The Portal and Hepatic Venous System in Shock: *

An Angiographic and Manometric Study in the Dog

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A CONTROVERSIAL aspect of prolonged hemorrhagic shock is the possible major role of splanchnic *pooling* in causing irreversibility.[13, 24, 31, 32] In the dog this is thought to result from an obstruction to the venous outflow of the liver, with damming of blood in the liver and portal system, causing engorgement and enlargement of the liver and congestion and hemorrhages in the intestines. Several authors[4, 6, 10, 12, 28, 29] have described sphincteric mechanisms, either functional or structural, in the venous outflow system of the liver. These may be located at one of four possible sites:

1. The hepatic vein—spasm may occur at its junction with the inferior vena cava[4, 29] or the whole hepatic venous system may react by intense vasoconstriction,[12] which may occur in a spiral fashion giving the vessels a corkscrew appearance.[28]
2. The sublobular veins.[6]
3. The *small sluice channels of Deysach*[6] which drain a number of hepatic sinusoids and enter either a central or sublobular venule.
4. The hepatic sinusoids.[10]

Data from studies of prolonged hemorrhagic hypotension in the dog from this laboratory have not supported these concepts.[26] The present study was undertaken to investigate the radiologic appearance of and the pressure changes in the portal and hepatic veins and the inferior vena cava before and after hemorrhage and after reinfusion of the shed blood. At the same time, changes in the volume, shape and color of the liver were also studied.

Methods

Forty adult mongrel dogs (15 females and 25 males) weighing between 10.0 and 24.1 Kg. were studied. The venous pressures were measured in 35 animals, and changes in liver volume were studied in five animals.

All were anesthetized with intravenous pentobarbital sodium (27 mg./ Kg.), and an endotracheal tube was passed to insure a clear airway. The abdomen was opened through an upper midline incision. The portal vein was cannulated via a large branch of the splenic vein except for two experiments where the cannulation was performed via a branch of the superior mesenteric vein in one and the left branch of the portal vein in the other. The left hepatic vein was exposed between the left central and left lateral lobes of the liver and a cannula inserted according to the method of Shoemaker *et al.*[23] This method was preferred to the alternative of inserting a cannula into the inferior vena cava and thence into a hepatic vein, as we wished to avoid mechanical interference with any possible sphincteric mechanism at the junction of these two vessels.

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The inferior vena cava was cannulated via the right common femoral vein, the tip of the cannula being placed opposite the point of entry of the left hepatic vein. The position was checked by palpation and by radiography, and was later confirmed by direct examination at autopsy. This careful positioning of the vena caval catheter was necessary to insure an accurate comparison between the pressures in the vena cava and left hepatic vein. Otherwise, the pressure gradient that normally exists between the caudal and cephalic portions of the abdominal and thoracic portions of this vessel would have caused misleading results.

In some dogs a second cannula was inserted into the lower vena cava for injecting contrast medium. The aorta was cannulated via the femoral arteries, one cannula being used for bleeding the animal and the second was connected to either a mercury manometer or a Statham pressure transducer and Grass polygraph for measuring arterial blood pressures. Each venous cannula was connected to a saline manometer, all measurements being referred to the level of the right atrium. The dogs were heparinized (5 mg. heparin/Kg.).

Serial radiographic studies were made in 13 dogs, each of the cannulated veins being injected in turn with 7.0 ml. of 50 per cent diatrizoate sodium (Hypaque). A series of three to six exposures was made at 0.5- to 0.7-second intervals using the Sanchez-Perez rapid cassette changer. Angiograms were made before hemorrhage, at half-hour intervals during a two- to four-hour period of severe oligemia and hypotension and at half-hour intervals after re-infusion of the shed blood until the experiment was terminated or the animal died. In another seven animals, using the x-ray image intensifier, cineangiograms (at 30 frames/sec. in six animals and 60 frames/sec. in the seventh) were made before, during and after hemorrhage and re-infusion. In four of the dogs Hypaque was used as described

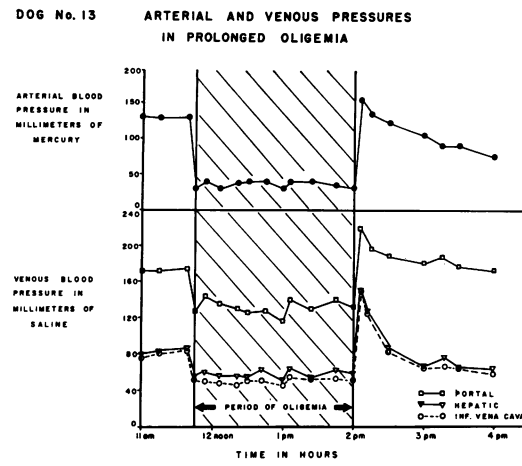

FIG. 1. Dog 13. Pentobarbital sodium anesthesia, 27 mg./Kg. Note that hepatic venous pressure remained above vena caval throughout experiment; portal venous pressure rose above control level following re-infusion, but if the rise in vena caval pressure is subtracted from the portal pressure, there is no real rise in portal pressure.

above, while in the remainder 6.0 ml. of 25 per cent thorium dioxide (Thorotrast) was used for each injection. In one animal a constant pressure injector (injecting at a rate of 10 ml./sec.) was used. In the remaining animals injections were made manually with equal rapidity by the same person each time. The results obtained with the two technics were identical.

The dogs were bled to a mean arterial pressure of 30 to 35 mm. Hg (the animals losing an average of 44% of their estimated blood volume**) and then kept at this level for two to four hours, after which the shed blood was returned to the animals.

