Evaluation of the Hemodynamics of Portal Hypertension in the Selection of Patients for Shunt Surgery

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THE HISTORY OF portal-systemic shunts begins with the first description of an experimental portacaval shunt carried out on a small series of animals by Nicholai Eck in 1877.[5] This report served only to demonstrate that the construction of this type of shunt was compatible with survival in the dog and no shunt problems or observations were described. In 1893, Hahn and colleagues [10] working in Pavlov's laboratory described a neurological syndrome occurring in dogs with constructed Eck fistulas which they ascribed to dietary factors and referred to this syndrome as "meat intoxication". Over the subsequent decades, intermittent interest was evinced in this association of hepatic disease, shunts, and central nervous system symptoms but no definitive studies were carried out. Burchi [2] in 1923 suggested that in the presence of defective urea synthesis, ammonia might be a toxic factor. Subsequently, Van Caulaert,[23] Kirk [12] Gaustad [9] and others reported observations on the ingestion of ammonium salts, the measurement of ammonia in collateral circulation in the abdominal wall and clinical disorders of mentation relating to this general area of hepatic disease and encephalopathy. It was not until 1953, however, that a series of reports from investigators working with Davidson in the Thorndike Laboratories at the Boston City Hospital defined a syndrome of impending hepatic coma precipitated by the ingestion of various nitrogenous materials and ion exchange resins releasing ammonia in the gastrointestinal tract.[8,19,22] At about the same time, we reported our initial observations on patients in whom the portal vein had been resected for invasive cancer of the head of the pancreas and an anastomosis constructed between the superior mesenteric vein and the inferior vena cava.[13] The initial case report and subsequent observations [14,11] would indicate that every patient with a normal hepatic and portal circulation in whom a shunt is constructed would develop severe postshunt encephalopathy. Subsequent to these observations, it became apparent that this syndrome also occurred in a significant number of patients in whom portal-systemic shunts had been constructed in the presence of intrahepatic block and portal hypertension.[15] Evidence accumulated that hyperammoniemia might be a factor in the production of this syndrome and during the past decade, a number of long-term observations placed the incidence of postshunt encephalopathy in the range of 25% of the operated cases (Table 1). During the past few years, increasing interest has been focused on the factors involved in the production of the encephalopathy. The exact biochemical changes affecting the central nervous system are still unsettled but, relative to the material in this particular report, various hemodynamic observations from experimental and clinical studies emphasize the importance of hepatic blood flow as well as the factor of the shunting of portal blood around the liver. Warren and Zeppa [20,24,25] in particular have emphasized the importance of maintenance of hepatic blood flow if the shunt is to be constructed and it has already been recognized that, while a standard Eck fistula was accompanied by the universal appearance of encephalopathy and

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varying degrees of deterioration in hepatic function, a portacaval transposition[21] protected experimental animals against this series of postoperative metabolic problems.

The present report is concerned with hemodynamic observations in our own series of shunting procedures and with some of our own observations in experimental animals, all of which tend to support the thesis of Warren and Zeppa relative to the importance of the maintenance of hepatic blood flow.

Methods and Material

In previous reports, we have emphasized the very significant differences between dogs with a standard portacaval shunt and those in whom hepatic blood flow has been maintained by portarenal transposition.[17,18] The technic of portarenal transposition is shown in Figure 1. Hepatic blood flow measurements in these experimental animals was determined by the disappearance curve of injected radioactive colloidal gold (Au 195) and the estimated flow reported in terms of percentage of effective circulating blood volume per minute.

The clinical material which was analyzed in terms of hemodynamics was drawn from a series of 410 elective portacaval and splenorenal shunts carried out between 1945 and 1965. Hepatic blood flow determinations in these patients were carried out by technic originally described by Dobson[4] utilizing chromic phosphate labeled with P32 and the flow calculated in terms of per cent of effective circulating blood volume. In 83 of these patients, prospective studies included the measurement of free portal pressure (FPP), hepatic occluded pressure (HOPP) in which the portal pressure was measured manometrically on the hepatic side of the occluded portal vein. Splanchnic occluded portal pressures (SOPP) were also measured but these data are not included in this report because there is no apparent relevance to the particular aspect of the hemodynamics under immediate study.

