The Circulation in Portal Hypertension\textsuperscript{1,2}

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Received November 22, 1974

While increased resistance to portal blood flow is a central feature of portal hypertension, the varied clinical presentations of this syndrome and their relation to the underlying divergent splanchnic hemodynamic patterns remain puzzling. Some patients present with massive ascites, repeated hemorrhage from ruptured esophageal varcies, and severe hypersplenism, whereas others with equivalent or even higher portal pressure readings are symptom-free. Nonetheless, each of these serious complications is generally conceded to be somehow a direct consequence of high portal pressure. Portal pressure, however, depends not only upon resistance to portal flow through the liver and through portasystemic collaterals bypassing the liver, but also upon the volume of splanchnic blood feeding into the portal system from the gastrointestinal tract, pancreas, and spleen. Thus, at any given moment, the level of portal pressure is the resultant of a whole set of rapidly changing interrelated flows and vascular resistances in the splenic, mesenteric, hepatic, and systemic circulations (1).

Less than 30 yr ago, the “syndrome” of pulmonary hypertension appeared equally perplexing. Pulmonary artery pressure likewise depends upon a complex set of rapidly changing interrelated flows and vascular resistances albeit in the systemic and pulmonary circulations. But then the cardiac catheter was introduced into the heart and great vessels, and blood flow and vascular pressure measurements were made at key points in these two circulations. Today, a variety of forms of pulmonary hypertension are recognized which have their own distinctive clinical presentations and are defined by specific hemodynamic criteria (2). Unfortunately, the events in portal hypertension take place in the relatively inaccessible splanchnic bed, and methodology continues to be a major stumbling block in obtaining complete hemodynamic data. Direct measurement of individual organ blood flow usually must be made under artificial or less than ideal conditions (e.g., at laparotomy), and indirect quantitation of portasystemic shunted flow is at best a rough approximation (3). Thus, “catheterization data” (simultaneous measurements of flow and pressure) at key points in the splanchnic circuit (splenic, mesenteric, hepatic, and portal) in patients with portal hypertension comparable to “catheterization data” in patients with pulmonary hypertension are simply not available.

The influence of splanchnic blood flow on portal dynamics is well illustrated in experimental right-sided congestive heart failure in the dog. Banding of the pulmonary artery alone or in combination with disruption of the tricuspid valve regularly produces marked systemic venous hypertension, massive hepatomegaly, engorge-

\textsuperscript{1}Supported in part by grants from the USPHS (HL 13390 and 13341). Some of these patients were studied in the NIH Clinical Research Center in Surgery at the Arizona Medical Center.

\textsuperscript{2}Based on a seminar at the West-Haven Veterans Administration Hospital, New Haven, CT on May 20, 1974, Dr. Harold O. Conn, Guest Editor.

\textsuperscript{3}Currently the recipient of a USPHS Career Research Development Award.
ment of hepatic hilar lymphatics, and weeping of ascitic fluid from the liver. The spleen, however, is shrunken (Fig. 1), and lymphatics draining the extrahepatic portal bed are not prominent (4). In this model, blood flow into the splanchnic viscera decreases in response to the over-all reduction in cardiac output, peripheral resistance rises, and arteriovenous oxygen extraction widens (passive congestion) (5–7). Thus, despite increased resistance to the return of blood via the great veins, simultaneous reduction in flow into the splanchnic bed minimizes or negates any rise in portal pressure and modifies the intensity and severity of congestion in the digestive tract and spleen.

In striking contrast to the dog with right-heart failure is the patient with portal hypertension from hepatic cirrhosis. In this disease (but not in portal hypertension from isolated portal vein occlusion) peripheral pulses are often bounding, cardiac output increased, systemic vascular resistance low (8, 9), and arteriovenous oxygen extraction narrow (10). Moreover, splenomegaly is prominent and occasionally massive, splanchnic arteries particularly to the spleen may be enlarged (11, 12), mesenteric and splenic lymphatics are widely dilated, and peritoneal surfaces of the bowel and mesentery are the predominant source of ascitic fluid (13). Furthermore, after reduction in splanchnic arterial flow through selective infusion of pitressin (a potent splanchnic vasoconstrictor) into the superior mesenteric and splenic arteries, portal pressure falls acutely and esophageal varix hemorrhage temporarily ceases (14). Thus, whereas increased resistance to portal flow is present in both right-heart failure (transmitted back from the central veins) and hepatic cirrhosis (transmitted back from the scarred regenerating liver), only in cirrhosis where splanchnic blood flow is maintained does portal hypertension and extrahepatic portal congestion develop.

