Splanchnic Hemodynamics and Oxygen Utilization During Hemorrhagic Shock in the Dog

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Portal vein and hepatic artery flow were measured with bristle flowmeters. Based on such measurements, oxygen utilization by both the intestine and liver was found to be significantly reduced after prolonged hypotension. Splanchnic vascular resistance did not increase significantly during hypotension, and following transfusion there was a phase of marked reduction particularly in the mesenteric component. This was followed by some degree of compensation which persisted until the terminal stages when splanchnic vascular resistance again declined. Terminally, mesenteric resistance again appeared to be the component of total splanchnic resistance which manifested failure of compensation. It is suggested that impaired oxygen utilization by the intestine and liver may be a key mechanism accountable for the inadequate splanchnic vascular compensation during hypotension and its ultimate failure.

Various investigations of the influence of hemorrhage on splanchnic hemodynamics and oxygen utilization in which indirect hepatic dye removal methods were used in dogs do not permit assessment of the specific roles of the intestine and liver. The methodologic restrictions have also made it difficult to evaluate the effect of prolonged hemorrhagic hypotension, and particularly the behaviour of the splanchnic bed during the post-transfusion phase of hemorrhagic shock. Other limitations of the above cited studies include the fact that measurements taken with indirect methods do not permit continuous flow recording. The purpose of the present study was, therefore, to investigate splanchnic hemodynamics in shock by measuring blood flow directly with instruments which afforded continuous flow recording.

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METHOD

Bristle flowmeters* were employed to measure the flow characteristics of the portal vein and hepatic artery throughout the course of a standardized hemorrhagic shock procedure. These meters combine adequate sensitivity and high frequency with low hydraulic resistance, making them suitable for measurement of venous flow with minimal distortion of normal flow characteristics. Phase flow could be electrically integrated to give mean flow and this was combined with simultaneous measurement of mean blood pressure to provide factors needed for computing vascular resistance throughout the course of the experiment. In addition, arterial, portal vein and hepatic vein blood samples were taken during various stages of the experiment and analyzed for oxygen content; this combined with flow measurements furnished information concerning oxygen utilization of the intestine and liver during shock.

Dogs ranging in weight from 17 to 29 Kg. and anesthetized with 30 mg./Kg. of pentobarbital sodium were used. Details of pressure and flow recording are illustrated in figure 1. The right flank was incised for exposure of the portal vein and common hepatic artery. Particular care was taken not to damage nerve fibers accompanying the vessels during cannulation. As illustrated, owing to size restrictions, a flowmeter could not be directly inserted into the hepatic artery; hence the flowmeter was placed in a carotid-hepatic artery perfusion circuit. The gastroepiploic branch of the hepatic artery was not ligated. Hepatic vein pressure and blood samples were taken through a
metal sound introduced via an external jugular vein; its position was verified by direct palpation through the flank incision at the beginning and at the end of the experiment. The 0 reference point for all pressure measurements was the level of the inferior vena cava. No corrections were made for intra-abdominal pressure, under the assumption that this approximates atmospheric pressure when the abdomen is open.

The standardized shock procedure employed involved bleeding into a constant pressure reservoir attached to the femoral artery until a level of 55-60 mm. Hg carotid arterial pressure was attained. This was maintained for 90 min. when further hemorrhage brought the pressure to about 40 mm. Hg for 45 min. The reservoir blood was then warmed and filtered through gauze and retransfused into the femoral vein during an interval of about 10 min. Blood samples for the respective O2 content analyses were taken simultaneously during the control, 1 hour after hemorrhage to 60 mm. Hg, 30 min. after hemorrhage to 40 mm., and 1 hour and 1½ hours after completion of transfusion. Oxygen content was measured by the Scholander method by 2 operators, checking with a mean difference of 0.12 volume per cent for duplicate checks. Hematocrit determinations were made on the arterial blood sample of each set.

Flow and pressure measurements were usually made every 5 min. during the experiment, except late in normovolemic shock when definite trends had been established; then readings were taken only at 10 min. intervals. Measurements were made during the expiratory pause. Most of the records were taken at slow kymographic speed (5 mm./sec.) with flows integrated. But during each stage of the experiment at least 1 record was taken at fast speed (25 to 75 mm./sec.) with the flowmeter amplifiers adjusted for registration of phasic flow changes. The flowmeters were calibrated at the termination of the experiment with the animal's own blood for a series of flows spanning the range encountered in the experiment. Adequate heparinization (10 mg. total dose every 30 min. after a priming dose of 4 mg./Kg.) plus siliconizing the bristle prevented fibrin formation in the meters.