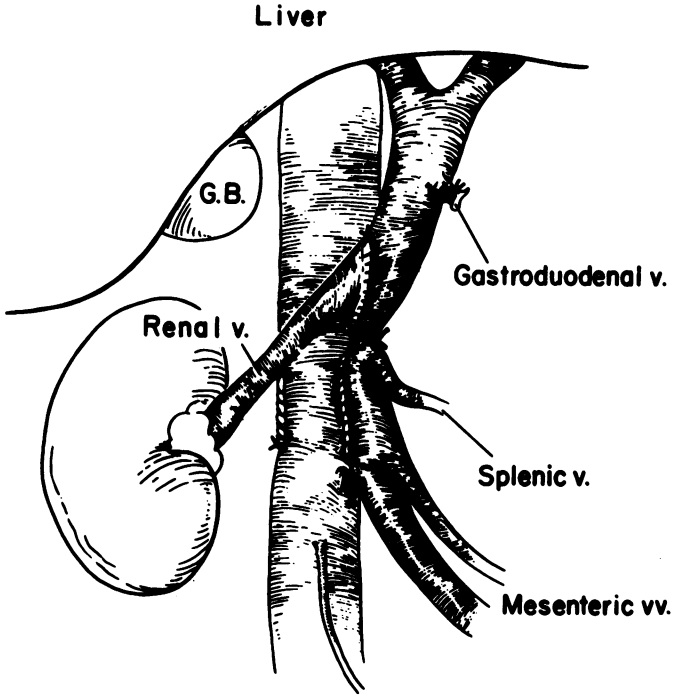

FIG. 1. Technic of Portarenal Transposition in the Dog. (Reproduced with permission from *Surgery*, 64:214, 1968).

In the estimate of operative risk, Child's categorization[3] has been utilized in which patients have been divided into A (good), B (fair), and C (poor).

Results

Experimental

In Figures 2 and 3, data are presented which illustrate the striking difference in hepatic blood flow between the

TABLE 1. *Summary of Elective Portal-Systemic Shunts*

Author	Date	Hospital Mortality	Incidence of Rebleeding from Varices	5 Year Survival	Post-Shunt Encephalopathy	Peptic Ulcer
McDermott	1961	9.0%	15.0%	68.0%	18.0%	15.0%
Walker	1961	6.0%	12.0%	70.0%	20.0%	—
Sedgwick	1966	21.5%	21.2%	57.1%	22.5%	5.0%
Voorhees	1970	12.0%	2.0%	58.0%	34.0%	—
Child	1956	14.0%	—	—	—	—
Palmer	1957	10.5%	14.0%	—	—	—
Foster	1971	19.0%	10.0%	40.0%	19.0%	4.0%
Akkary (Schistosomiasis)	1962	23.0%	10.0%	—	26.0%	—
Zuidema	1961	20.0%	—	—	15.0%	—
Schwarr	1968	5.0%		47.0%	30.0%	—
Barnes	1971	9.0%				
Patton	1959	19.0%	—	—	39.0%	8.0%
Ellis	1956	11.0%	14.9%	50.0%	—	—
Welch	1957	15.0%	20.0%	—	—	—
Wantz	1961	11.3%	—	—	21.8%	—
Voorhees	1970	12.0%	3.0%	37.0%	34.0%	12.0%

