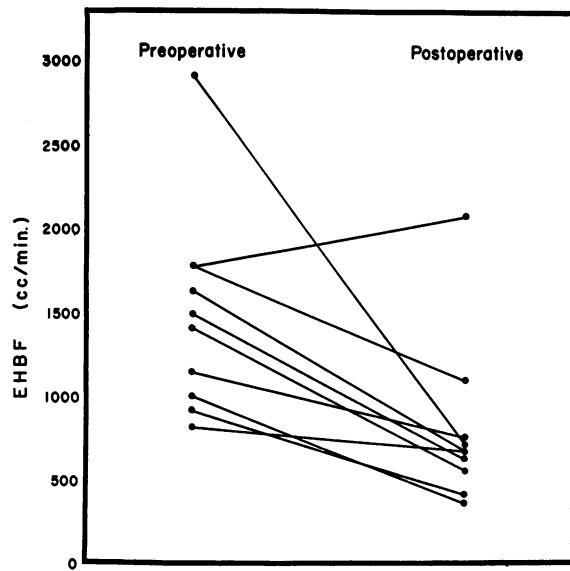
FIG. 1. EFFECT OF PORTACAVAL SHUNT ON ESTIMATED HEPATIC BLOOD FLOW

calculated from the product of the arterial-hepatic venous oxygen difference and the hepatic blood flow. The value no longer includes oxygen uptake of the other abdominal viscera since there is no portal blood entering the liver.

RESULTS

Estimated hepatic blood flow (EHBF)

The EHBF preoperatively ranged from 815 to 2,910 ml. per minute, and averaged 1,490 (±182)[4] ml. per minute. After the shunting operation, the hepatic blood flow ranged from 365 to 2,080 ml. per minute with a mean value of 800 (±93) ml. per minute (Table I, Figure 1).

In 9 of the 10 patients, the EHBF decreased following surgery, while in one instance (Patient T. S.), it increased 16 per cent. The percentage decrease in flow ranged from 15 to 75 per cent, and the average change in the EHBF following the portacaval shunt was a decrease of 46 per cent. In Patient R. R. the preoperative value for the EHBF was unusually high (2,910 ml. per minute). If we were to exclude this value from the results for the EHBF, the adjusted mean preoperatively would be 1,335 (±111) ml. per minute and the percentage decrement following surgery would be 40 per cent. However, since the maximum rate of change of the arterial plasma BSP concentration during that measurement was only 0.0002 mg. per ml. per minute, the EHBF

4 Standard error of the mean.

value, in accord with the aforementioned criterion, was considered valid.

It should be pointed out that there are several potential sources of error in the measurement of the EHBF by the bromsulfthalein method, some of them undoubtedly operative in our patients. If, as reported (12), the plasma volume is greater than normal in cirrhosis, then the correction for the changing plasma BSP level will be larger than calculated. This will result in the EHBF being overestimated when plasma BSP levels are rising, and being underestimated when they are falling. Fortunately, in most instances in our patients, plasma BSP levels rose comparably in the preoperative and postoperative studies so that any error introduced by low estimates of plasma volume would tend to be systematic and not contributory to differences between pre- and postoperative flows. Only in Patients M. S. and C. H. were plasma BSP levels rising during the preoperative flow determination, and falling during the postoperative measurement. Since the rate of change of plasma BSP concentration was not excessive in either of these patients, the potential error in the EHBF calculation attributable to incorrect estimation of plasma volume is not excessive. In Patient M. S., for example, if plasma volume is
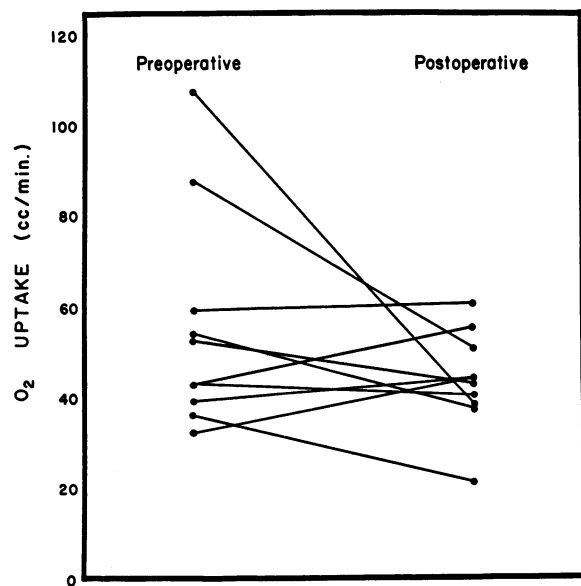

FIG. 2. EFFECT OF PORTACAVAL SHUNT ON HEPATIC OXYGEN UPTAKE

The preoperative figures refer to total splanchnic oxygen uptake, and the postoperative figures to hepatic oxygen uptake.

actually 50 per cent greater than has been assumed, the preoperative EHBF is 90 ml. per minute too high, and the postoperative value 40 ml. per minute too low.

The influence of the level of arterial BSP concentration on the estimation of hepatic blood flow is a matter of debate. Sherlock, Bearn, Billing, and Paterson felt that arterial BSP levels below 1 mg. per 100 ml. resulted in falsely high EHBF because of the increased importance of extrahepatic BSP removal (13). Bradley, Ingelfinger, and Bradley, on the other hand, has disagreed with this contention (14). Our own opinion is that the arterial BSP concentration is not a critical factor in the measurement of the EHBF, and that extrahepatic removal of BSP is important only when it represents a significant fraction of the BSP removal rate (*i.e.*, when the latter is small). Nevertheless, it would be preferable to make comparative pre- and post-operative EHBF measurements with the same arterial BSP levels, and we were unable to accomplish this in all of our patients.