Donor blood was given prior to the start of the control observations to compensate for any blood lost as the result of surgery and to fill the shunt circuit; additional blood was given to replace that removed for blood gas analysis. Rectal temperature was observed throughout; a warming device on the dog board was turned on when necessitated.

Calculations

Splanchnic vascular resistance was calculated from the ratio:

\[
\frac{\text{portal vein flow} + \text{hepatic artery flow (ml./min.)}}{\text{arterial blood pressure}} - \frac{\text{hepatic venous pressure (mm. Hg)}}{\text{Mesenteric vascular resistance (intestine plus spleen):}}
\]

\[
= \frac{\text{portal vein flow (ml./min.)}}{\text{Arterial b.p.} - \text{portal venous pr. (mm. Hg)}}
\]

Hepatic vascular resistance was analyzed as two components, (A) hepatic artery and (B) intra-hepatic portal vein resistance.

\[
\begin{align*}
(a) & \quad \text{hepatic artery flow (ml./min.)} \\
& \quad \text{Art. b.p.} - \text{hep. v. p. (mm. Hg)} \\
(b) & \quad \text{Portal vein flow (ml./min.)} \\
& \quad \text{Port. v. p.} - \text{hep. v. p. (mm. Hg)}
\end{align*}
\]

The units thus derived have been designated: "peripheral resistance units" (P.R.U.).

Oxygen utilization*

Mesenteric:† Portal vein flow × (art. - port. v. O2 diff.)

Liver: The sum of hepatic artery and portal vein contribution:

\[
\begin{align*}
(a) & \quad \text{hepatic artery flow × (art. - hep. v. O2 diff.)} \\
(b) & \quad \text{Portal vein flow × (port. v. - hep. v. O2 diff.)}
\end{align*}
\]

* It is important to emphasize that oxygen utilization is calculated here from differences in O2 content, rather than from per cent saturation. Such calculations assume that hemoglobin concentration is unaffected by volume changes occurring while blood flows through the organ. To the extent that this may occur in the liver the present computations may be in error. The exercising of care to observe simultaneous sampling of blood minimized another potential source of error in this connection.

† This represents utilization by all tissues which drain into the portal vein. This is presumed to represent largely the uptake by the intestines, but the spleen may play a role. Smith and associates found the O2 content of portal vein blood in intact and splenectomized dogs not to differ significantly (15.51 volume per cent in intact, 14.12 volume per cent in splenectomized). However, the difference in portal oxygen saturation (72.06 per cent in intact, 65.02 per cent in splenectomized) was statistically significant.
General Data

Major emphasis is placed on 9 animals which survived for varying periods of time into the post-transfusion period. Average survival time was 4 hours, with all but 2 in the range 3½ to 6 hours. Two died at 68 and 97 min., respectively, after transfusion. Three others succumbed during hypotension, presumably of respiratory failure. Another animal, although surviving hypotension, had abnormally low portal vein flow throughout the experiment (averaging 88 ml./min. during the control) and was not included in the mean figures, although the trend of events paralleled the major group of animals. No explanation for the abnormally low flow in this animal was forthcoming.

Phasic Variations in Flow and Pressure

Segments of records from a representative experiment are presented in figure 2. Record A...
was taken during the control period, B during the 40 mm. Hg period of hypotension, specifically at 172 minutes. Records C and D were taken during the post-transfusion phase at 220 and 342 min. (For time sequence, see fig. 5).

Phasic variations are attributable to both cardiac and respiratory influences. These are best illustrated in the control record (A), in relation to a representative respiratory cycle (inspiration, lines 1–2; expiration, lines 2–3), based on the intrathoracic pressure variation (third tracing). This ranged between about −2 to −8 mm. Hg. During inspiration carotid blood pressure (first tracing) and hepatic vein pressure (second tracing) decreased by the approximate magnitude of the respiratory negative pressure variation. Portal venous pressure (fifth tracing) showed smaller but consistent variations of a different type. This was a small increase during inspiration, followed by an abrupt decrease during expiration, to return shortly to the initial resting level. Sometimes an initial tendency for it to decrease early in inspiration was noted, as in segment A. Hepatic artery flow decreased during inspiration, related to the fall in arterial pressure. Portal vein flow also characteristically declined during inspiration. This decrease was related to the brief increase in portal pressure.