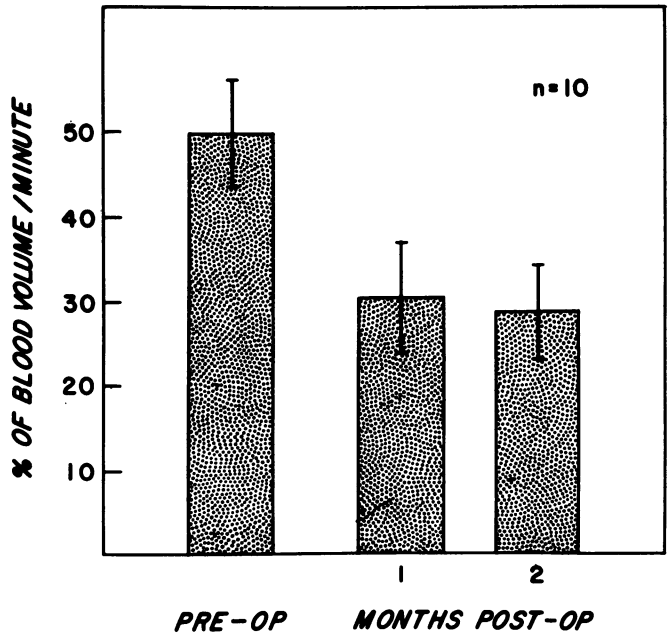

FIG. 2. Effect (average of 10 dogs) of end-to-side portacaval shunt on liver blood flow.

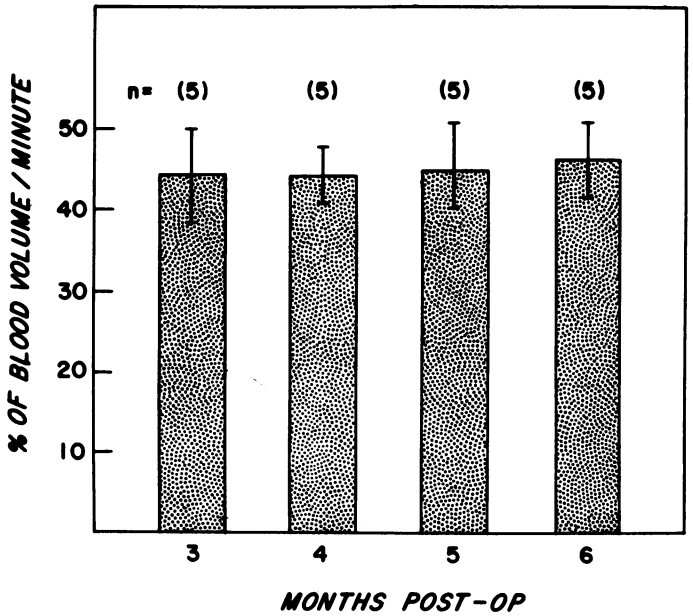

FIG. 3. Effect (average of 5 dogs) of portarenal transposition on liver blood flow.

standard portacaval shunt in dogs and the portarenal transposition. Figure 4 illustrates the protection against hyperammoniemia afforded by portacaval transposition and data previously reported by us has demonstrated the effectiveness of this type of transposition in preventing weight loss and deterioration in a number of parameters of hepatic function.

Clinical

The data relative to the occurrence of encephalopathy in 410 portacaval and splenorenal shunts constructed between 1945 and 1965 are shown in Table 2. The reason for the apparent increase in incidence over the years cannot be exactly defined but may relate to increasing awareness and recognition of this postoperative complication or perhaps to variations in the selection of patients for operation over the years. In a number of series reported between 1956 and 1970, the incidence has ranged from a low of 15% to a high of 39%. Most observers would accept an overall incidence of between 20 and 25% and in terms of severity of encephalopathy, it has been customary to grade this clinically from 1–4 with 1 representing minor and transient changes in central nervous system function to Grade 4 in which the patient lapses intermittently into deep and unresponsive coma.

In the analysis of our own series, it was apparent that this complication is age dependent with an incidence of less than 20% in those patients under 20 years of age to a high of nearly 40% in those patients over 70 years of age (Fig. 5). In our own series, a few patients who were originally free of encephalopathy for a varying number of years following operation, began to develop varying degrees of central nervous system symptoms as they moved into the older age brackets. Because the disease itself is not associated with a large number of long-term survivors and because the procedure has only been carried out for approximately 20 years in any significant numbers, more evidence must be accumulated before this impression can be substantially supported.

