Dynamic and Neurogenic Factors Determining the Hepatic Arterial Flow after Portal Occlusion

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Acute ligation of the portal vein in the barbital-anesthetized dog produces a significant increase in the hepatic arterial flow when the perfusion pressure remains elevated in the artery. Evidence is presented which supports the concept that the immediate readjustment is solely dependent on dynamic changes. The late readjustments are probably conditioned by the interplay of neurogenic and humoral factors.

The magnitude of the functional intercommunications between the hepatic arterial and portal venous radicles in the liver remains in doubt. Two reports would suggest that exclusion of the portal circulation in such fashion as to maintain a steady hepatic arterial perfusion pressure results in augmentation of blood flows in this vessel in the dog and the cat. Whether this is due to hemodynamic factors or results from vasomotor adjustments is not known. A detailed and systematic study of this problem and its controlling mechanism is not available in the literature.

This report deals with a series of experiments which were primarily designed to investigate (1) the effect of portal ligation on hepatic arterial flow, and (2) the role of the hepatic nerve plexus in the regulation of the changes which might follow portal ligation.

Since it is well known that portal vein ligation significantly reduces venous return and cardiac output, so that extreme arterial hypotension supervenes in the dog and cat (though not in the macacus monkey), the problem was studied by perfusion of the hepatic artery under a reasonably constant perfusion pressure.

Materials and Methods

Adult mongrel dogs weighing between 15 and 21 Kg. were given morphine and anesthetized with intravenous sodium barbital (180 mg. per Kg.). Flows were measured directly in the hepatic artery with a calibrated photoelectric bubble flowmeter described by Selkurt. The hepatic artery was perfused directly from a constant perfusion pressure system. This was accomplished by diversion of blood from a femoral artery by means of a finger cot into an elevated reservoir prior to delivery into the meter, as shown in figure 1. Arterial pressures were recorded via Gregg manometers of suitable sensitivity and their mean obtained by planimetric integration. Mean perfusion pressures were simultaneously inscribed through a side connection to the flow meter bubble trap.

Through a midline abdominal incision, the portal vein was dissected free, and a loose thread placed around it. The pancreatico-duodenal vein and artery were ligated. The hepatic artery was isolated, care being taken to preserve the periarterial nerve plexus and the loose areolar tissue bearing the vasa nervorum. The hepatic nerve plexus was then carefully stripped parallel to the long axis of the artery and preserved intact.

To avoid major arterial anastomotic connections, the hepatic artery was perfused through a number 220 polyethylene tube connected to the base of the flowmeter trap and inserted into the exposed hepatic artery beyond the last gross anastomotic branch near the liver hilus. Exclusion of flow through remaining anastomotic channels was checked...
in the following manner: Prior to initiation of perfusion, the bubble trap outlet of the flowmeter was opened and the polyethylene tube inspected for backflow into the saline system. In the experiments analyzed, no backflow was noted against a hydrostatic pressure of 12 cm H$_2$O, thus eliminating the existence of significant arterial collaterals. Small amounts of saline were added periodically to the jugular vein funnel to maintain a fairly constant hematocrit level; this was checked at intervals throughout the experiment.

Following a one-hour period of observation, the portal vein was ligated. Flow and pressure recordings were obtained every five minutes from the beginning of the observation period until death. At the end of each experiment, the hepatic artery was sectioned distal to the tip of the indwelling polyethylene tube, and the flow capacity of the perfusion system was tested in order to make certain that there were no kinks or other obstructions to flow at the point of cannulation. This was never less than 120 cc per minute with a perfusion pressure of 80 mm Hg and a hematocrit level of 50 per cent.

**RESULTS**

In six dogs with an intact hepatic nerve plexus, the hepatic artery was perfused under a pressure of circa 80 mm Hg. Flows recorded soon after hepatic arterial intubation were variable and showed transient changes, then stabilized and remained fairly constant by the end of 30 minutes. In all instances, portal vein ligation was followed by an increase in hepatic arterial flow.

Figure 2 presents a typical experiment. Immediately following portal vein ligation (A), there was a steep rise in hepatic arterial flow (HAF), and a marked decrease in hepatic arterial resistance; the systemic arterial pressure (MAP) decreased rapidly, but perfusion pressure (MPP) remained unaltered throughout the course of the experiment. In 3 of a total of 12 dogs (see below) portal vein ligation was followed by a transient period (of 5 to 10 minutes), during which hepatic arterial flow was greatly reduced or ceased entirely before increases in flow greater than the basal values.
were noted. This transient reduction observed in these three cases occurred regardless of the continuity or severance of the hepatic nerve plexus.