It is our belief that descent of the diaphragm during inspiration compresses the liver momentarily and impedes briefly the portal flow. This explanation is strengthened by the fact that portal flow overshoots during the succeeding expiration. These effects are reproduced exactly by brief compression of the portal vein.

Vertical line 4, drawn through the peak of systole of a cardiac cycle late in the expiratory pause, serves for orientation of events ascribable to heart action. Variation in hepatic artery flow corresponded closely to arterial pressure variation, with a slight delay apparently resulting from the more rapid propagation of the pulse wave. (It will be noted that with the more rapid hepatic arterial inflow in segment C that this interval was reduced.) Portal flow manifested an interesting variation in flow referable to the cardiac cycle, with a peak occurring just after the systolic peak in hepatic artery flow. Hepatic venous pressure variations are undoubtedly distorted by cardiac impact on the recording cannula, but a negative variation is clearly discernible which is probably a negative variation of a retarded central venous pulse wave. Cardiac variations of the portal pulse recorded by very sensitive manometers have been described by Feil and Forward, but these were barely discernible in the present record with the manometric sensitivity employed.

The above respiratory variations persisted during severe hypotension (segment B), but cardiac variations were usually somewhat damped due to diminished stroke volume. Respiration was more rapid and shallower (fourth tracing), and the resting intrathoracic pressure had decreased to 6 mm. Hg. The increase in portal pressure with inspiration persisted. The apparent influence of respiration on portal flow had diminished but there was usually still a variation relative to total flow which had diminished severely.

Although carotid arterial pressure recovered to only 123/85 mm. Hg on transfusion, both hepatic artery flow and, particularly, portal vein flow were increased above control following transfusion (segment C, fig. 2). Hepatic artery flow showed marked systolic/diastolic variation, reflecting the greater pulse pressure and, presumably, increased stroke volume. Although not clear in this segment due to the coincidence of a 0-reference calibration, other portions of the record revealed persistence of the respiratory influence on portal flow, with decrement during inspiration, and exaltation of flow during expiration. Portal venous pressure (fifth tracing) had risen above the control value, as had the hepatic venous pressure.

Segment D illustrates the progressive phase of normovolemic shock. Both hepatic artery and portal vein flow were decreased compared to C. All pressures had receded, so that phasic variations had been damped, approaching the situation observed in B. Cardiac rate had accelerated to 194 beats/min. (control, 168), accounting for the small pulse pressure in the top tracing.
Mean trends in hemodynamics during standardized shock procedure. A. oligemic shock; B. normovolemic shock; P, venous pressure; P/F, ratio of arterial-hepatic venous pressure over total splanchnic blood flow (portal plus hepatic artery).

Hemodynamic Changes During Hemorrhagic Shock

These can best be discussed by consideration of figure 3 in which the mean trends for the 9 experiments have been summarized. The mean plot was carried only to 150 min. post-transfusion because of different survival times beyond this period. The degree of hemorrhage needed to precipitate the changes is shown by the bottom curve.

Changes in Pressure. Mean carotid arterial pressure changes appear in the upper curve. These were kept reasonably constant at the prescribed pressures during the hypovolemic phase. Upon transfusion, incomplete recovery of arterial pressure was the rule, the average being 96 mm. as compared to the control average of 128 mm. Hg. This was reasonably well maintained for about 2 hours, then began to decline by varying degrees in different animals.

Portal venous pressure averaged about 8 mm. Hg during control, diminished to 4.5 mm. following hemorrhage, then gradually returned to 6 mm.; on further hemorrhage to 40 mm. arterial pressure it decreased to 5 mm. Hg. Coincident with return of blood it was briefly elevated to an average of 12.5 mm., then declined to an average of 7 mm. later in the experiments.