In five dogs the experiment was modified to measure changes in the volume of the liver. Only the two aortic cannulas were inserted. A balloon, enclosed in a rigid oval carboard cylinder was placed around a portion of the left central lobe of the liver and was fixed to it by means of a suture. The balloon was inflated with air at a pressure of 30 mm. saline and was connected via a Statham pressure transducer to a Grass

** Blood volume estimated at 9.0 per cent of body weight.

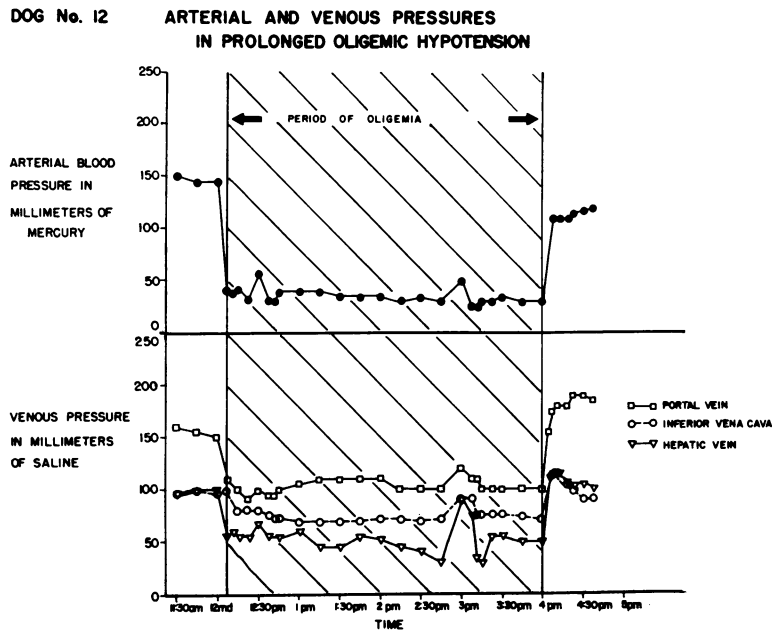

FIG. 2. Dog 12. Pentobarbital sodium anesthesia, 27 mg./Kg. Note that hepatic venous pressure fell below vena caval during entire period of oligemia; portal venous pressure showed moderate elevation above control levels with re-infusion and was still raised at end of experiment, 45 minutes after re-infusion.

polygraph for recording changes which would be proportional to changes in liver volume following bleeding and re-infusion as described.

In four dogs the liver and an adjacent ruler were photographed in color at intervals before bleeding, during a two-hour period of oligemia and following re-infusion. An identical technic was used for all the photographs.

Twenty-one of the 40 animals died either toward the end of the period of oligemia, shortly after re-infusion, or within two hours after re-infusion. The remaining animals were sacrificed 45 minutes to four hours after re-infusion. Autopsies were performed in all the animals. The color, size and shape of the liver were noted and the positions of the vena caval and hepatic vein catheters were checked.

Results

Pressures. All the venous pressures fell concomitant with the drop in arterial blood pressure. The mean pressure in the left hepatic vein (measured in 22 dogs) was usually higher than or equal to that in the vena cava opposite the left hepatic vein orifice (Fig. 1). The two pressures behaved similarly throughout the experiment, remaining low during the period of oligemia, and rising together after re-infusion to levels above the control in nine of 13 animals. In three dogs, however, the mean hepatic venous pressure fell below the mean caval pressure as soon as bleeding commenced and remained at this level until the animal was re-infused (Fig. 2). Hepatic venous pressure fell from 0.4 to 5.2 cm. of saline solution below vena caval pressure. In four other dogs the hepatic vein pressure was 0.4 to 1.5 cm. of saline solution below caval during oligemia, for periods ranging from ten to 45 minutes.

Additional data relating to these observations were obtained as follows in three dogs before bleeding: First, the left branch of the portal vein was clamped. Twenty minutes later the left branch of the hepatic artery was clamped, each clamp being left in position for a further 20 minutes. The pressure in the hepatic vein fell slightly and transiently, but remained higher than or equal to that in the vena cava. Thus,

the lower than caval pressures in the left hepatic vein were not to be explained by reduced inflow into the left lobe of the liver.

In nine dogs hepatic venous pressure following re-infusion exceeded the control figure. However, in three of these the absolute rise was no longer apparent when the concomitant rise in vena caval pressure was subtracted from it. The absolute rises in hepatic venous pressure were 1.5, 2.0 and 6.7 cm. of saline solution, respectively, while the rises in vena caval pressures were 1.8, 2.0 and 6.9 cm. of saline solution, respectively. Six of the nine animals showed relative as well as absolute rises in hepatic venous pressure. In these six the mean rise from control was 3.9 cm. of saline solution (range 1.1 to 9.2 cm.). The mean rise in vena caval pressure was 0.3 cm. of saline solution (range 0 to 1.4 cm.). The mean rise in hepatic venous pressure above the mean rise in vena caval pressure was 3.6 cm. of saline solution.

Of the remaining 22 dogs, nine died before or during re-infusion while in three the pressure equalled the control figure and in one it remained below the control. Of the six dogs which showed an increase in hepatic venous pressure following re-infusion, five had an associated marked increase in portal venous pressure.

Portal pressures fell immediately with hemorrhage (Fig. 1–3), but tended to rise toward normal during the latter part of the oligemic period (Fig. 3). In 27 of 35 dogs the pressure rose well above control levels after re-infusion, but in four there was no significant rise of pressure above control. Four dogs died before re-infusion. The pressures then fell, this fall being closely related to arterial blood pressure, falling to control levels within 15 to 30 minutes in animals showing a rapid decline in blood pressure, and falling more slowly in those where the decline in blood pressure occurred more slowly.