Hemodynamics

Initial studies on hepatic blood flow on some of these patients was reported by Nardi *et al.*[16] In these reported

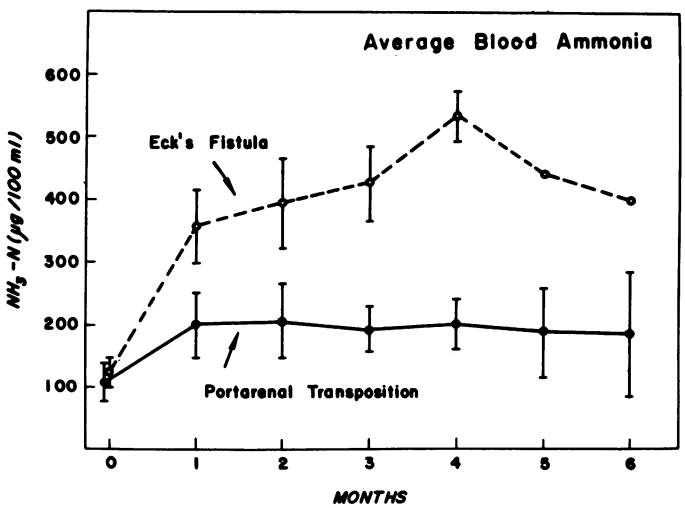

FIG. 4. Comparison of the effects of portacaval shunt and portarenal transposition on ammonia levels in dogs. (Reproduced with permission from *Surgery*, 64:214, 1968).

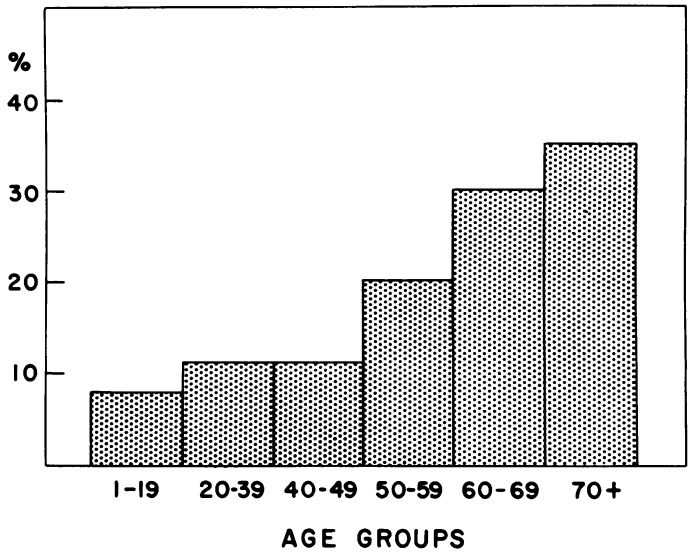

FIG. 5. Relationship of post-shunt encephalopathy to age.

data and in subsequent observations, hepatic blood flow in terms of percentage of effective circulating blood volume has ranged from 40% (normal) to 19%. There has been no correlation between measurement of initial hepatic blood and prognosis in terms of survival or incidence of encephalopathy. A significant drop in heptic blood flow following operation, however, was associated with a higher mortality and with the development of encephalopathy.

Pressure Studies: In 83 of the 410 shunts, pressure studies were carried out as described above. These observations are shown in Table 3 and the focus has been directed on the difference recorded between free portal pressure (FPP) and hepatic occluded pressure (HOPP). The cases have been arbitrarily divided into those in whom the drop was greater than 10 cm. of saline (Group I), those in whom the drop was between 5 and 10 cm. of saline (Group II), and those in whom the pressure either increased on the occluded side of the portal vein, remained essentially the same or showed a drop of less than 5 cm. of saline (Group III). Not only was the incidence of encephalopathy higher but the severity according to the standard clinical gradation from 1–4 was greater in Group I. Late mortality during the first postoperative year was 30% in Group I in contrast to 19% in Group III. These observations seem to have particular significance when attention is directed to the tabulation of the patients according to Child's category of risk. In Group I, all of the patients were classified in the good or fair category whereas in Group III, 87% of the patients fell into the fair to poor category; therefore, the difference in the incidence of encephalopathy and in the clinical course during the first postoperative year could in no way be ascribed to hepatic function or reserve. The data on the patients in Group II fall, as might be expected, between Groups I and III. Obviously one could arbitrarily select a number of different dividing lines in terms of pressure changes but this particular tabulation seems to emphasize the differences most significantly. The immediate operative mortality was higher (12%) in Group III than in Group I (5%); this is the only area in which estimate of hepatic function in reserve affected the overall clinical problem more than did the pressure changes. The data in terms of pressure and flow were not collected consistently enough in the same patients to establish a valid statistical correlation between a postoperative drop in the hepatic blood flow and a drop in hepatic occluded pressure in HOPP as recorded at the time of operation but in a few cases in which all hemodynamic studies were available, those patients with a significant drop in hepatic blood flow also had a fall in HOPP. The collection of a more organized set of hemodynamic data in the future may establish a better correlation between these changes in pressure and flow.