Hepatic venous pressure during control averaged 2 mm. Hg. Following the initial hemorrhage it decreased to —2 mm., then to a minimal value of —3.2 mm. during the 40 mm. period. A transient increase to 1.5 mm. coincided with complete restoration of blood volume, but ultimately pressure stabilized at about 0. Although respiration is not portrayed in this figure, the hepatic venous pressure was observed to parallel closely the changes in intrathoracic pressure, as was made evident during consideration of figure 2. This pressure became more negative during hypotension. It is probable that the direct communication of the hepatic veins with the inferior vena cava at the level of the diaphragm accounted for the dependent relationship. The decrease in intrathoracic pressure was probably a reflection of the increased respiratory effort consequent to hemorrhage, manifested by increased rate and often increased depth of respiration. In addition, perhaps blood volume depletion in some manner altered the hydrostatic pressure relationships in the hepatic veins. One of the determinants of the pressure here should be the inferior vena cava pressure. This was found to decrease during hemorrhagic hypotension in another study.

Changes in Flow. Portal vein flow averaged 300 ml./min. during control. This decreased significantly \((p = <.01)\) to 127 ml./min. on hemorrhage to 60 mm., but then increased to 155 ml./min. as pressure was held at approximately this level for 90 min. On further hemorrhage to reduce arterial mean pressure to 40 mm., flow decreased to 100 ml./min. Portal flow increased markedly to an average of 470 ml./min. at 30 min. post-transfusion. This increase bordered on being statistically significant \((p = .064)\). Hyperemia persisted for 1 hour, 40 min. after the start of transfusion.

Hepatic artery flow was reduced from 175 ml./min. to 100 ml./min. \((p = <.01)\) by the initial hemorrhage, then increased to 130 ml./min. On further hemorrhage it was reduced to 71 ml./min. Following transfusion hepatic
artery flow returned to approximately control value.

Changes in Vascular Resistance. The control average splanchnic vascular resistance was 0.264 PRU (0.149–0.378). Its greatest increase was to 0.340 (0.213–0.655) following hemorrhage, but this increase proved not to be statistically significant (p = 0.2). There was some reduction of this resistance with maintained hypotension accounting for the slight improvement in flow during this interval. A comparable increase to 0.348 PRU was observed following the second hemorrhage (p = 0.3); this too was not maintained during the remainder of the 40 mm. period. A striking reduction of resistance was observed immediately after transfusion to 0.147 PRU (0.087–0.237), a highly significant change (p < 0.01). As can be seen in the figure, this reduced resistance persisted for a considerable time in the post-transfusion period, then reverted to near the control value at an average time of 2 hours and 40 min. after transfusion. However, this upward trend was not maintained, but actually later manifested a downward trend in the majority of the animals as they entered the terminal stage of shock. In 8 of the animals of this series splanchnic resistance was lower than control terminally, and the entire group averaged 0.180 PRU (0.079–0.306) (p = <0.01).

Territorial Vascular Resistance. Mesenteric bed and hepatic artery resistances generally paralleled total splanchnic resistance as described above during the 60 mm. period, but mesenteric resistance tended to decline somewhat during the 40 mm. period, while hepatic artery resistance generally increased somewhat further. This is shown in the representative experiment in figure 4. However, considering the group as a whole, variations did not prove to be statistically significant. After transfusion, mesenteric resistance decreased on the average to 58 per cent of the control average (p < .01), while hepatic artery resistance declined to 71 per cent (p < .01). During the final half-hour mesenteric resistance was 58 per cent of control (p < .01), but hepatic artery resistance was 87 per cent of control (p = .50).

![Figure 4](http://circres.ahajournals.org/)

**Fig. 4.** Representative experiment illustrating trends in regional splanchnic vascular resistance. A: oligemic shock; B: normovolemic shock. The lower curves of the figure show changes in hepatic artery resistance and mesenteric resistance. (The phasic segments shown in figure 2 were taken from this experiment.)
Although small in absolute magnitude, intrahepatic portal vein resistance showed the greatest change. It increased from 0.021 to 0.074 (p = .03) following the first hemorrhage, then to 0.123 (p < .01) following the second hemorrhage. On transfusion it returned to control (0.026), and averaged 0.048 terminally. The latter 2 values were not statistically significant.