The differing effects of stagnant as opposed to hyperdynamic blood flow in the

![FIG. 1. Massive hepatomegaly (680 g) and splenic atrophy (15 g) in dog, 4 wk after banding of the main pulmonary artery with an ameroid constrictor (casein hydrolysate). Gradual swelling of the constrictor (hydrophilic) promoted progressive right-sided heart failure with systemic venous hypertension and massive ascites. Despite prominent engorgement of the liver, congestion of the extrahepatic portal bed was minimal.](image-url)
pathophysiology of portal hypertension are seen in experiments carried out acutely in dogs. After marked constriction of the portal vein (to approximately 25–50% of the original diameter), portal pressure rises sharply and concomitantly lymph formation in the extrahepatic portal bed increases, mesenteric vascular resistance rises, arterial inflow decreases, and arteriovenous oxygen extraction across the gut widens as oxygen delivery falls (the pattern of "passive congestion") (Fig. 2). On the other hand, doubling or even tripling mesenteric blood flow by intravenous infusion of glucagon does not produce significant portal hypertension (Fig. 3). When, however, intravenous infusion of glucagon is combined with only minimal constriction of the portal vein (to approximately 80–90% of the original diameter), portal pressure and extrahepatic lymph production increase sharply, but the entire physiologic pattern differs from that induced by portal vein constriction alone. Specifically, mesenteric blood flow and oxygen delivery to the gut are preserved, and mesenteric venous blood is highly saturated with oxygen ("active congestion") (Fig. 4). Although these experiments confirm the necessity of some degree of increased portal vascular resistance in the production of portal hypertension, they also demonstrate that forced maintenance of "forward flow" in the splanchnic bed in the face of increased portal vascular resistance reproduces more closely the findings of portal hypertension in hepatic cirrhosis.

Splenomegaly, a common feature in portal hypertension, also provides a clue to the role of arterial flow in the genesis of portal hypertension. Although the enlarged spleen is usually viewed as the end result of transmission of high portal venous pressure backward into the spleen ("passive congestion") (16) the degree of splenomegaly correlates poorly with the level of portal pressure (17, 18) or the severity and duration of portal or splenic venous obstruction (19, 20). Moreover, the spleen may be greatly enlarged and congested in the absence of portal hypertension (21), splenic venous blood in patients with portal hypertension is typically highly saturated with oxygen (10) (in contrast to "passive congestion"), reduction of portal pressure by portasystemic shunt often does not appreciably reduce splenic size (18) and neither sustained congestive splenomegaly nor persistent elevation in splenic venous pressure follows chronic obstruction to splenic venous flow in experimental animals (10, 22, 23). Splenic size does correlate, however, with the magnitude of splenic arterial flow which may be three to five times normal in patients with massive splenomegaly (Fig. 5). Yet abrupt interruption of splenic inflow (e.g., by ligation of the splenic artery) rarely lowers pressure to normal and sometimes barely affects it at all (21, 24) suggesting that other hemodynamic variables (e.g., mesenteric blood flow and portal vascular resistance) curiously adjust to sustain the elevation in portal pressure (25). Nonetheless, occasionally splenectomy or splenic artery ligation with preservation of splenic venous collaterals suffices to control esophageal varix hemorrhage or ascites (vide infra).