In some of our patients there was a considerable variation in hemoglobin levels between the preoperative and postoperative EHBF measurements. Other things being equal, a fall in hemoglobin would be expected to cause a rise in the EHBF. In Patients M. S. and M. L., the rise in hemoglobin at the time of the postoperative measurement may have contributed to the observed fall in EHBF. On the other hand, postoperative declines in hemoglobin in Patients C. M., T. S., and J. R. may have minimized the fall in the EHBF in these cases. Since the mean preoperative hemoglobin level of 10.9 Gm. per 100 ml. differs little from the mean postoperative value of 11.0 Gm. per 100 ml., it is assumed that the net effect of the changes in hemoglobin level on the EHBF is insignificant.

Oxygen consumption

Preoperatively, the average value for SOC was 55.5 (±7.4) ml. per minute, while the mean HOC postoperatively was 43.8 (±3.2) ml. per minute (Table I, Figure 2). On the average, postoperative HOC was 21 per cent below preoperative SOC, being lower in six cases and higher in four. This difference is of doubtful significance, statistically. If the data for Patient R. R. are excluded because of marked variation from the mean of the remaining results, preoperative SOC averages

TABLE I

*Hepatic vein catheterization data before and after end-to-side portacaval anastomosis ***

Subject	Days from surgery Pre	Post	PBSP (mg./100 ml.) Pre	Post	ABSP (mg./ml./min.) Pre	Post	RBSP (mg./min.) Pre	Post	EBSP (%) Pre	Post	EHBF (ml./min.) Pre	Post	WHVP (mm. Hg) Pre	Post	H.R. (arb. units) Pre	Post	Art. O2 content (ml./100 ml.) Pre	Post	H.V. O2 content (ml./100 ml.) Pre	Post	Art.-H.V. O2 diff. (ml./100 ml.) Pre	Post	O2 uptake (ml./min.) Pre	Post
R. R.	27	40	1.23	1.49	+0.00020	+0.00016	3.19	3.28	17.1	53.0	2,910	710	14	11	0.48	1.26	15.6	16.2	11.9	10.7	3.7	5.5	107.7	39.0
C. M.	2	107	2.29	1.35	+0.00016	+0.00014	3.28	2.44	10.8	23.0	1,790	1,105	17	13	0.95	1.18	14.7	11.5	12.3	7.8	2.4	3.7	42.9	40.9
T. S.	0	21	1.32	1.24	+0.00026	+0.00012	2.95	2.58	18.9	13.7	1,790	2,080	17	10	0.95	0.48	11.8	8.9	8.5	6.0	3.3	2.9	59.0	60.4
J. R.	49	259	0.85	0.84	−0.00008	+0.00009	2.69	1.74	23.6	41.7	1,630	695	21	11	1.29	2.16	12.3	10.3	6.9	2.9	5.4	7.4	88.0	51.3
M. S.	23	66	0.88	1.36	+0.00018	−0.00015	3.02	2.93	30.6	47.0	1,500	630	22	12	1.46	1.74	7.0	13.5	3.5	6.7	3.5	6.8	52.5	42.8
M. L.	55	54	1.25	2.07	+0.00013	+0.00020	1.99	2.31	15.2	37.6	1,410	570	21	12	1.49	2.11	8.2	18.6	5.4	10.8	2.8	7.8	39.5	44.5
C. W.	22	55	0.76	1.48	−0.00007	+0.00020	2.40	1.44	40.8	18.2	1,150	755	15	9	1.31	1.59	12.5	13.8	9.7	7.9	2.8	5.9	32.2	44.5
J. A.	22	19	0.96	1.46	+0.00004	+0.00023	2.55	1.81	36.5	51.7	1,020	365	18	9	1.76	2.46	11.3	13.7	7.7	7.8	3.6	5.9	36.7	21.5
C. H.	21	15	0.59	1.40	+0.00006	−0.00026	2.46	2.78	65.6	77.1	920	410	20	13	2.12	2.20	15.6	15.4	9.7	6.2	5.9	9.2	54.2	37.7
J. J.	0	21	0.99	1.34	0.00000	+0.00015	2.70	2.33	51.2	36.5	815	690	19	13	2.33	1.89	13.8	12.7	8.5	4.6	5.3	8.1	43.1	55.9
Mean											1,493	801	18	11	1.41	1.70					3.8	6.3	55.5	43.8
S. E. of mean											±182	±93	±0.6	±0.3	±0.16	±0.13					±0.3	±0.5	±7.4	±3.2
S. E. of the difference between means											204		0.6		0.20						0.57		8.0	

* Abbreviations: PBSP = arterial plasma bromsulfalein concentration; ABSP = rate of change of plasma level of BSP; RBSP = hepatic removal rate of BSP; EBSP = hepatic BSP extraction percentage; EHBF = estimated hepatic blood flow; WHVP = wedged hepatic venous pressure; H. R. = hepatic postsinusoidal vascular resistance.
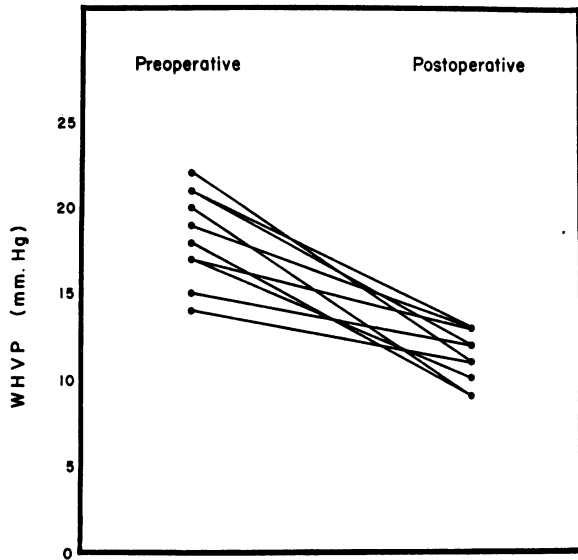
FIG. 3. EFFECT OF PORTACAVAL SHUNT ON WEDGED HEPATIC VENOUS PRESSURE

49.7 (±5.0) ml. per minute, and the percentage decrement following the shunt is 11 per cent.