The decrease in portal vein and hepatic artery flows following the initial hemorrhage was somewhat greater than the reduction in arterial pressure. Over the next hour there was some improvement in flow in the order of about 25 per cent. This appeared to be the result of remission of the initial increase in splanchnic vascular resistance. Partial recovery of flow after hemorrhage has been observed by others using dye removal technics, the extent of recovery of flow apparently depending on the severity of hemorrhage. It is important to note that the second hemorrhage to bring the animal to the approximate range of 40 mm. arterial pressure also did not incur a lasting increase in splanchnic resistance, and that at the end of this period the P/F ratio had returned approximately to the control average. Hence, continued vasoconstriction in response to hemorrhage was not seen under the present experimental conditions. Since the spleen, from other evidence, contracts, the apparent unresponsiveness of the intestinal vasculature is even more striking. This unresponsiveness was noted in an earlier study in which mesenteric artery flow was measured. Changes in hepatic artery vascular resistance were not generally significant, although in the previous series a greater tendency was noted for the hepatic artery resistance to increase, particularly during the 40 mm. Hg period. In the present series, intrahepatic portal vein resistance consistently increased to a highly significant degree. Although small in absolute magnitude, this operates in a low pressure system. Thus, increased resistance here contributed to the gradual increase in portal pressure noted here during hypotension by Wiggers, Opdyke and Johnson, and confirmed by others.

Following transfusion, the most striking observation was the large increase in portal vein flow resulting from markedly reduced vascular resistance. Since intrahepatic portal vein resistance had returned to the control value, this hyperemia was largely accountable for the significant increase in portal pressure that occurred concurrently. The site of mesenteric vascular dilatation is not precisely known, nor is the cause of the observed hyperemia understood. In the preceding study mesenteric artery resistance was found to be decreased during this phase. In addition, Alexander has noted a reduction in venoconstriction corresponding to this phase. During the intermediate phases of normovolemic shock, splanchnic vascular resistance was restored to approximately the control average. Of significance is the fact that terminally this resistance declined again. Similarly, venoconstriction declined terminally. The degree to which changes in venoconstriction participate in the over-all changes in splanchnic resistance is not known, but undoubtedly they are contributory. The liver does not participate in the terminal venoconstriction.

The possibility of a pyrogenic reaction was considered. Using rectal temperature as a criterion, this seemed unlikely. The average rectal temperature about 30 min. after transfusion, at a time when mesenteric vascular resistance was still markedly reduced, was 37.6 C. (36.3-30.7), compared to the average temperature of 38.5 during the 40 mm. period. In one instance an increase from 36 to 36.3 C. was noted.
SPLANCHNIC CIRCULATION IN HEMORRHAGIC SHOCK

Table 1.—Statistical Summary of 9 Experiments on Splanchnic Blood Flow and Oxygen Utilization During Hemorrhagic Shock

### Blood Flow* (ml./min.)

<table>
<thead>
<tr>
<th>Exp.</th>
<th>Control</th>
<th>Hypotension</th>
<th>Post-transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H.A. P.V.</td>
<td>H.A. P.V.</td>
<td>H.A. P.V.</td>
</tr>
<tr>
<td></td>
<td>60 mm.</td>
<td>40 mm.</td>
<td>1/4 hr.</td>
</tr>
<tr>
<td>Av.</td>
<td>175</td>
<td>309</td>
<td>110</td>
</tr>
<tr>
<td>S.E.</td>
<td>18.53</td>
<td>29.44</td>
<td>15.35</td>
</tr>
<tr>
<td>T</td>
<td>3.50</td>
<td>5.93</td>
<td>6.90</td>
</tr>
<tr>
<td>P</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

### A-V O2 Difference (vol./%)

<table>
<thead>
<tr>
<th>Exp.</th>
<th>Control</th>
<th>Hypotension</th>
<th>Post-transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A-P H</td>
<td>A-P H</td>
<td>A-P H</td>
</tr>
<tr>
<td></td>
<td>60 mm.</td>
<td>40 mm.</td>
<td>1/4 hr.</td>
</tr>
<tr>
<td>Av.</td>
<td>18.07</td>
<td>11.57</td>
<td>9.16</td>
</tr>
<tr>
<td>S.E.</td>
<td>0.985</td>
<td>0.810</td>
<td>1.154</td>
</tr>
<tr>
<td>T</td>
<td>2.21</td>
<td>7.35</td>
<td>5.13</td>
</tr>
<tr>
<td>P</td>
<td>0.06</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