TABLE 2. *Incidence of Post-shunt Encephalopathy in a Series of 410 Elective Portal-systemic Shunts in Man.*

	Total	Encephalopathy	Portacaval	Encephalopathy	Splenorenal	Encephalopathy
1945–58	237	28(12%)	71	12(17%)	166	16(9%)
1959–65	173	47(27%)	100	33(33%)	73	14(20%)
	410	75(18%)	171	45(26%)	239	30(12%)

Discussion

It has become increasingly clear that the syndrome of postshunt encephalopathy involves considerably more than the simple phenomenon of shunting of portal blood with its high concentration of ammonia and other absorbed products of protein digestion and bacterial enzymatic action in the gastrointestinal tract. The mechanism by which ammonia and other absorbed products may affect the central nervous system is also far from clarified. It has been suggested on the basis of experimental and clinical evidence that the pNH_3 rather than the total ammonia content of blood is important and therefore, the degree of metabolic disorder is dependent on the acid-base balance. More recently Fischer and James [6,7] have implicated certain amines as false neurotransmitters and, tied in with this concept, L-dopa has been shown to improve the central nervous system function of patients in deep hepatic coma. A detailed discussion of the biochemical mechanisms within the central nervous system is, however, beyond the scope of this report.

Of the factors involved in the induction of encephalopathy, *age* is certainly important and, as has been indicated, the incidence of postshunt encephalopathy in-

creases with each decade of life in which a shunt is constructed.

Hepatic blood flow following a shunt is certainly of great significance. The observations on experimental animals indicate that maintenance of hepatic blood flow following a shunt will almost completely negate the adverse effects in terms of encephalopathy, weight loss, malnutrition and a number of parameters of hepatic function. In clinical studies the incidence of encephalopathy bore no relationship to the preoperative hepatic blood flow but a drop in hepatic blood flow from whatever initial level was associated with neurological complications and frequently with progressive hepatic deterioration. While interesting, these observations do not permit any prediction in terms of prognosis after shunt operation.

Pressure studies can be recorded, however, prior to the construction of a shunt and from the data reported would appear to serve as a rough index of the amount of prograde flow to the liver in the portal vein and therefore can be used as a guide to the proportion of the total hepatic blood flow provided by the portal vein. In our data a drop in the hepatic occluded pressure from the initial free portal pressure of greater than 100 ml. of saline was associated with an incidence of encephalopathy to approximately three times that of patients in whom there was either an increase, a minimal decrease (less than 50 ml. of saline) or no significant change in the hepatic occluded pressure; in addition, despite the fact that patients categorized as Group I were better risks by clinical assessment and by hepatic function, the late mortality during the first postoperative year was higher than the poor risk group of patients included in Group III.

Clinical evaluation and assessment of hepatic function are certainly a gauge of immediate operative risk but are of little value in determining either the longterm results or the likelihood of post-shunt encephalopathy. Rapid deterioration of some of the best risk patients occurs with disturbing frequency. Similar deterioration occurs frequently if a portal-caval shunt is constructed for portal hypertension resulting from schistosomiasis, to the extent that many surgeons in the areas where schistosomiasis is endemic have avoided shunt operation and relied on various types of disconnection procedures to control the hemorrhage.