In 9 of the 10 patients, the arterial-hepatic venous oxygen difference increased after portacaval anastomosis, averaging 3.8 (±0.36) volumes per 100 ml. before and 6.3 (±0.58) volumes per 100 ml. after surgery. The increase in this value following surgery was due to a decrease in hepatic venous oxygen content in all but three of these nine patients. In these three patients (M. S., M. L., and J. A.) there was a higher hepatic venous oxygen content after surgery because of a postoperative rise in hemoglobin, but the arterial-hepatic venous oxygen difference was still increased. The arterial-hepatic venous oxygen difference was slightly decreased postoperatively in one patient (T. S.), and in this patient the EHBF increased slightly.

Wedged hepatic vein pressure (WHVP)

Preoperatively, the WHVP was elevated in all patients, and ranged from 14 to 22 mm. Hg and averaged 18 (±0.63) mm. Hg. Normal values in our laboratory are from 2 to 6 mm. Hg. The WHVP decreased in every instance postoperatively, falling on the average to 11 (±0.31) mm. Hg and ranging from 9 to 13 mm. Hg (Table I, Figure 3). This represented a mean fall in the WHVP of 38 per cent as compared to the mean

decrease in the EHBF of 46 per cent. The largest decrements in the WHVP (Patients M. S., J. A., and C. H.) were associated with postoperative decreases in the EHBF of considerable magnitude (50 per cent, 50 per cent, and 55 per cent, respectively), and in the group as a whole, the fall in the WHVP was correlated with the decrease in the EHBF.

Hepatic resistance

The values for postsinusoidal hepatic resistance, expressed in arbitrary units, ranged from 0.48 to 2.33 preoperatively and from 0.48 to 2.46 postoperatively (Table I, Figure 4). The mean values were 1.41 (±0.16) before, and 1.70 (±0.13) after surgery. In a limited number of patients with no evidence of hepatic disease, we have obtained values of from 0.1 to 0.35 for this measurement.

DISCUSSION

In the end-to-side portacaval anastomosis, the portal venous blood is totally diverted from the liver into the inferior vena cava, and the hepatic stump of the portal vein is ligated. Although means for direct measurement of the portal blood flow are not available, an estimate of the value in cirrhosis can be obtained from the difference in hepatic blood flow before and after an end-to-side shunt. The hepatic hemodynamic changes observed following this procedure can be as-
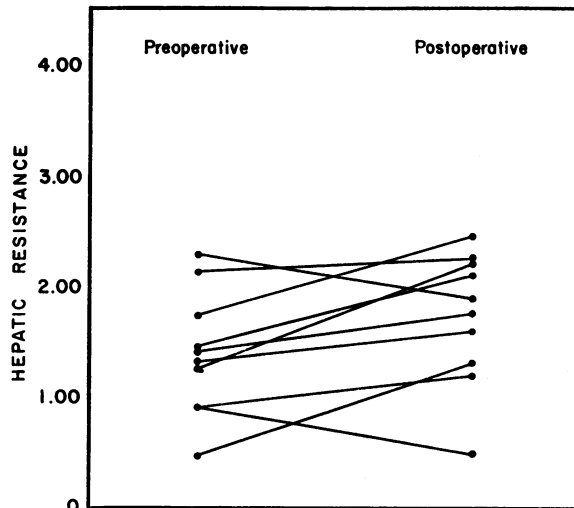

FIG. 4. EFFECT OF PORTACAVAL SHUNT ON CALCULATED HEPATIC POSTSINUSOIDAL VASCULAR RESISTANCE (ARBITRARY UNITS)

cribed only to exclusion of the portal blood from the liver, plus possible readjustments in hepatic arterial inflow. If, following the shunt, no significant change in hepatic arterial flow occurs, then the fall in the EHBF (averaging 46 per cent) presumably represents the portal venous component of the preoperative total liver blood flow. On the other hand, a postoperative compensatory increase in hepatic arterial inflow would modify the fall in total liver blood flow, and imply an even larger magnitude to the portal venous component than the observed 46 per cent. The observed fall in the EHBF, averaging 690 ml. per minute in our 10 cases, must, therefore, be considered a minimal estimate of the size of the portal blood flow. It appears that a very significant portion of the total blood flow of the liver is provided by the portal vein, even in patients with advanced cirrhosis and extensive collateral circulation. This agrees with the findings of Myers who, by administering sodium sulfathiazole orally and comparing simultaneous sulfathiazole levels in hepatic venous and abdominal collateral vein blood, estimated that portal flow ranged between 75 per cent and 25 per cent of the total liver blood flow in three patients with advanced cirrhosis (15). The hypothesis that only a small amount of portal venous blood actually enters the cirrhotic liver, the major portion circumventing it through collateral venous channels, is not compatible with our finding since, under these circumstances, an end-to-side portacaval shunt would be expected to have little or no effect on total liver blood flow. Moreover, if the abnormal hepatic arterial-portal venous communications, which have been described in human cirrhotic livers (16), were significant factors in the genesis of portal hypertension, retrograde flow in the portal vein might be expected to occur, and portal ligation incident to the shunt could actually increase the total liver blood flow.