Control levels usually were reached within one to one-and-a-half hours after re-infusion. However, in four animals

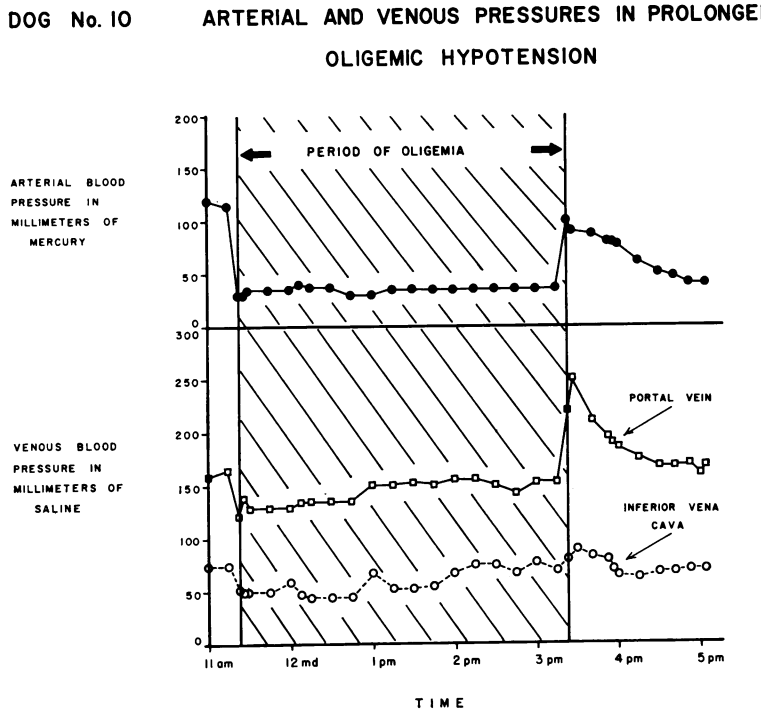

FIG. 3. Dog. 10. Pentobarbital sodium anesthesia, 27 mg./Kg. Note that portal venous pressure tended to rise toward control level in latter part of oligemic period. It rose well above control level with re-infusion and fell with decline in arterial blood pressure. It reached control level just over an hour after re-infusion.

which showed little decline in arterial blood pressure at the time they were sacrificed (45 minutes to two hours after re-infusion)

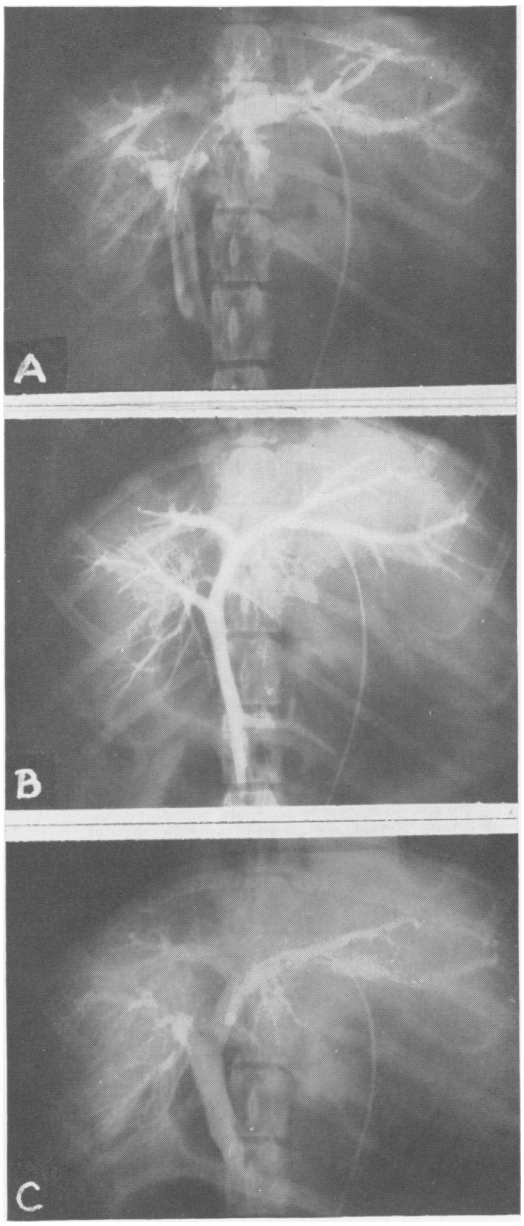

FIG. 4. Dog 10. Pentobarbital sodium anesthesia, 27 mg./Kg. Cannula in portal vein. A. Portal phlebogram before hemorrhage. B. Phlebogram during oligemia showing narrowing of portal venous tree with increased opacification. Note, also, retrograde filling of splenic vein and superior mesenteric veins. C. Phlebogram after re-infusion, showing return of portal vein to normal caliber and reduced opacification.

the portal pressures remained above control levels.

Radiologic Findings. *Portal System.* Before bleeding, injections of contrast medium outlined the portal vein and its branches as illustrated in Figures 4A and 5A. The portal phlebograms were similar in all cases, showing the major branches and the numerous intrahepatic ramifications of the vein. Immediately after hemorrhage the portal phlebogram showed clear diminution in caliber (Fig. 4B, 5B), which persisted throughout the period of oligemia. There was better visualization of the vein and its branches than before oligemia and hypotension, because the flow was slower and there was less dilution of the injected contrast medium by the blood stream. In three animals, portions of the intrahepatic portal system failed to fill with contrast medium during oligemia. Four of the 20 animals studied died before re-infusion. Of the remaining animals 11 demonstrated return of the portal vein to normal caliber following re-infusion (Fig. 4C) associated with a rise of arterial blood pressure to control or near control levels. In five animals, however, the vein and its branches remained narrowed and radiologically dense (Fig. 5C), though not quite as dense as in the period of oligemia. In four of these animals arterial blood pressure rose, with re-infusion, to a mean of 68 per cent of the control blood pressure, while in the fifth animal it returned to control levels.