### O2 Utilization (cc./min.)

<table>
<thead>
<tr>
<th>Exp.</th>
<th>Control</th>
<th>Hypotension</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mesent. Liver</td>
<td>Mesent. Liver</td>
<td>Mesent. Liver</td>
</tr>
<tr>
<td></td>
<td>60 mm.</td>
<td>40 mm.</td>
<td>1/4 hr.</td>
</tr>
<tr>
<td>Av.</td>
<td>10.00</td>
<td>24.15</td>
<td>12.68</td>
</tr>
<tr>
<td>S.E.</td>
<td>2.21</td>
<td>4.27</td>
<td>2.60</td>
</tr>
<tr>
<td>T</td>
<td>2.88</td>
<td>1.60</td>
<td>3.29</td>
</tr>
<tr>
<td>P</td>
<td>0.02</td>
<td>0.15</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

* Blood flow data represent half-hour averages of all readings taken during 15 minutes preceding and following the removal of blood samples for O2 utilization.
† Time given represents that after completion of transfusion.
‡ Mesenteric, or extrahepatic splanchnic O2 utilization, taken to be largely intestinal O2 consumption.


**Oxygen Utilization**

Mean trends of O2 A-V gradients in the splanchnic bed and O2 utilization are given in figure 5, and in table 1. No significant alteration occurred in arterial O2 content during the time interval indicated in the figure, but both portal vein and hepatic vein O2 content showed highly significant reduction in O2 content during the hypotensive period (p < .01), as the A-P A-V O2 difference increased from 6.50 to 10.28 (60 mm. Hg period) and 11.46 volume per cent (40 mm. period), and the A-H A-V O2 difference from 8.91 to 12.68 and 15.00 volume per cent respectively. At 1/4 hour and 1 1/2 hours after completion of transfusion, O2 content in the portal and hepatic vein was not significantly different from the control values. A-V O2 differences had restored to 3.79 and 5.60 volume per cent (A-P), and 7.06 and 9.05 volume per cent (A-H), respectively.

After 1 hour of the 60 mm. period mesenteric O2 utilization had decreased from 19.0 to 12.68 cc./min., a change bordering on significance (p = .02). During the 40 mm. period, utilization was further reduced to 10.46 cc./min. (p < .01). At these time intervals, liver utiliza-
tion had decreased from 24.15 cc./min. to 16.95 cc./min. (60 mm. period), but was not statistically significant \( p = 0.15 \). A significant reduction in utilization occurred during the 40 mm. period to 12.83 cc./min. \( p < .01 \). Following transfusion, liver \( O_2 \) utilization returned to approximately the control rate. Intestinal utilization remained reduced at about 14 cc./min., but this reduction proved not to be statistically significant \( p = 0.25 \) to 0.15).

Computations showed that during the control period the hepatic artery supplied 35.7 per cent (range, 24.7 to 52.3) of the total blood supply, and 70 per cent of the total \( O_2 \) supply (range, 34 to 100 per cent). Following hemorrhage, the proportion of blood supplied by the hepatic artery increased slightly to 44.9 per cent (34.7–60.6 per cent) 60 mm. period, and 41.6 per cent (16.6–60.0 per cent) 40 mm. period. Percentage \( O_2 \) supply increased to 80.44 per cent (52–100 per cent) 60 mm. period and 76.6 per cent (58–99 per cent) 40 mm. period, but statistical analysis indicated that these increases were probably not significant \( p = .05 \) and .20 respectively.

The portal vein became the more important source of \( O_2 \) supply in the immediate post-transfusion period as it supplied now an average of 70.5 per cent of the total liver blood flow (range 57.3–84.5 per cent, 1/2 hour post-transfusion), and 51.8 per cent of the total \( O_2 \) supply (range, 21–79 per cent), a significant change from the control \( p = <.01 \). At 1 1/2 hours post-transfusion, the proportion of blood supply and \( O_2 \) supply by the hepatic artery was not significantly different from the control averages (35.3 per cent of blood supply and 60.4 per cent of \( O_2 \) supply). Unfortunately, data are not available for the terminal stages of shock.