In the fasting cirrhotic patient, the oxygen content of portal blood is only 1 to 2 volumes per 100 ml. less than arterial blood (4, 17). One might, therefore, expect the large drop in portal blood flow, following a portacaval shunt, to critically reduce the oxygen supply to the liver. Superficially, the 21 per cent difference between preoperative SOC and postoperative HOC would suggest that such a reduction has occurred. How-

ever, it must be recalled that in the preoperative patient, the product of the total hepatic blood flow and the arterial-hepatic venous oxygen difference represents the total splanchnic oxygen consumption. Because of the small arterial-portal venous oxygen difference, splanchnic oxygen consumption exceeds the hepatic oxygen consumption by a few ml. per minute. After ligation of the portal vein, only hepatic arterial blood perfuses the liver, and the same calculation gives a value for true hepatic oxygen consumption. The 21 per cent difference between preoperative SOC and postoperative HOC is, therefore, largely, if not entirely, due to inclusion of nonhepatic splanchnic oxygen uptake with the former. Further evidence against a fall in hepatic oxygen uptake is provided by the consistent increase in arterial-hepatic venous oxygen difference, seen postoperatively in all nine patients in whom the EHBF fell. It seems likely that the liver, by extracting increased amounts of oxygen from the arterial blood, is able to maintain its oxygen supply even in the face of a marked fall in total liver blood flow. Of course, since these studies were performed in the fasting state, they may not depict accurately the situation during peak metabolic demands on the liver. In addition, if there were any hepatic cells supplied only by branches of the portal vein, their oxygen supply would be expected to be compromised by a portacaval shunt.

Even though hepatic oxygen uptake is not reduced, the question nevertheless arises concerning what detrimental effects such a striking decrease in liver blood flow might have on a liver whose function has already been impaired by cirrhosis. Table II contains the results of certain standard hepatic function tests performed within a few days of the preoperative and postoperative catheterizations. It is apparent that there are no significant differences in these tests after the shunt, in spite of the magnitude of the decrease in liver blood flow. In a number of other patients whom we have observed following portacaval anastomosis, the standard tests of hepatic function have not been significantly altered except during a 4 to 12 week postoperative period when moderate jaundice and a decrease in serum albumin are the rule. We have not felt this temporary decline in liver function to be out of proportion to that observed in any patient with severe cirrhosis following a

Patient	Preoperative	Postoperative	Time from surgery
R. R.	A/G 4.0/2.0 II 20 BSP 14%	A/G 4.2/3.4 BSP 29%	6 weeks
C. M.	A/G 4.2/3.6 II 7 BSP 24%	A/G 3.4/3.8 BSP 24%	15 weeks
T. S.	A/G 3.7/2.2 II 7 BSP 20%	A/G 3.6/2.0 II 8 BSP 18%	3 weeks
J. R.	A/G 3.3/2.0 II 8 BSP 14%	A/G 3.5/2.5 II 23 BSP 21%†	34 weeks
M. S.	A/G 4.1/1.8 II 13 BSP (less than 10%)	A/G 3.9/3.2 BSP 15%	10 weeks
M. L.	A/G 3.4/2.2 II 22	A/G 3.5/2.8 II 7 BSP 30%	8 weeks
C. W.	A/G 3.3/2.5 II 17 BSP 21%	A/G 3.5/3.0 II 6 BSP 16%	8 weeks
J. A.	A/G 3.6/1.7 II 10 BSP 25%	A/G 3.4/3.2 II 15 BSP 30%	3 weeks
C. H.	A/G 4.0/2.3 II 9 BSP 10%	A/G 3.5/2.7 II 13 BSP (less than 10%)	2½ weeks
J. J.	A/G 3.6/3.6 BSP 19%	A/G 2.7/3.6	3 weeks

* Abbreviations: A/G = Albumin-globulin ratio (Gm. per 100 ml.); II = Icterus index; BSP = BSP retention after 30 minutes (5 mg. per Kg.).
† BSP retention after 45 minutes (5 mg. per Kg.).

major surgical trauma rather than to the drop in liver blood flow.

Of course, diversion of the portal blood from the liver may have more subtle effects on liver function than are measured by the standard tests. For example, "episodic stupor" has been observed to have its onset after portacaval shunt (18, 19). Although it appeared in 2 and possibly 3 of the 10 cases included in this report (Patients J. A., J. R., and J. J.), it has not been a frequent complication of the operation in our experience. These three cases afford us an opportunity to observe any possible relationship between the functional disturbance and magnitude of the post-

operative fall in liver blood flow. Although Patients J. R. and J. A. both had large percentile falls in their EHBF, there is no clear cut difference in this respect between these two and the remainder of the group. Patient J. J. actually had a relatively minor change in his EHBF, but it is questionable whether he fits into the category of "episodic stupor." When last seen, he had apparently been showing mental deterioration for approximately two months, and we were unable to determine if it was in any way episodic.

The WHVP was significantly elevated in all patients prior to the portacaval shunt. By this technique the occluding tip of the catheter is, in effect, extended via a static column of blood along the hepatic venule in the direction of the portal system. Presumably, this static column of blood extends no further towards the portal system than the nearest site of freely anastomosing vessels. This site of anastomosis can be termed the "sinusoid," whether one accepts the cord theory or the plate theory of liver anatomy. In cirrhotics with portal hypertension, the WHVP is elevated to a level approximately 20 per cent below portal venous pressure (20). Therefore, the area between the catheter tip and the "sinusoid" can be said to include the major share of the vascular resistance in the liver (excluding presinusoidal hepatic arterial resistance).

Figure 5 is a diagrammatic representation of hepatic circulation, designed to clarify the information provided by the wedge hepatic venous pressure data. In Figure 5a, values for pressure and flow in the hepatic artery, portal vein, and hepatic vein have been assigned commensurate with the catheterization findings in the 10 patients in this paper. Pressure at S is that obtained by wedging the catheter into an hepatic venule (WHVP). The value given for portal vein pressure is based on the assumption that the WHVP is 80 per cent of the portal vein pressure (20). The three resistances R1, R2, and R3 can be calculated by dividing the pressure gradients by the appropriate blood flows and multiplying by 100 to give values (in arbitrary units) of 9 (R1), 0.65 (R2), and 1.21 (R3).

Figure 5b illustrates comparable values for the normal liver. These are necessarily gross approximations, since we have even less data in the normal liver than in the cirrhotic concerning

sinusoidal pressure and the relative contributions of hepatic artery and portal vein to the total liver blood flow. With the values as assigned, R1 is 17; R2, 0.30; and R3 0.33 units. Clearly, R2 and R3 are increased in cirrhosis. If the values for blood flow given in Figure 5b are even gross approximations of the true values, then the major increase in resistance in cirrhosis is on the hepatic venous side of the sinusoid (R3). This is in keeping with the anatomical evidence represented by Kelty, Baggenstoss, and Butt (21).