The increased rate of hepatic arterial flow and the decreased resistance following portal ligation remained constant until late in the shock state. In the experiment illustrated in figure 2, there were noted terminally a late decrease in hepatic arterial flow, an increase in calculated resistance, and an agonal rise in systemic arterial pressure (B), rapidly eventuating in death of the animal (C). There was a great variability, however, in the events observed late in the shock stage. The agonal rise in systemic arterial pressure was often insignificant or did not occur at all, particularly in dogs surviving ligation less than one hour. In some instances, the increase in hepatic arterial flow and the decreased hepatic arterial resistance following portal ligation remained constant until or even several minutes after death. This was noted whether the nerve plexus was severed or intact.

That the nerve plexus when intact plays some part in the usual terminal decrease in hepatic arterial flow and increase in resistance is illustrated by the experiment shown in figure 3. The last part of a sustained series of flows following portal ligation is shown. There was then a decrease in flow which became pronounced after 220 minutes. Section of the hepatic plexus (A) resulted in a restoration of high flow levels (B), but terminally a decrease was again noted persisting until death (C). Similar observations were made in four experiments.

With the purpose of further investigating the influence of the hepatic nerve plexus on the increased arterial flow attendant to portal ligation, and the reversibility of the process, the same procedure as outlined was repeated in a group of six dogs. A perfusion pressure of 60 mm. Hg was arbitrarily employed for perfusion of the hepatic artery. Similar results were obtained in each experiment, as typified in figure 4.

The final flow of a one hour basal period is shown at the start of the graph. Immediately following portal clamping (A) there was a definite and progressive increase in flow (HAF). After 30 minutes, upon release of the portal vein (B), hepatic arterial flow decreased; section of the hepatic plexus at the nadir (C) did not alter flow. At the 125-minute period, (D) the portal vein was again clamped, with a second increase in flow which mirrored the pattern noted after the first clamping (A).
Repeated portal inflow release (E) again reproduced the initial hepatic flow decrease (B). Calculated hepatic arterial resistance (HAR) showed, as before, changes opposite to those occurring in the flow.

A sudden decrease in the circulating blood volume provides an alternative method whereby sudden lowering of portal flow may be achieved. With the portal vein unobstructed, a period of rapid bleeding reduced the systemic arterial pressure to 44 mm. Hg (F). There was an immediate increase in hepatic arterial flow which remained sustained for 25 minutes. At this point, flow progressively decreased until death 28 minutes later (G).

The effect of bleeding was observed on two other occasions and yielded similar immediate increases in flow; in one instance a late rise in calculated hepatic arterial resistance was noted, but not in the other. In both cases, the hepatic plexus had been preserved intact.

**DISCUSSION**

The evidence presented demonstrates that exclusion of the portal inflow with a sustained pressure head in the hepatic artery leads to an increase in hepatic arterial flow. The increase in hepatic arterial flow and decrease in calculated hepatic resistance are sustained until the animal approaches the terminal stage. The mechanism is purely dynamic, and is not dependent on the continuity of the autonomic nerve supply to either hepatic arterial or portal radicles; it still occurs when the hepatic plexus is sectioned and the periportal tissue is destroyed. In addition, the process is reversible. In these experiments, no attempt was made to insure destruction of grossly invisible adventitial nerve fibers by phenol application. The role played by such fibers may be discounted, since it has been satisfactorily demonstrated that the electric stimulation of the smaller visible individual nerve fibers produces no significant increase in hepatic arterial resistance.8

Neither would the evidence implicate hypoxia as a factor. In one instance, a 100 percent increase in hepatic arterial flow was demonstrated within 10 seconds following portal ligation—hardly a sufficient period of time to allow for a hypoxic effect. This view is supported by the marked increase in hepatic arterial flow, which follows a period of rapid bleeding, an event which leads to reduction of portal inflow.9

The intrinsic intrahepatic mechanism, however, remains unexplained. Two alternative hypotheses may be invoked: either a direct resistance drop across hepatopetal communications, or a decrease in volumetric encroachment by distended portal radicles upon arterial channels. Likewise unexplained are the terminal phenomena which show variations despite unaltered perfusion pressures. When the late resistance increase occurs, its temporary decrease following nerve section and the subsequent resumption of this increase point to the possible participation of neurogenic and humoral factors late in the hypotensive stage.

**SUMMARY AND CONCLUSIONS**

1. The hepatic arterial flow was measured by means of a photoelectric bubble flowmeter in a series of barbital-anesthetized dogs. A constant perfusion pressure was maintained in the hepatic artery by means of a finger cot pump.

2. Portal ligation was followed by an immediate increase in hepatic arterial flow, which was sustained until the terminal stage was approached, at which time it decreased abruptly or gradually.

3. Nerve plexus section had no effect on the initial postligation augmentation of flow, but temporarily augmented the flow following a late decrease in the terminal shock stages.

4. The evidence supports the view that the early augmentation of hepatic arterial flow which follows portal ligation is a purely dynamic response, and is not related to a local or central nerve reflex or to hypoxia, whereas late events may be controlled by either neurogenic or humoral factors.

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