As the blood pressure declined during normovolemic shock the vessels again became narrow. As the condition of the animals deteriorated tributaries of the portal vein which had previously not filled with contrast medium became progressively more demonstrable (Fig. 5D) until, with the death of the animal, widespread filling of the portal system resulted. The portal venous pressures showed no tendency to rise at this stage. This retrograde filling occurred within ten to 15 minutes of the

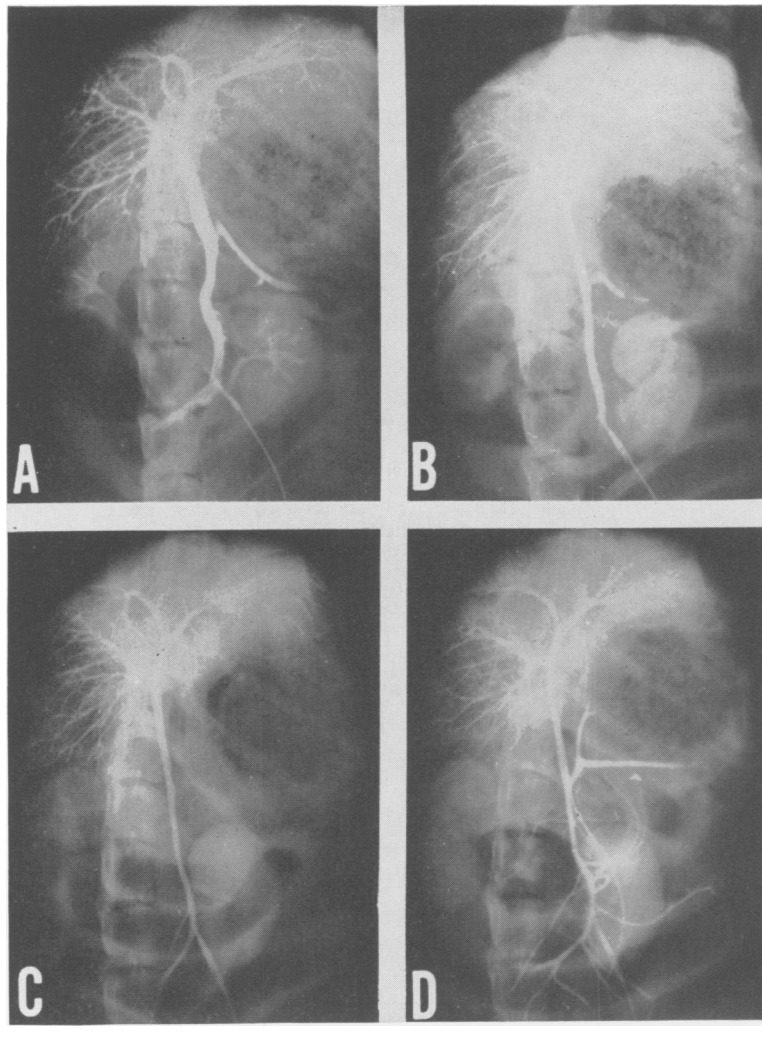

FIG. 5. Dog 2. Pentobarbital sodium anesthesia, 27 mg./Kg. Cannula in branch of superior mesenteric vein. A. Portal phlebogram before hemorrhage. B. Phlebogram during oligemia showing narrowed vessels. C. Phlebogram 35 minutes after re-infusion and 105 minutes before death; arterial blood pressure at this time: 25 mm. Hg. Further narrowing of the vessel has occurred and retrograde filling of tributaries has commenced. D. Phlebogram 15 minutes before death; arterial blood pressure at this time: 15 to 20 mm. Hg. Retrograde filling has become much more extensive.

death of the animal, with the exception of one animal, in which it commenced 105 minutes before death, when its blood pressure had declined to 25 mm. Hg.

Hepatic Vein. The picture obtained depended upon which direction the catheter was directed. If the tip was passed toward the sinusoids the oncoming blood as well as the outflowing blood was opacified and a long length of the vein could be demonstrated (Fig. 6). If the tip was passed toward the junction with the vena cava only the outflowing blood was opacified and a relatively short length of the vein could then be shown radiologically (Fig. 7).

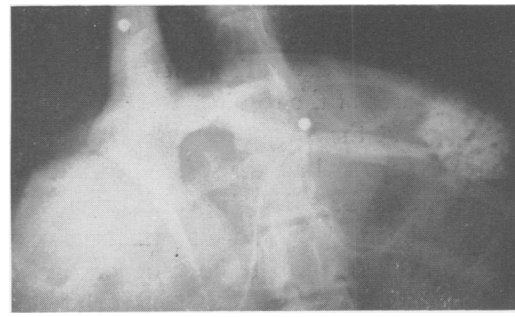

FIG. 6. Dog 14. Pentobarbital sodium anesthesia 27 mg./Kg. Catheter in main left hepatic vein with tip directed toward sinusoids. Phlebogram during oligemia showing narrowed vessel, with increased opacification. Reflux has occurred into distal vena cava, into orifice of right hepatic vein and into vein draining left posterior lobe of liver. No evidence of a sphincter or other obstructing mechanism in vein can be seen.

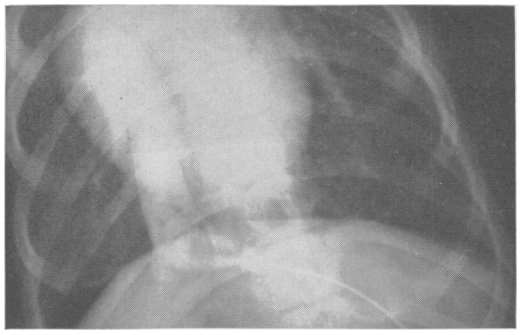

FIG. 7. Dog 7. Pentobarbital sodium anesthesia, 27 mg./Kg. Cannula in left hepatic vein with tip directed toward vena cava. Phlebogram before hemorrhage. Relatively short segment of hepatic vein shown, clearly outlining junction with vena cava. An almost identical picture was obtained after re-infusion.