Although the WHVP fell in all patients after the portacaval shunt, it still remained abnormally elevated. This continued elevation is to be expected if there is no change in intrahepatic vascular anatomy with the operation. In Figure 5c, are charted the mean postoperative values for

the blood flow and WHVP in our 10 subjects. R3 is now 1.38, not significantly different from the preoperative level. If the postsinusoidal vascular resistance remains unchanged after the shunt, then the sinusoidal pressure should drop in proportion to the fall in total blood flow. Comparison of the decrements in the WHVP and EHBF in the 10 individual patients indicates that, in general, the two variables did fall proportionately after the portacaval shunt and that the calculated postsinusoidal vascular resistance did not change markedly.

The continued elevation of the WHVP after portacaval shunt does not mean persistence of portal hypertension, since the portal vein has been disconnected from the liver and the WHVP no longer bears any relationship to portal pres-
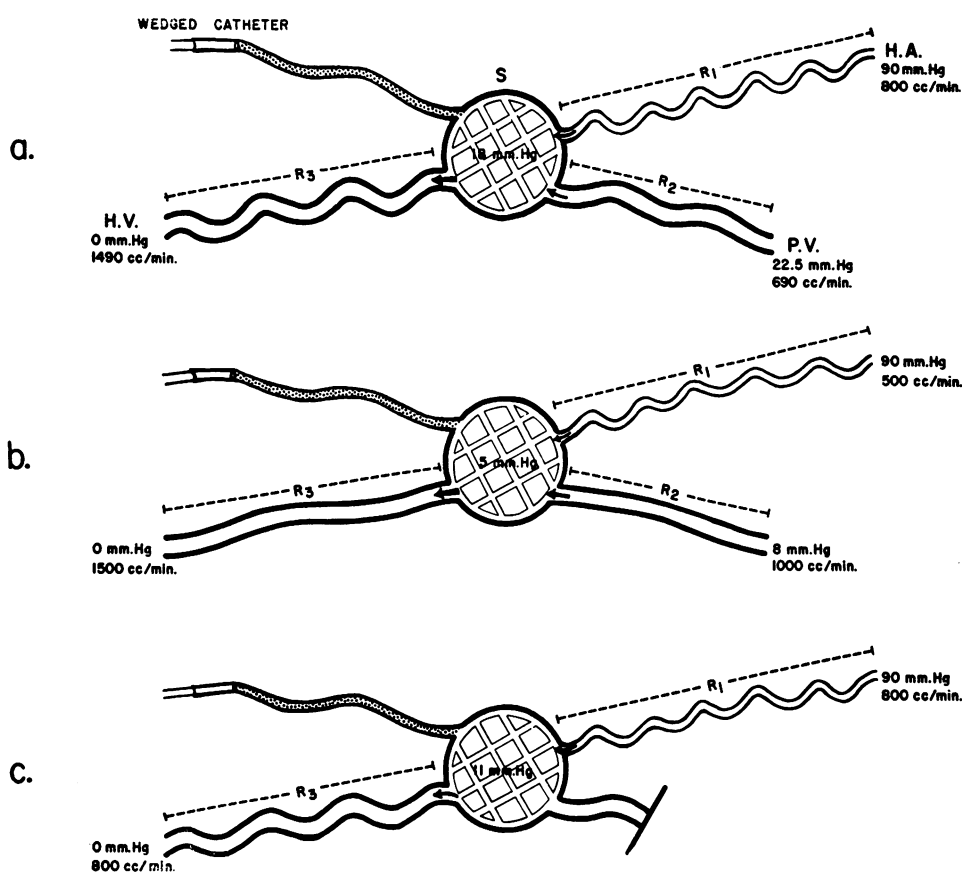

Fig. 5. Diagrammatic Representation of Hepatic Circulation Showing Blood Flow and Mean Pressure in Hepatic Artery (H. A.), Portal Vein (P. V.), Hepatic Vein (H. V.), and Sinusoid (S)

Resistances are indicated by R1, R2, and R3. a, cirrhotic liver; b, normal liver; c, cirrhotic liver after end-to-side portacaval shunt.

sure. The elevated WHVP simply reflects the unchanged hepatic vascular resistance. Portal vein pressures actually fall to insignificant levels after end-to-side portacaval anastomosis, as indicated by direct measurements at surgery and by postoperative catheterization of the portal vein itself, directly through its anastomosis to the inferior vena cava (17).

The therapeutic implications of the above-noted hemodynamic changes should be considered. The volume of portal blood flowing through the liver in patients with advanced cirrhosis and portal hypertension is surprisingly large. Though the end-to-side portacaval shunt has proven to be eminently satisfactory for the prevention of bleeding from esophageal varices, it has the disadvantage of diverting this portal blood from the liver. Although our data do not demonstrate any deterioration in function tests, or any lowering of hepatic oxygen uptake after the operation, it is possible that the reduction in blood flow may interfere with hepatic regeneration or affect other functions that we cannot measure. Consequently, the end-to-side portacaval shunt may eventually prove not to be the best surgical approach to the problem of portal hypertension.

The splenorenal shunt, judging from the data of Bradley and co-workers (4), and Nardi (5), causes less lowering of liver blood flow, probably because of a smaller anastomotic orifice. Pressure in the portal system is seldom lowered to the same degree that it is following a portacaval shunt and, since the portal vein is still open, some portal blood may still perfuse the liver. Unfortunately, there is a significant incidence of recurrent variceal bleeding following splenorenal shunt (2), presumably either because of thrombosis of the anastomosis, or inadequate decompression of the varices. Therefore, as presently performed, splenorenal shunt has definite drawbacks.