**DISCUSSION**

As stated, during control the hepatic artery supplied 70 per cent of the total \( O_2 \) to the liver. This compares with 37.5 per cent for the cat, while by contrast in the rabbit a relatively insignificant amount of \( O_2 \) is supplied to the liver by the portal vein because of greater intestinal utilization. Blalock and Mason found that in 5 dogs the hepatic artery \( O_2 \) supply was in the range of 22–38 per cent; in 2 other animals the hepatic artery supplied 38 and 62 per cent of the liver’s \( O_2 \). In their group the hepatic artery supplied only 18 per cent of the total liver blood supply, while in our series the hepatic artery supplied an average of 36 per cent, accounting for the greater prominence of its role in oxygen delivery to the liver. Portal flow averaged 374 ml./min., compared to our value of 309 ml./min. Portal vein oxygen content was very similar in both studies, 10.51 as compared to 11.57 volume per cent; but hepatic vein \( O_2 \) content was lower in Blalock and Mason’s group of dogs, 6.42 as compared to 9.16 volume per cent in the present series with arterial content of 16.13 as compared to 18.07 volume per cent respectively.

It is believed that continuous simultaneous measurement of hepatic artery and portal vein flow constitutes a more reliable method of measuring the respective flows than the technic employed by Blalock and Mason of brief occlusion of the hepatic artery to measure the differential flow, since the possibility exists that portal vein flow may be disturbed by manipulation of the hepatic artery. Nevertheless, it is important to note that the total oxygen supply to the liver by both portal vein and hepatic artery, irrespective of differing proportions, is almost the same in our control series, 24.15 cc./min., as Blalock and Mason’s average of 23.8 cc./min. Results expressed in terms of gram of liver weight are also very similar, .0445 (range, .021–.096) compared to .045 (range, .025–.065). Total splanchnic \( O_2 \) consumption averaged 2.01 cc./min./Kg. (range, 1.14–3.89). This compares with Hamrick and Myers’ combined control average of 2.12 cc./min./Kg. (range, 1.4–3.9).

The observation has been made by others that following hemorrhage increase in A-V \( O_2 \) across the splanchnic bed provides the liver with a reasonably constant supply of oxygen despite reduction in blood flow. In the present study, although A-V \( O_2 \) differences increased markedly, they did not appear to increase to the extent that the splanchnic blood flow was reduced, so that total splanchnic utilization decreased significantly during the 40 mm. period. Hamrick and Myers also ob-
served a reduction in splanchnic oxygen consumption in their group of "sustained shock" dogs, although it was unchanged in their "single hemorrhage" group. The cause of the reduction of oxygen consumption is not entirely known. Presumably when oxygen saturation of the venous blood reaches a low critical level, certain tissues in the splanchnic bed, particularly in areas where flow is markedly reduced, will have received blood in which the level of saturation is so low that no further oxygen extraction can occur. This explanation would appear reasonable in the present series, since hepatic venous $O_2$ content at the first observations during hypotension averaged 3.22 volume per cent, and was only 1.17 volume per cent or less in 4 animals of this group. During the 40 mm. period, hepatic venous content averaged 2.06 volume per cent.

It was noted that utilization was diminished in both the mesenteric (intestinal) tissues and in the liver in approximately equal proportions. Impaired $O_2$ utilization by an organ as metabolically important as the liver must have important significance in an understanding of the metabolic derangements of shock; the possible significance of reduced utilization by the extrahepatic components of the splanchnic bed (e.g., the intestine) is presently obscure.

The important problem of establishing a causal relationship between hypoxic states of the liver and intestine to the alterations in splanchnic hemodynamics remains. Two tentative links are herewith proposed: (A) The hypoxic liver may release vasodepressor substance(s), a "washout" phenomenon may account for the marked hyperemia following transfusion; and (B) based on unpublished observations which showed that intestinal ischemia produced a hyperemic response of its vasculature, it is possible that the hypoxia of the intestine during hemorrhagic hypotension creates a similar response. Neurogenic mechanisms appear to supervene during the compensated phase of normovolemic shock, but these do not persist, and a final reduction of splanchnic vascular resistance signals the demise of the animal.

**Summary**

Phasic and mean variations of flow and pressure in the portal vein and hepatic artery were studied during the course of standardized hemorrhagic shock in dogs. Phasic variations related both to respiration and the cardiac cycle were discerned. These were characteristically modified during hemorrhage.

Mean portal vein flow averaged 309 ml./min., and hepatic artery flow 175 ml./min. during the control observations. These diminished to 100 and 71 ml./min. respectively during the period of lowest mean blood pressure. On transfusion, portal flow exceeded control to attain a peak average flow of 470 ml./min. at 20 min. after completion of transfusion. A marked increase in portal vein pressure was associated with the mesenteric hyperemia. Hepatic artery flow was restored to the control average. Terminally, hepatic artery flow decreased more than portal vein flow.