The changes in the hepatic vein were similar to those described in the portal vein except that narrowing of this vessel during oligemia was less apparent than in the portal vein. No sphincteric mechanism could be demonstrated either at the junction of the hepatic vein with the vena cava or anywhere along the course of the hepatic vein (Fig. 6, 8C). At all times there was a free flow of the contrast medium into the vena cava. In fact, it was not uncommon to see reflux of the contrast medium from upper parts of the vena cava into the orifices of the right and left hepatic veins (Fig. 6) and into the inferior vena cava distal to them. This reflux appeared to coincide with the contractions of the right atrium and in one animal it was related to the phases of the respiratory cycle, reflux occurring at the height of expiration.

In the terminal stages before death, tributaries of the hepatic vein which previously had not been visible became progressively more obvious until at the time of death, the hepatic venous system and inferior vena cava could easily be outlined (Fig. 8D).

With the exception of four dogs which were kept in the left oblique position, all studies were done with the animal supine, as autopsy studies showed that in this position the left hepatic vein and inferior vena cava were roughly in the same horizontal plane. However, one dog's position was changed from time to time to study the effects of gravity. During the control period, posture did not affect the emptying of the vein. However, during oligemia, with the dog in the right lateral position, there was more rapid emptying of the left hepatic vein, while in the left lateral position the already sluggish circulation in this vein became even slower, resulting in a considerable delay in emptying of the vein following the injection of the contrast medium. These results suggest that at the low venous pressures present in severe oligemia gravity may play a part in causing blood to be detained in the more dependent regions of the liver. Possibly the high specific gravity of the contrast medium may contribute to this effect.

Inferior Vena Cava. The findings here were similar to those already described for the portal and hepatic veins, with marked slowing of the circulation and greater opacification occurring during oligemia. On occasion, only during oligemia, reflux of contrast medium occurred from the inferior vena cava into the left and right hepatic veins (Fig. 8B). However, there was no constant relationship between free reflux and the occasional recording of hepatic venous pressures below those in the vena cava.

At no time was any gross dilatation of the vena cava seen to suggest the possibility of *pooling* of blood in the vena cava as the animals deteriorated. Vena caval dilatation was noted only as a terminal event shortly before death (Fig. 8D) in all animals who died during the course of the experiment.

Changes of Liver Volume. The balloon used was enclosed in a rigid cardboard cylinder to prevent pressure on it from movement of the diaphragm. Although it was not possible completely to eliminate respiratory artifacts, they were not sufficient

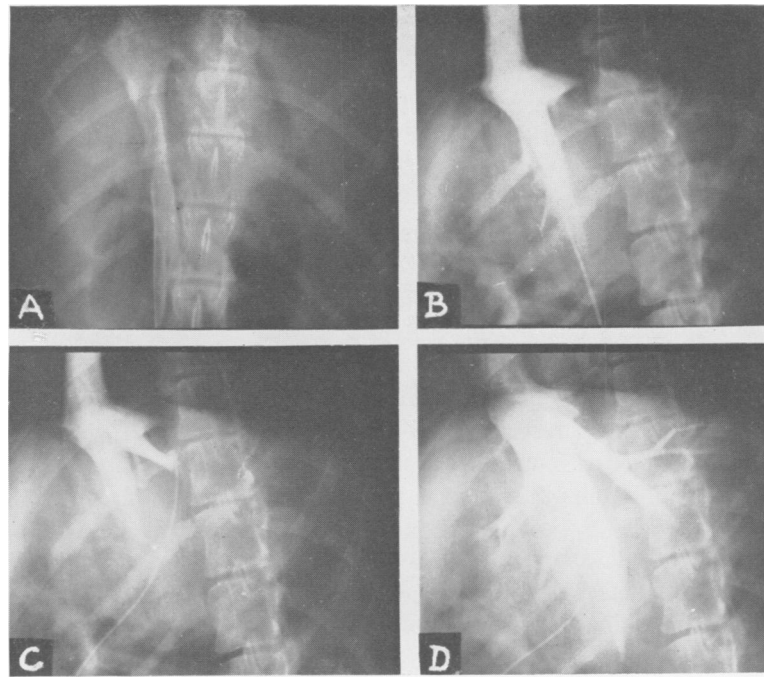

FIG. 8. Dog 13. Pentobarbital sodium anesthesia, 27 mg./kg. One catheter in inferior vena cava, a second in left hepatic vein with tip directed toward inferior vena cava. A. Vena caval phlebogram before hemorrhage. B. Vena caval phlebogram during oligemia, showing increased opacification and reflux into right and left hepatic veins. C. Left hepatic plebogram during oligemia, showing narrowing, increased opacification and, reflux into distal vena cava. No sphincteric constriction was demonstrable. D. Left hepatic phlebogram a few minutes before death, showing widespread retrograde filling of left and right hepatic veins, distal vena cava, and left inferior phrenic vein.

to interfere with the recordings, and the instrument provided a sensitive index of changes in liver volume. Bleeding resulted in an obvious decrease in liver volume while re-infusion resulted in enlargement of the liver to normal or near normal volume. All changes occurred promptly following hemorrhage or re-infusion. At no stage did we find an increase in liver volume suggestive of the hepatic engorgement which has been reported for the dog when shock becomes irreversible.[13]

If the re-infused dog was then made hypervolemic by a transfusion of donor blood or low molecular weight dextran, the volume of the liver increased further and reached levels above the control level. If such an animal was subsequently bled the liver volume again decreased.