Two other possible surgical approaches to portal hypertension may be worth further evaluation. One is arterialization of the stump of the portal vein after end-to-side portacaval shunt. This is feasible (22) but technically difficult. The other is creation of a side-to-side portacaval shunt with an anastomotic orifice of limited size designed to relieve, but not entirely eliminate, portal hypertension and thus preserve some portal blood flow through the liver.

SUMMARY

Measurements of the estimated hepatic blood flow, arterial-hepatic venous oxygen difference, hepatic oxygen consumption, and wedged hepatic venous pressure were made in 10 patients before and after an end-to-side portacaval anastomosis. The hepatic postsinusoidal vascular resistance (the ratio of wedged pressure to hepatic blood flow) was determined pre- and postoperatively. Hepatic function, estimated from the usual laboratory tests, was compared before and after the shunt.

Estimated hepatic blood flow fell in 9 of the 10 subjects following the shunt. In the group as a whole, blood flow fell from 1,490 ± 182 ml. per minute to 800 ± 93 ml. per minute, a mean percentage decrease of 46 per cent. Hepatic oxygen consumption was essentially unchanged after the surgery. Arterial-hepatic venous oxygen difference increased, averaging 3.8 ± 0.36 volumes per 100 ml. before and 6.3 ± 0.58 volumes per 100 ml. after the shunt. Wedged hepatic venous pressure decreased in every instance, falling on the average from 18 ± 0.63 to 11 ± 0.31 mm. Hg, a mean percentage decrease of 38 per cent. The nearly proportional decrease in wedged pressure and hepatic blood flow resulted in essentially unchanged values for the hepatic vascular resistance.

The large fall in hepatic blood flow after the shunt presumably represents the portal component of the preoperative total hepatic blood flow. In spite of the large drop in flow, hepatic function tests were not significantly altered.

CASE REPORTS

R. R. (#1560–837), a 51 year old white male with a history of heavy alcoholic intake for many years, was admitted to the hospital on March 6, 1955. Hematemesis and melena had occurred earlier that day and the hemoglobin level on entry was 8.0 Gm. per cent. Emergency treatment included the use of the Sengstaken-Blakemore tube and 10 transfusions. At that time there was hepatomegaly, and the tip of the spleen was palpable. There was no ascites. A few days later, laboratory studies were as follows: icteric index, 20 units; cephalin-cholesterol flocculation, 0; serum protein, 6.0 Gm. per cent (A/G, 4.0/2.0); and BSP retention of 14 per cent after 30 minutes. Needle biopsy of the liver revealed portal cirrhosis. X-ray examination showed large esophageal varices. Hepatic venous catheterization was performed on March 30, 1955. On April 27, 1955, an end-to-side portacaval anastomosis was made; portal venous pressure fell from 340 to 200 mm. saline. Liver biopsy again

revealed portal cirrhosis. Convalescence was uneventful, and he left the hospital 10 days after the surgery. Hepatic venous catheterization was repeated on June 7, 1955: at that time moderate hepatosplenomegaly persisted and laboratory studies showed: serum protein, 7.6 Gm. per cent (A/G, 4.2/3.4) ; and BSP retention of 29 per cent after 30 minutes. X-rays on July 7, 1955, and on February 14, 1956, showed persistence of the esophageal varices, although greatly diminished in size. He has done well since the shunt, and has returned to full activity.

C. M. (#632–014), a 48 year old Mexican woman with a history of chronic alcoholism for many years, was admitted to the hospital on September 16, 1954, because of sudden onset of hematemesis and melena beginning two days before entry. Frequent episodes of epistaxis had occurred during the previous three years, and a clinical diagnosis of cirrhosis was made four months before admission when she complained of recurrent mild epigastric discomfort. Hepatosplenomegaly was noted on admission. There was no ascites or icterus. X-ray examination revealed esophageal varices. Hepatic venous catheterization was performed on October 27, 1954. Laboratory studies at this time were as follows: icterus index, 7 units; serum protein, 7.8 Gm. per cent (A/G, 4.2/3.6) ; and BSP retention of 24 per cent after 30 minutes. An end-to-side portacaval anastomosis was performed on October 29, 1954. Liver biopsy at operation revealed portal cirrhosis. She recovered uneventfully and X-ray study on January 10, 1955, failed to demonstrate any varices. Postoperative hepatic venous catheterization was done on February 16, 1955, at which time laboratory studies showed: serum protein, 7.2 Gm. per cent (A/G, 3.4/3.8) ; and BSP retention of 24 per cent after 30 minutes. She has done fairly well since the shunt, except for an episode of mild pancreatitis with elevation of the serum amylase in May, 1956. There has been no further gastrointestinal bleeding.

T. S. (#1523–196), a 45 year old white woman with a history of chronic, severe alcoholism, was admitted to the psychiatric unit in September, 1954, for delusions and hallucinations. Hepatomegaly, spider angiomata and icterus were noted, and she was transferred to the medical service. On November 2, while in the hospital, massive hematemesis and melena occurred. Bleeding ceased with the use of the Sengstaken-Blakemore tube but was followed by the appearance of ascites, increasing icterus, oliguria and coma. There was gradual recovery complicated by three small hematemeses. Esophageal varices were not demonstrated by X-ray examination, but esophagoscopy revealed large varices in the distal one-third of the esophagus. The ascites and icterus slowly disappeared. On January 5, 1955, hepatic venous catheterization was performed and a few hours later that day, an end-to-side portacaval anastomosis was performed. Laboratory studies prior to surgery revealed: icterus index, 7 units; cephalin-cholesterol flocculation, 2+; serum protein, 5.9 Gm. per cent (A/G, 3.7/2.2) ; and BSP retention of 20 per cent after 30 minutes. Liver biopsy at operation showed portal cirrhosis, and the portal vein

pressure was 370 mm. saline. Except for transient icterus, the postoperative course was uneventful and hepatic venous catheterization was repeated on January 26, 1955. Laboratory studies at this time showed: icterus index, 8 units; cephalin-cholesterol flocculation, 0: serum protein, 5.6 Gm. per cent (A/G, 3.6/2.0) ; and BSP retention of 18 per cent after 30 minutes. X-ray examination in April, 1955, again failed to demonstrate esophageal varices. Esophagoscopy has not been repeated. She had had persistent mild ankle edema, but has otherwise been well to date.