In diseases placing a sustained excess "work load" on the reticuloendothelial system (e.g., production of abnormal erythrocytes in hereditary spherocytosis or accumulation of macromolecular cerebrosides in Gaucher's disease), splenic enlargement and increased splenic blood flow accompanies reticuloendothelial proliferation (21, 26, 27). Similarly, in primary disorders of the reticuloendothelial system and blood-forming organs (e.g., myeloid metaplasia or the dysproteinemias), the spleen participates in the pathologic process, and splenomegaly with hyperdynamic splenic blood flow is often observed (26, 28, 29). In portal hypertension, too, the enlarged spleen demonstrates prominent white pulp hyperplasia in addition to red pulp congestion (20). This reticuloendothelial response is likely related to reduction in
FIG. 2. Circulatory dynamics in the extrahepatic portal bed of the dog after induction of portal hypertension by narrowing of the portal vein. Note the sharp fall in superior mesenteric arterial (SMA) flow and rise in mesenteric vascular resistance accompanied by progressive decline in oxygen saturation (HbO₂) of mesenteric venous blood and widened arterial–mesenteric venous (A–MV) oxygen extraction. Thoracic duct lymph (TDL) flow also increased, whereas thoracic duct lymph-serum (TDL/S) protein decreased. These findings represent "stasis" or "passive congestion" of the portal system. *PRU = peripheral resistance units (arterial–mesenteric venous pressure) (mmHg)/SMA flow (ml/min). (Reprinted with permission of Annals of Surgery) (15)
FIG. 3. Circulatory dynamics in the extrahepatic portal bed of the dog after induction of hyperdynamic mesenteric blood flow by systemic infusion of glucagon. Despite doubling of superior mesenteric arterial (SMA) flow, portal pressure, mesenteric venous oxygen saturation (HbO₂), and arterial-mesenteric venous (A–MV) oxygen extraction were minimally altered. Mesenteric vascular resistance decreased as SMA flow increased. There was also a modest increase in thoracic duct lymph (TDL) formation and a slight fall in thoracic duct lymph/serum (TDL/S) protein ratio. *PRU = arterial-mesenteric venous pressure (mmHg)/SMA flow (ml/min) (Reprinted with permission of *Annals of Surgery*) (15).
FIG. 4. Circulatory dynamics in the extrahepatic portal bed of the dog after induction of portal vein constriction combined with systemic infusion of glucagon. Superior mesenteric arterial (SMA) flow was slightly increased and mesenteric vascular resistance lowered. Mesenteric venous oxygen saturation ($HbO_2$) remained high and arterial–mesenteric venous (A–MV) oxygen extraction unaltered. Thoracic duct lymph (TDL) formation is similarly increased and thoracic duct lymph/serum (TDL/S) protein content reduced. These findings represent "active congestion" in contrast to "passive congestion" of the portal system (see Fig. 6). *PRU = arterial–mesenteric venous pressure (mmHg)/SMA flow (ml/min). Reprinted with permission of Annals of Surgery (15).
FIG. 5. Correlation of splenic weight in patients with congestive splenomegaly with level of portal pressure (left) and rate of splenic arterial inflow (right). Whereas, there is no correlation between spleen weight and level of portal pressure ($r = 0.20, n = 11, P > 0.50$) there is a significant correlation between spleen weight and rate of splenic arterial inflow ($r = 0.86, n = 10, P < 0.01$). In calculation of regression correlation the patient illustrated by an open square was omitted. Despite intense red pulp congestion the bulk of splenic enlargement in this patient derived from extramedullary hematopoiesis (see Fig. 8). Reprinted with permission of *Gastroenterology* (21).
transhepatic portal flow and/or depression of reticuloendothelial activity in the liver (30, 31). Thus, while the specific etiology may differ, the basic stimulus for splenomegaly and hyperdynamic splenic blood flow—namely, reticuloendothelial hyperplasia—is similar in diseases as diverse as hereditary spherocytosis and cirrhosis of the liver.

The critical role of the spleen in portal hypertension is well shown by hemodynamic data before and after splenectomy in a middle-aged woman with hepatic cirrhosis, massive splenomegaly, and intractable ascites. This patient exhibited a markedly hyperdynamic splenic circuit, rapid portal flow, and only minimally elevated portal vascular resistance (Fig. 6). After ligation of a greatly enlarged splenic artery (blood flow estimated at 1200 ml/min), portal pressure fell from 39 to 25 cm saline. Despite increased resistance to transhepatic portal flow, the major factor responsible for her severe portal hypertension was a massive influx of splenic blood into the portal system. Splenectomy alone was performed and ascites has not returned. Reexamination of portal dynamics 5 yr later revealed normal transhepatic blood flow with only mild portal hypertension (Fig. 7). Similar splenic hemodynamics in other patients with portal hypertension are shown in Figs. 8 and 9.

Muscle and skin are other sites of hyperdynamic blood flow in patients with portal hypertension from hepatic cirrhosis (36). The spider angioma, a common cutaneous “stigma” of this disorder, consists of a plexus of dilated arterioles as nicely illustrated by arteriography (Fig. 10) and comparative blood gases (Table 1). In contrast to the splanchnic bed where hyperdynamic blood flow is met by increased venous resistance through the cirrhotic liver, rapid flow in the skin (and elsewhere outside the abdomen) does not ordinarily encounter increased venous resistance and, therefore, regional venous hypertension does not develop.