Splanchnic vascular resistance did not increase significantly during hemorrhagic hypotension. Following transfusion there was a marked reduction in splanchnic vascular resistance. After partial restoration during the compensated phase of normovolemic shock it declined again, leading to the final collapse. In the terminal phase reduced splanchnic vascular resistance was largely the result of reduced resistance in the mesenteric (intestinal) vasculature. Hepatic vascular resistance did not change significantly terminally.

Hepatic oxygen utilization averaged 24.15 cc./min., and mesenteric (intestinal) 19.0 cc./min. during control. Both declined during hemorrhagic hypotension, reaching significantly low values during the period of drastic hypotension, 12.83 cc./min. for liver, and 10.46 cc./min. for mesenteric utilization. On transfusion, liver utilization returned to normal, but mesenteric only to 74 per cent of control.

It is concluded that hemorrhagic hypotension of the degree and duration employed in these experiments is capable of causing significant impairment of the mechanisms for oxygen utilization of both the liver and mesenteric bed. Final mechanisms are not known, but
it is suggested that this may be a key mechanism accountable for the observed inadequate or incomplete vascular compensation during hypotension and the ultimate failure terminating normovolemic shock.

**Summary in Interlingua**

Variationes phasic e medie del fluxo e del pression in le vena portal e le arteria hepatic esseva studiate in le curso de standardisate choc hemorrhagic in canes. Variationes phasic relationate al respiracion e al cyclo cardiac esseva discernibile. Illos esseva modificate characteristicemente durante le hemorrhagia.

Le fluxo medie intraindividual del vena portal amontava a un nivello medie interindividual de 309 ml/min in le observationes de controlo. Le correspondente valor pro le fluxo del arteria hepatic esseva 175 ml/min. Iste nivello descendeva a 100 e 71 ml/min durante le periodo del plus basse pression medie del sanguine. Post transfusion, le fluxo portal exceedeva le nivello de controlo. Illo attingeva un maximal fluxo medie de 470 ml/min 20 minutas post le completion del transfusion. Un marcate augmento del pression in le vena portal esseva associate con le hyperemia mesenteric. Le fluxo del arteria hepatic esseva restaurate al nivello medie del observationes de controlo. Terminalmente, le fluxo del arteria hepatic decreceseva plus que le fluxo del vena portal.

Le splanchnic resistentia vascular non montava significative durante le hypotension hemorrhagic. Post le transfusion il occurreva un marcate reduction del splanchnic resistentia vascular. Post un restauration partial durante le phase compensate del choc normovolemic, illo redescendeva ante le col-lapso final. Durante le phase terminal, un reduceite splanchnic resistentia vascular esseva in grande mesura le resultato del reduceite resistentia in le vasculatura mesenteric (intestinal). Le hepatic resistentia vascular non exhibiva un significative alteration terminal.

Le utilisation hepatic de oxygeno amontava durante le periodo de controlo a un nivello medie de 24,15 cm³/min. Le correspondente nivello mesenteric (intestinal) esseva 19,0 cm³/min. Ambie iste valores descendeva du-

**REFERENCES**

vascular circuits during hemorrhagic shock.

Avitaminosis A and Experimental Hydrocephalus

Progress in the treatment of human afflictions has been achieved through their reproduction in experimental animals. In the repair of congenital defects this has been possible by surgical creations of lesions similar to those arising from congenital causes. In a recent editorial (Circulation 4: 511, 1956) the congenital defects following dietary deficiencies in animals were reviewed and the importance of such experiments in the prevention of congenital defects of the heart and large vessels in the human new-born was stressed.

Attention is called in a recent paper to the fact that it has now proved possible to produce nearly 100 per cent hydrocephalic offspring in rabbits if avitaminosis A is induced in the mother 20 weeks before mating. "Until this technique for producing hydrocephalus was discovered, the only available method for providing animals with hydrocephalus for the study of possible therapeutic measures for the condition, was by tedious surgical intervention of doubtful validity."

Splanchnic Hemodynamics and Oxygen Utilization During Hemorrhagic Shock in the Dog

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