Discussion

Measurements of blood pressure in the portal vein, the hepatic vein and the vena cava, and study of serial radiographs and cine-angiograms in various stages of hemorrhagic hypotension and shock failed to support the concept that one cause, if not the principal cause in the dog, of fatal normovolemic shock is a damming of blood behind the venous outflow of the liver, the excess of blood thus detained in the hepatic and splanchnic area being unavailable for the cardiac output. Were the data to have supported the concept of a sphincteric effect in the vena caval end of the hepatic vein, then the hepatic venous pressures should have increased when the animals which had been kept oligemic and hypotensive sufficiently long were re-infused, or when they began to deteriorate at a later stage. By the same mechanism, the portal venous pressures should have increased. If the sphincteric mechanism were at the level of the intrahepatic sinusoids, then one might have observed an increase in portal venous pressure with no change or possibly a decrease in hepatic venous pressure.

These effects did not occur. In seven of 13 dogs in which hepatic venous pressure was measured after re-infusion there was no rise in pressure above control levels. In

the remaining six animals hepatic venous pressures were elevated immediately after re-infusion, but there was no associated radiographic evidence of retention of blood in the hepatic vein to account for this. On cine-angiography the injected contrast medium flowed into the vena cava without delay. The rise in hepatic venous pressure must, therefore, have resulted from an increased blood flow into and through the liver, as borne out by the fact that in five of these six animals there was an associated rise in portal venous pressure.

While portal pressures were elevated in nearly all cases after re-infusion, this change, in some, was more apparent than real. Thus, in a previous group of experiments there was no real increase in one fourth of the cases.[26] In the present series, eight of 31 dogs (26%) showed either no rise above control levels of portal pressure relative to vena caval pressure or a rise which was of no significance. In five of these eight animals there was a poor response of the arterial blood pressure to re-infusion and the animals died within 15 minutes after re-infusion. In the remaining three animals, arterial pressure did rise to control levels, but was sustained until termination of the experiment in only one. These data suggest that the raised portal pressure is dependent more on elevation of mean arterial pressure (and, therefore, mesenteric and hepatic arterial pressure) to control levels than on increased resistance to outflow from the liver. This is supported by the fact that these rises in pressure were only temporary. They began to fall, on many occasions, before the mean arterial pressure began to fall and may simply represent a temporary increase in splanchnic flow following the prolonged period of splanchnic relative ischemia. On no occasion did the hepatic and portal pressures remain elevated while the systemic (and hepatic and mesenteric) arterial pressures fell.

These observations differ from those of several workers[7, 13, 24, 30-32] who have shown[24, 31] that immediately after re-infusion hepatic blood flow does not exceed control values. They attributed the increase in portal pressure to an increased outflow resistance in the liver, which may be secondary to liberation of norepinephrine,[24] acidosis without hypoxia,[16, 26] hypoxia without acidosis[26] or a combination of acidosis and hypoxia.

On the other hand, the data presented are in keeping with the findings of other workers[2, 5, 19, 20, 27] who demonstrated a *reactive hyperemia*[20] of the splanchnic area following re-infusion. They found diminished splanchnic vascular resistance, which persisted for approximately 30 minutes after re-infusion, and resulted in increased portal venous flow.

The concept that increased splanchnic flow is the cause of the raised portal pressure after re-infusion is further strengthened by the work of Shaldon *et al.*[22] who, in studies of portal hemodynamics in normal and cirrhotic patients, showed the converse, namely, that if the splanchnic resistance is increased by administration of vasopressin (Pitressin), hepatic blood flow was reduced by 40 per cent, and portal venous pressures fell by 39 per cent of the control figure.

If increased splanchnic flow is the mechanism responsible for the raised portal pressure we would expect to find an increase above control levels of the oxygen content of the portal venous blood after re-infusion, in keeping with *reactive hyperemia* in other areas. Selkurt and Brecher[19] have shown this, in fact, does occur.

Increased splanchnic blood flow rather than damming of blood in the portal system may explain the characteristic congestion, hemorrhages and necrosis seen in the intestines of dogs subjected to severe hemorrhagic hypotension. Thus, Lillehei[11] has shown that these changes still occur even in animals where the portal system was decompressed by the prior construction of an Eck fistula. The hemorrhages and necrosis,

under these conditions, were apparently the result of critical ischemia occurring during the shock period, with subsequent leakage of blood from the reopened anoxic vessels. If pooling of blood in the portal system is a major factor in causing irreversibility, one would expect a significant increase in the weight of the intestines after re-infusion. In fact, it has been shown that this does not occur.[21]

Further evidence against the concept of damming of blood behind an obstruction in the venous outflow of the liver is provided by the angiographic studies. These showed that following re-infusion there was no hold-up of portal blood flow through the liver, at a time when the portal pressure was markedly elevated. The previously narrowed portal veins returned to their normal caliber except in the animals in which arterial blood pressure failed to return to control levels. In general, the angiograms failed to show the disparity in caliber between the intrahepatic and extrahepatic portions of the portal vein reported by Friedman *et al.*[7] and to which was attributed the damming of blood in the portal system. Friedman *et al.* noted further constriction of the portal veins as the normovolemic period progressed, whether or not there was a fall in systemic arterial pressure. On the other hand, we found that this change occurred only with a decline in arterial blood pressure.

Retrograde filling of the portal venous tributaries (associated with prograde filling as well) was not a prominent feature during the period of oligemia occurring in only three animals (Fig. 4B). During normovolemic shock the portal venous bed opened only as a terminal event a short time before death. At this stage portal venous pressure was lower than the control level and showed no tendency to rise as one would have expected if the changes were due to an obstruction to the outflow through the liver.

Retrograde filling of tributaries was not confined to the portal system, but was also observed in the hepatic veins and in the inferior vena cava. This may have represented a loss of venomotor tone in keeping with the finding of Alexander [1] of a fall in venomotor tone as the animal's condition continued to deteriorate.

Finally, in no case was there any suggestion that an obstruction, either functional or anatomic, developed along the course of the hepatic vein.