Thus, while resistance to portal flow may be the sine qua non in the pathogenesis of portal hypertension, the magnitude of portal pressure elevation and the varied clinical sequelae that ensue probably reflect the broad spectrum of blood (and lymph) circulatory dynamics in the splenic, mesenteric, portal, and hepatic systems in this syndrome. In the care of patients with pulmonary hypertension, surgical treatment often depends upon hemodynamic data acquired through cardiac catheterization. For example, “high flow” pulmonary hypertension from patent ductus arteriosus responds nicely to ligation of the ductus, whereas the same operation with “high resistance” pulmonary hypertension may be catastrophic. Similar considerations may indeed apply to the syndrome of portal hypertension. Thus, when a hyperdynamic splenic circuit is the major factor generating portal hypertension, splenectomy alone or splenic artery ligation without complete diversion of the portal stream may be the preferable operation (38–40). On the other hand, when high-resistance portal hypertension predominates, this particular approach may be ineffective or even hazardous and portasystemic shunt operations may be necessary. It is suggested, therefore, that the hemodynamics of the splanchnic bed be clarified in patients suffering from the complications of portal hypertension particularly if standard drug therapy is unsatisfactory and operation is contemplated.

A close correlation exists between the size of the splenic artery on celiac angiography or at operation and the rate of splenic blood flow (38, 41, 42). Our own estimated formula is a flow rate of 100 ml/min/mm of splenic artery diameter. A diameter of >8 mm signifies that splenic blood flow contributes to portal hypertension (21).
FIG. 6. Splenoportography (A) and celiac angiography (B) (reprinted with permission of *J. Amer. Med. Assoc.*) (32) in a 41-yr-old woman with posthepatitic cirrhosis and massive ascites. Hemodynamic findings indicated a hyperdynamic splenic circulation with slightly increased postsinusoidal hepatic resistance to portal flow. Splenic arterial flow was 1.2 liters/min and hepatic arterial flow was 670 ml/min (measured at laparotomy with a noncannulating electromagnetic flowmeter). Total liver blood flow was 2270 ml/min (indocyanine green extraction) and calculated portal flow was 1.6 liters/min. Portal vascular resistance was slightly increased (hepatic wedge pressure-free hepatic vein pressure = 44–16 cm saline). After splenectomy portal pressure fell from 38 to 25 cm saline (see Fig. 3).
FIG. 7. Venous phase of a superior mesenteric arteriogram in a 41-yr-old woman 5 yr after splenectomy for treatment of ascites secondary to hepatic cirrhosis and portal hypertension. Estimated hepatic blood flow (indocyanine green extraction) which before splenectomy was 2270 ml/min was now 1350 ml/min. Hepatic wedge pressure-free hepatic vein pressure was now 21–15 cm saline (see Fig. 6). (Reprinted with permission of J. Amer. Med. Assoc.) (33).
FIG. 8. Selective splenic arteriogram (top) in a middle-aged woman with polycythemia vera, massive splenomegaly, ascites, and varix hemorrhage. Venous phase (outlined) demonstrates huge, tortuous splenic and portal vein (bottom). Spleen (inset) weighed over 3 kg and splenic arterial flow was 1500 ml/min (noncannulating electromagnetic flowmeter). Splenectomy lowered portal pressure from 28 to 20 mmHg. Although the patient's disease has progressed to myelogenous leukemia, she is free of ascites and esophageal varix hemorrhage. (Reprinted with permission of Marcel Dekker, Inc.) (34).
FIG. 9. Selective splenic arteriography in a frail 59-yr-old woman with postnecrotic cirrhosis, marked splenomegaly, severe thrombocytopenia with easy bruisability, and epistaxis. Note the enlarged, tortuous splenic artery (A) and huge splenic vein that drains via a large coronary vein into prominent esophageal varices (B). At laparotomy splenic arterial flow was 850 ml/min (noncannulating electromagnetic flowmeter), and splenectomy lowered portal pressure from 28 to 22 cm saline. (Reprinted with permission of Ann. Surg.) (35).
FIG. 10. Subclavian arteriogram of a large spider angioma of the arm in a patient with hepatic cirrhosis. Note the single arteriole "feeding" into a racemose vascular network (A) with prompt drainage via a solitary venous tributary (arrow) into the basilic vein (B). (Reprinted with permission of South. Med. J.) (37).

|             | $PO_2$ (mmHg) | $PCO_2$ (mmHg) | pH   |
|-------------|---------------|----------------|------|
| Vascular spider | 63            | 33             | 7.42 |
| Radial artery  | 63            | 33             | 7.42 |
| Basilic vein   | 38            | 36             | 7.37 |

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