J. R. (#1542–751), a 55 year old white man with a history of alcoholism for many years, entered the hospital on August 8, 1955, for fever and abdominal pain. Pyelonephritis was diagnosed and treated. During investigation of the abdominal complaints, X-ray studies revealed esophageal varices. Physical examination disclosed hepatosplenomegaly, mild ascites, spider angiomata and "liver palms." There was also a history of heart failure of unknown etiology, controlled with digitalis for the past three years. On October 19, 1955, he suffered a small hematemesis. Hepatic venous catheterization was done on November 1, 1955. Laboratory studies at this time revealed: icterus index, 8 units; serum proteins, 5.3 Gm. per cent (A/G, 3.3/2.0) ; and BSP retention of 14 per cent after 30 minutes. An operation was recommended, but refused by the patient. Hematemesis recurred on November 26, 1955, requiring the use of the Sengstaken-Blakemore tube and was followed by a transient period of coma. An end-to-side portacaval anastomosis was finally performed on December 20, 1955. Portal venous pressure fell from 350 to 210 mm. saline. Liver biopsy showed portal cirrhosis. The immediate postoperative period was complicated by a thrombophlebitis of the right leg and a pulmonary embolism. While receiving heparin therapy, severe bleeding from the surgical incision occurred requiring many transfusions. Disorientation and a "flapping" tremor were noted frequently during this period. He slowly recovered and did well until August 23, 1956, when a small hematemesis occurred. X-ray examination failed to demonstrate either esophageal varices or an ulcer. The liver remained enlarged, but the spleen could no longer be felt. There was mild ankle edema but no ascites. Laboratory studies at this time showed: icterus index, 23 units; serum proteins, 6.0 Gm. per cent (A/G, 3.5/2.5) ; and BSP retention of 21 per cent after 45 minutes. Hepatic venous catheterization was repeated on September 4, 1956. There has been no further hemorrhage but he has since suffered repeated periods of mental deterioration associated with gross "flapping" tremor.

M. S. (#1296–971), a 48 year old white woman, was hospitalized on June 10, 1955, for hematemesis and melena. She had used alcohol excessively for many years, but none in the past four years. Cirrhosis was diagnosed in 1952, during an episode of ascites, edema and jaundice. She had suffered hematemesis in September, 1954, and again in March, 1955. X-ray studies then failed to dis-

close the source of the bleeding. On admission, there was hepatosplenomegaly, but no ascites. The hemorrhage ceased with the use of the Sengstaken-Blakemore tube. Laboratory studies revealed: icterus index, 13 units; serum protein, 5.9 Gm. per cent (A/G, 4.1/1.8) ; and normal BSP retention. Hepatic venous catheterization was done on June 28, 1955. Hematemesis recurred on three occasions during the next few days, and was accompanied by transient icterus. An end-to-side portacaval anastomosis was done on July 22, 1955, with a fall in portal venous pressure from 350 to 225 mm. saline. Liver biopsy showed portal cirrhosis. The postoperative course was complicated by mild icterus and a parotitis requiring surgical drainage. She continued to improve and there was no further hemorrhage, although hepatosplenomegaly persisted. The postoperative catheterization was performed on September 27, 1955. Laboratory studies at this time were: serum protein, 7.1 Gm. per cent (A/G, 3.9/3.2) ; and BSP retention of 15 per cent after 30 minutes. X-ray studies revealed no evidence of esophageal varices. She began heavy drinking in December, 1955, became deeply jaundiced and expired in hepatic coma on April 5, 1956. Postmortem examination revealed cirrhosis, a functioning end-to-side portacaval anastomosis, and no evidence of esophageal varices.

M. L. (#1328-681), a 49 year old Mexican man, had been a chronic alcoholic for many years. From 1952 until December, 1954, ascites had appeared from time to time, responding fairly well to diuretics and sodium restriction. Abdominal paracentesis was done twice in 1953. A sudden hematemesis required hospital admission on December 12, 1954, and a Sengstaken-Blakemore tube was passed with control of the hemorrhage. Ascites and hepatomegaly were present at this time. On January 11, 1955, hepatic venous catheterization was done. Laboratory studies at that time showed: serum proteins, 5.6 Gm. per cent (A/G, 3.4/2.2) ; icterus index, 22 units; and prothrombin time, 68 per cent. X-ray examination in January, 1955, showed large esophageal varices. The formation of ascites gradually ceased, and an end-to-side portacaval anasomosis was done on March 9, 1955, with portal venous pressure falling from 440 to 150 mm. saline. Splenomegaly was noted at operation, and liver biopsy revealed portal cirrhosis. Except for mild transient jaundice, the postoperative course was uncomplicated, and he left the hospital in two weeks. A repeat hepatic venous catheterization was done on May 3, 1955. There was no ascites or icterus at that time, and laboratory studies showed: serum proteins, 6.3 Gm. per cent (A/G, 3.5/2.8) ; icterus index, 7 units; and BSP retention of 30 per cent after 30 minutes. There was no evidence of esophageal varices on X-ray examination. He has remained free from jaundice or ascites since that time and there has been no gastrointestinal bleeding.