Once could speculate that the progression of intrahepatic portal bed block, particularly in cirrhosis, may often result in a progressive decrease in flow to the liver via the portal vein. If not compensated by an increase in hepatic arterial flow sufficient to support the remaining functioning hepatic parenchyma, the natural history may be one of steady deterioration and death from hepatic failure. On the other hand if compensation occurs through increase in arterial flow, a relative stable situation may result and bleeding from esophageal varices as a complication of the portal hypertension lead to a portal-systemic shunt. The data presented would support the concept that the ultimate success of shunt operation in terms of survival and freedom from encephalopathy may depend primarily on low prograde flow in the portal vein with a compensatory increase in arterial flow through the hepatic artery; under these circumstances the construction of a shunt with diversion of portal flow would not alter significantly the existing hemodynamics.

If these concepts are supported by further observations and studies, more exact means of evaluating the hemodynamics of the liver will be essential to proper preoperative evaluation. If a high risk group of patients can be satisfactorily identified, then procedures other than the standard types of portal-systemic shunts are indicated. Superficially one might say that any type of side-to-side decompressions from the portal to the systemic circulation would provide maintenance of flow to the liver but in fact, in the presence of the elevated intrahepatic pressure this type of shunt results in retrograde flow from the liver through the shunt. Warren, Zeppa and Fomon [25] and Britton [1] have described newer modifications of shunting procedures which are designed to maintain hepatic blood flow after selective decompression of esophageal varices; whether these will achieve the ultimate objective of adequate decompression and freedom from postshunt complications will await a longer period of evaluation than exists at the moment. Our own prefer-

TABLE 3. *Hemodynamic Studies on 83 Patients with Portal Hypertension as Related to Post-shunt Complications.*

	Difference between FPP and HOPP	Total Cases	Postshunt Encephalopathy			Category of Risk (Child's Classification)			Deaths			
			Grade 1 2 3 4	Total		A	B	C	3 mos.	3–6 mos.	6–12 mos.	Total (1 year)
Group I	>10 cm. saline	17	1 1 4 3	9 (53%)		6 (35%)	11 (64%)	0 —	4	—	1	5 (30%)
Group II	5–10 cm.	25	2 4 2 2	10 (40%)		7 (28%)	15 (60%)	3 (12%)	4	1	2	7 (28%)
Group III	<5 cm.	41	4 1 2 1	8 (18%)		5 (12%)	26 (63%)	10 (24%)	4	1	3	8 (19%)

ence in the high risk patients at the moment is the use of portal-azygous disconnection similar to the procedure which has been used for many years by Tanner rather than any type of portal-systemic shunt.

Summary

1. Experimental and clinical data have been presented relative to factors influencing post-shunt encephalopathy and hepatic failure.

2. Post-shunt encephalopathy increases with each decade of life.

3. Maintenance of hepatic blood flow is vital to a satisfactory result following shunt operation.

4. Measurement of FPP and HOPP can be used as an indicator of prograde flow in the portal vein and as a rough predictor of the likelihood of post-shunt encephalopathy.

5. Technics of hemodynamic evaluation should be amplified and used prior to contemplated operation for portal hypertension in order to identify high-risk patients and to select the appropriate operative procedure.

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Discussion

Dr. Frederick A. Reichle (Philadelphia): I wish to describe and comment on a method which is available now, and which we have been using to determine the preoperative portal vein blood flow in the unanesthetized, unsedated human being. This can be done, in principle, by installation of radiopaque water immiscible droplets into the main stem portal vein, by filming droplet motion by cineradiography and then with certain assumptions one can calculate portal blood flow.

(Slide) The technic of umbilical vein cannulation is illustrated here. This is done before the day of testing, preferably under field block or regional anesthesia, and preferably extraperitoneally. Then on a subsequent day an inner catheter can be passed through the umbilical vein retrograde in the left portal vein and into the main stem portal vein in a hepatofugal direction to the the region of the confluence of the splenic vein and mesenteric vein. Then by slowly introducing small amounts of Lipiodol, a water immiscible material, small droplets can be formed, and their motion in the portal vein can be observed by subsequent analysis of cineradio-