"The much discussed but infrequently demonstrated sphincteric mechanism in the hepatic veins" [13] is still the subject of much controversy. Guntheroth and Mullins [9] have pointed out that many of the *physiologic* studies on which the existence of these sphincters is based were largely pharmacologic studies, often with extirpated organs, usually with indirect methods and under unnatural conditions.

Inspection of the liver throughout the course of the experiment supported by subsequent studies of photographs in color, also failed to support the concept of damming of blood in the liver. The expected purple engorgement of the tense liver was not found after rapid infusion of reservoir blood following prolonged oligemia and hypotension. At autopsy this organ retained the reddish brown color it had at the commencement of the experiment. It did not appear to be enlarged and, with rare exceptions, had well defined sharp edges. Engorgement and enlargement of the liver with rounding of the edges was found only in four animals made hypervolemic with donor blood or dextran, and in five animals whose condition was deteriorating and which were re-infused very rapidly with reservoir blood. These developed very high vena caval, hepatic and portal pressures, indicating terminal failure of the heart. They died very promptly after re-infusion.

Certain other findings deserve comment. In seven of 22 animals the hepatic venous pressure apparently fell below vena caval pressure during oligemia. This finding could

be attributed to technical error,[8, 14] but other explanations are possible. The failure to find a significantly lower pressure in the left hepatic vein after clamping the left hepatic artery and left branch of the portal vein suggests that the fall in hepatic venous pressure below vena caval pressure could not be attributed to a reduction in blood flow into the left lobe of the liver.

A possible explanation for this apparently paradoxical pressure difference is a Bernoulli effect resulting, possibly from the hepatic inflow of blood being slowed more than the linear velocity of flow in the vena cava is slowed.

Another possible explanation is offered by the report of Nakata *et al.*[14] who observed, in the rat, that hepatic venous flow is intermittent and related to the respiratory cycle. They demonstrated that retrograde flow may occur from the vena cava into the hepatic veins with inspiration. A similar mechanism may come into play at the low venous pressures in severe oligemia, but radiologically demonstrable reflux was present only at the height of expiration instead of inspiration.

Radiologic narrowing of the hepatic vein during oligemia was not as great as that of the portal vein confirming a finding of Friedman *et al.*[7] This effect possibly is due to liberation of epinephrine during oligemia, as these authors found that in the normal dog administration of epinephrine caused greater constriction of the portal vein than of the hepatic vein.

The marked narrowing seen in the portal vein during oligemia may be a purely passive phenomenon, the vessels merely accommodating themselves to the diminished amount of blood in the splanchnic system. On the other hand, active constriction of the vessels could be involved. Several factors favor the latter interpretation. There is a well developed muscular coat in the portal vein[3] which is capable of strong contraction as is often seen when dissecting the vein or its tributaries. Isolated segments of the portal vein constrict with epinephrine[3] which is liberated in large quantities into the circulation after hemorrhage.[18] The concept of active constriction is supported by Reynell *et al.*[17] who, on the basis of splanchnic blood flow and splanchnic volume studies after hemorrhage, concluded that the splanchnic vasculature contributes actively to circulatory homeostasis by a reduction in capacity.

The finding in three animals that portions of the intrahepatic portal system failed to fill during severe oligemia, is in keeping with the observation of Prichard and Daniel[15] in the normal rat that, at times, the circulation is maintained through the deeper regions of the liver, while the superficial parts fail to be perfused.

In conclusion, we believe that the raised portal and hepatic venous pressures following re-infusion are secondary to increased splanchnic blood flow, a *reactive hyperemia* occurring in the intestines just as it occurs in other organs subjected to a temporary ischemia. On the basis of our other findings, it is possible that in normovolemic shock there may be a general loss of venomotor tone with widespread retention of blood in the venous system as a whole, and not confined only to the splanchnic bed. This failure of venous return contributes materially to the ultimate circulatory failure.

Summary and Conclusions

Pressures in the portal vein, left hepatic vein and inferior vena cava were measured in 35 dogs before and after a severe hemorrhage and after re-infusion of the shed blood.

In another five dogs changes in liver volume, occurring under these conditions were studied.

In 20 of the dogs radiographic studies of the portal vein, hepatic vein and vena cava were made before and after hemorrhage and after re-infusion of the shed blood.

The rise in portal venous pressure following re-infusion began to decline soon after completion of the re-infusion and usually reached control levels within one to one-and-a-half hours. It thus appeared unlikely that progressive hepatic outflow obstruction could account for progressive deterioration of the animals by causing *pooling* or *damming* of blood in the liver and splanchnic bed.

An apparently reversed pressure gradient between the left hepatic vein and inferior vena cava was found during severe oligemia in seven out of 22 animals.

Radiologic narrowing of the portal vein and, to a lesser extent, of the left hepatic vein and inferior vena cava was observed during oligemia, with return to grossly normal, and not increased, caliber following re-infusion.

No evidence of a sphincteric mechanism could be demonstrated in the left hepatic vein.

Only in the very terminal stages, shortly before death, was evidence of *pooling* noted in the portal system. *Pooling* was not confined to this vascular bed but occurred, also, in the hepatic veins and inferior vena cava.

Possibly widespread loss of tone occurs in the venous system throughout the body so that large volumes of blood may be accommodated without rise in pressure in veins with loose perivenous support. This final and progressive venomotor paralysis could account for the decreased venous return to the heart and the progressive deterioration of the animal.