C. W. (#1086-949), a 47 year old white man, was admitted to the hospital on December 20, 1955, following sudden hematemesis and melena earlier that day. There was a history of heavy alcoholic intake for 25 years. Transient ascites and jaundice had occurred in 1948 and

again in 1952. At the time of entry to the hospital there was hypotension, the blood hemoglobin was 7.5 Gm. per cent, and hepatomegaly was noted. Bleeding promptly ceased with the use of the Sengstaken-Blakemore tube. Esophageal varices were subsequently demonstrated by both esophagascopy and X-ray examination. Laboratory studies on December 28, 1955, revealed: serum proteins, 5.8 Gm. per cent (A/G, 3.3/2.5) ; icterus index, 17 units; and BSP retention of 21 per cent after 30 minutes. Hepatic venous catheterization was done on January 10, 1956. At operation on February 2, 1956, chronic cholecystitis and cholelithiasis were discovered in addition to cirrhosis. A cholecystectomy and an end-to-side portacaval anastomosis were performed. Portal venous pressure fell from 360 to 150 mm. saline. His recovery was uneventful, without the appearance of icterus or coma, and complicated only by a curious neuritis of the left foot. The postoperative catheterization was done on March 27, 1956. Laboratory studies at this time showed: serum proteins, 6.5 Gm. per cent (A/G, 3.5/3.0) ; icterus index, 6 units; and BSP retention of 16 per cent after 30 minutes. Esophageal varices were still demonstrable on X-ray, although markedly reduced in size, on May 31, 1956. There has been no hemorrhage or jaundice since the shunt and he has remained fairly well.

J. A. (#1620-577), a 65 year old Mexican male, was admitted to the hospital on November 20, 1955, following a massive hematemesis. There was a history of heavy alcoholic intake for more than 20 years. One month prior to admission, he had entered another hospital for hematemesis and melena and had received two transfusions. An X-ray study there was reported to have shown a prepyloric ulcer and antacid therapy had been recommended. Peptic ulcer symptoms were denied. He continued to have melena, and an emergency laparotomy was done on November 22, 1955. A large, nodular liver and a large spleen were found. Duodenotomy revealed no evidence of an ulcer. An omental vein pressure was elevated (approximately 250 mm. saline). A liver biopsy showed portal cirrhosis. Laboratory studies after operation revealed: serum proteins, 5.3 Gm. per cent (A/G, 3.5/1.7) ; and icterus index, 17 units. Hepatic venous catheterization was done on December 6, 1955. At that time, the icterus index was 10 units and BSP retention was 25 per cent after 30 minutes. X-ray studies on December 7, 1955, showed large esophageal varices and no demonstrable ulcer. An end-to-side portacaval anastomosis was performed on December 27, 1955; portal venous pressure fell from 350 to 140 mm. saline. Three weeks after the shunt, mental confusion, but no tremor, was first noted. The repeat catheterization was done on January 17, 1956. Laboratory studies then showed: serum proteins, 6.6 Gm. per cent (A/G, 3.4/3.2) ; icterus index, 15 units; and BSP retention of 30 per cent after 30 minutes. Since then he has had periodic mental confusion and a continuous mild "flapping" tremor. In January, 1957, he suffered a period of marked disorientation accompanied by a gross "flapping" tremor from which he recovered rather rapidly. There have been several subsequent one to two day episodes of marked confusion and

gross tremor. There has been no recurrence of variceal bleeding.

C. H. (#1642–082), a white man aged 46 years, had consumed alcohol in moderate excess for many years. He had suffered hematemesis in April and in December of 1955. In October, 1955, diabetes mellitus was diagnosed and treatment instituted. Another large hematemesis occurred on February 2, 1956, and he was admitted to the hospital. Hepatosplenomegaly was present and, in addition, a large tortuous abdominal collateral vein was noted leading from the umbilicus to the right epigastrium, over which a loud continuous "hum" was audible. The bleeding ceased spontaneously, and hepatic venous catheterization was performed on February 28, 1956. At this time, laboratory studies showed: serum proteins, 6.3 Gm. per cent (A/G, 4.0/2.3) ; icterus index, 9 units; and BSP retention of 10 per cent after 30 minutes. X-ray examination revealed large esophageal varices. An end-to-side portacaval anastomosis was done on March 19, 1956, with portal venous pressure falling from 340 to 150 mm. saline. Convalescence was complicated only by a mild transient icterus. The repeat hepatic venous catheterization was performed on April 3, 1956. Laboratory studies then revealed: serum proteins, 6.2 Gm. per cent (A/G, 3.5/2.7) ; icterus index, 13 units; and BSP retention of 18 per cent in 30 minutes. X-ray examination in April, 1956, showed a marked diminution in the size of the esophageal varices. Except for periodic low grade jaundice and weakness, he has remained fairly well since that time. There has been no gastrointestinal bleeding.

J. J. (#1537–328), a 43 year old white man, was admitted to the hospital on November 20, 1954, for the complaint of ankle edema for five months. There was a history of excessive alcoholic intake and two years before, while in a state prison, he was told he had cirrhosis. There was no history of jaundice, ascites, hematemesis or melena. On admission, in addition to ankle edema, hepatosplenomegaly, spider angiomata and "liver palms" were noted. Laboratory studies revealed: serum proteins, 7.2 Gm. per cent (A/G, 3.6/3.6) ; and BSP retention of 19 per cent after 30 minutes. X-ray examination and esophagoscopy both revealed extensive esophageal varices. Hepatic venous catheterization was done on January 19, 1955, a few hours before an end-to-side portacaval anastomosis was performed. Portal venous pressure fell from 360 to 19 mm. saline after the shunt. Liver biopsy showed portal cirrhosis. The postoperative course was uneventful, including the absence of icterus. The postoperative catheterization was done on February 9, 1955. A marked reduction in the size of the spleen was noted at this time, and laboratory studies revealed: serum proteins, 6.3 Gm. per cent (A/G, 2.7/3.6). Ankle edema recurred and has persisted to date. X-ray evamination in October, 1955, still demonstrated esophageal varices, although greatly reduced in size. The patient was confined in the State Prison until July, 1955. After his release, he began drinking and using narcotics and was seen infrequently. When last examined in December, 1956, his behavior was irrational and there was a mild

"flapping" tremor of his hands. The serum proteins were 7.5 Gm. per cent (A/G, 3.1/3.4). He was again confined to prison. Detailed information could not be obtained regarding his mental state, other than to the effect that he showed evidence of mental deterioration during the two months he had spent in jail.

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