References

1. Alexander, R. S.: Venomtor Tone in Hemorrhage and Shock. Circulat. Res., **3**:181, 1955.
2. Ballinger, W. F. II, H. Vollenweider and E. H. Montgomery: The Response of the Canine Liver to Anaerobic Metabolism Induced by Hemorrhagic Shock. Surg. Gynec. & Obstet., **112**:19, 1961.
3. Bard, P.: Medical Physiology, St. Louis, C. V. Mosby Company. ed. 11. p. 241, 1961.
4. Bauer, W., H. H. Dale, L. T. Poulsson and D. W. Richards: The Control of the Circulation through the Liver. J. Physiol. (Lond.), **74**:343, 1932.
5. Cull, T. E., M. P. Scibetta and E. E. Selkurt: Arterial Inflow into the Mesenteric and Hepatic Vascular Circuits During Hemorrhagic Shock. Amer. J. Physiol., **185**:365, 1956.
6. Deysach, L. J.: Nature and Location of "Sphincter Mechanism" in Liver as Determined by Drug Actions and Vascular Injections. Amer. J. Physiol., **132**:713, 1941.
7. Friedman, E. W., H. A. Frank and J. Fine: Portal Circulation in Experimental Hemorrhagic Shock—in Vivo Roentgen Ray Studies. Ann. Surg., **134**:70, 1951.
8. Grindlay, J. H., R. Thors and J. L. Bollman: Effect of Occlusion of Vessels Entering the Liver on Hepatic Venous Pressure in Normal and Cirrhotic Dogs. Surg. Forum, p. 493, 1953.
9. Guntheroth, W. G. and G. L. Mullins: Liver and Spleen as Venous Reservoirs. Amer. J. Physiol., **204**:35, 1963.
10. Knisely, M. H., F. Harding and H. Debacker: Hepatic Sphincters: Brief Summary of Present Day Knowledge. Science, **125**:1023, 1957.
11. Lillehei R. C.: The Intestinal Factor in Irreversible Hemorrhagic Shock. Surgery, **42**: 1043, 1957.
12. Maegraith, B. G., W. H. H. Andrews and C. E. M. Wenyon: Active Constriction of Hepatic Venous Tree in Anaphyllactic Shock: Relation to Centrilobular Lesions, Preliminary Communication. Lancet, **2**:56, 1949.
13. Moore, F. D.: Relevance of Experimental Shock Studies to Clinical Shock Problems. Fed. Proc. Suppl. No. 9., p. 227, 1961.
14. Nakata, K., G. F. Leong and R. W. Brauer: Direct Measurement of Blood Pressures in Minute Vessels of the Liver. Amer. J. Physiol., **99**:1181, 1960.
15. Prichard, M. M. L. and P. M. Daniel: in "Visceral Circulation—A Ciba Foundation Symposium." Ed. Wolstenholme, G. E. W., Little, Brown and Co., Boston, p. 60, 1953.
16. Quintero, M., Y. Shibota, W. E. Neville and G. H. A. Clowes, Jr.: Acute Portal Hypertension and Congestion as a Cause for Unexplained Arterial Hypotension and Blood Loss from the Circuit During Perfusion in Dogs. Trans. Amer. Soc. Artif. Int. Organs, **5**:248, 1959.
17. Reynell, P. C., P. A. Marks, C. Chidsey and S. E. Bradley: Changes in Splanchnic Blood Volume and Splanchnic Blood Flow in Dogs after Hemorrhage. Clin. Sci., **14**:407, 1955.

18. Rosenberg, J. C., R. C. Lillehei, J. Longerbeam and B. Zimmerman: Endogenous Circulating Epinephrine, Nor-epinephrine and Serotonin in Hemorrhagic and Endotoxin Shock. Ann. Surg., **154**:611, 1961.
19. Selkurt, E. E. and G. A. Brecher: Splanchnic Hemodynamics and Oxygen Utilization during Hemorrhagic Shock in the Dog. Circulat. Res., **4**:693, 1956.
20. Selkurt, E. E.: Mesenteric Hemodynamics During Hemorrhagic Shock in the Dog with Functional Absence of the Liver. Amer. J. Physiol., **193**:599, 1958.
21. Selkurt, E. E.: Intestinal Ischemic Shock and the Protective Role of the Liver. Amer. J. Physiol., **197**:281, 1959.
22. Shaldon, S., W. Dolle, L. Guevera, F. L. Iber and S. Sherlock: Effect of Pitressin on the Splanchnic Circulation in Man. Circulation, **24**:797, 1961.
23. Shoemaker, W. C., W. F. Walker, T. B. Van Italie and F. D. Moore: A Method for the Simultaneous Catheterization of the Major Hepatic Vessels in a Chronic Canine Preparation. Amer. J. Physiol., **196**:311, 1959.
24. Shoemaker, W. C., W. F. Walker and L. N. Turk, III: The Role of the Liver in the Development of Hemorrhagic Shock. Surg. Gynec. & Obstet., **112**:327, 1961.
25. Shoemaker, W. C. and L. B. Fitch: Hepatic Lesion of Hemorrhagic Shock. Arch. Surg., **85**:492, 1962.
26. Simeone, F. A.: Some Issues in the Problem of Shock. Fed. Proc. Suppl., No. 9, p. 3, 1961.
27. Stewart, J. D., J. G. Stephens, M. B. Leslie, B. A. Portin and W. G. Schenk, Jr.: Portal Hemodynamics Under Varying Experimental Conditions. Ann. Surg., **147**:868, 1958.
28. Thomas, W. D. and H. E. Essex: Observations on the Hepatic Venous Circulation with Special Reference to the Sphincteric Mechanism. Amer. J. Physiol., **158**:303, 1949.
29. Walker, W. F., J. S. MacDonald and C. Pickard: Hepatic Vein Sphincter Mechanism in the Dog. Brit. J. Surg., **48**:218, 1960.
30. Wiggers, C. J., D. F. Opdyke and J. R. Johnson: Portal Pressure Gradients Under Experimental Conditions, Including Hemorrhagic Shock. Amer. J. Physiol., **146**:192, 1946.
31. Wiggers, C. J.: Physiology of Shock. Commonwealth Fund, New York, 1950.
32. Zweifach, B. W.: Aspects of Comparative Physiology of Laboratory Animals Relative to the Problem of Experimental Shock. Fed. Proc. Suppl., No. 9, p. 18, 1961.