Effect of Hemorrhage on Hepatic Blood Flow
Determined by Radioactive Colloidal Chronic Phosphate Removal

By Cheves McC. Smythe, M.D.

In a group of 18 anesthetized dogs hepatic blood flow measured by the BSP removal technique of Bradley and the radioactive colloidal chronic phosphate disappearance method of Dobson gave comparable results of 38.7 and 38.3 ml./Kg./min. respectively. In response to acute hemorrhage of 25 ml./Kg., hepatic blood flow fell from 42.3 to 35.4 ml./Kg. A more severe hemorrhage of 33 ml./Kg. produced a more profound decrease of hepatic blood flow, from 43.4 to 20.5 ml./Kg./min.

With indirect methods of measuring hepatic blood flow (HBF) dependent upon catheterization of the hepatic veins,1 hepatic venous outflow has been determined in man and dogs under a number of conditions including experimental hemorrhage.2,3 Other approaches dependent upon radioactive colloidal removal rates, which are technically simpler, have been introduced.4

A comparison of HBF, determined by the bromsulfalein (BSP) removal method of Bradley4 and determined by the radioactive colloidal chronic phosphate (RCCP) disappearance method of Dobson,4 has been made in animals at rest. The response of HBF to hemorrhage has been extensively described.2,3 Changes in RCCP following hemorrhage were also studied, and the results were compared with previously published data.

Methods

General. Fasting mongrel dogs were anesthetized with sodium pentobarbital, 25 to 30 mg./Kg. intravenously. A femoral artery, a peripheral vein, and a jugular vein were cannulated. Arterial pressure was measured with a capacitance electromanometer and recorded with an oscillograph. The method of determining HBF by BSP removal has been previously described.5 Most of the figures for HBF determined by the BSP method are means of two, three, or four determinations of HBF over eight minute periods. The figures for HBF determined by the RCCP removal method are each based on a single disappearance curve. No BSP determinations were made after hemorrhage because of spectrophotometric interference between BSP and T 1824.

Blood Volume. Plasma volume was determined by measuring T 1824 dilution in a single plasma sample taken at 10 minutes.0 There was no interpolation to zero time. The observed hematocrit was multiplied by 0.90 to correct for total body hematocrit and trapped plasma when blood volume was calculated from plasma volume. The single sample taken at 10 minutes without interpolation may result in artificially high figures for blood volume.

RCCP Method. Eight to 12 mc. of P32 labeled chronic phosphate were given intravenously in 0.4 to 1.5 ml. of solution. Samples were drawn from the femoral artery at 1 minute intervals (stop watch) beginning 2 minutes after the injection for a period of 10 to 15 minutes. Two ml. aliquots of whole blood were pipetted into standard-sized paper planchettes and counted with an end window GM counter. This method of counting has a mean error of ± 3.69 per cent. Net counts were plotted semilogarithmically against time, and the best slope was fitted visually. No effort was made to plot the terminal portions of the disappearance curves when this portion did not fit the initial slope, or to subtract such terminal portions from the initial slopes. This was because this slope has been shown to be determined by disappearance rates of small particles and to be unrelated to HBF.2

Hemorrhage. All the required blood samples necessitated a base line blood loss of 8 ml./Kg. (average). After determination of HBF by the two methods, the animals were bled neutely by syringe to a mean of 17 ml./Kg. in addition or a total hemorrhage of 25 ml./Kg. Immediately
following this, plasma volume (T 1824) and HBF by the RCCP method were redetermined.

Another group of animals was bled acutely by syringe to a mean arterial pressure of 40 mm Hg, and maintained at this level for 30 minutes by removing or infusing small aliquots of blood. A mean of 25 ml./Kg. (total of 33 ml./Kg.) of blood was removed to create and maintain this period of hypotension. At the end of 30 minutes HBF and plasma volume were measured.

RESULTS

During the resting or control periods, the figures for HBF determined simultaneously by the two methods were almost identical (table 1). In 18 animals, mean RCCP flow was 38.3 ml./Kg./min. with a range of 52.8 to 25.2 ml./Kg./min. The BSP method in the same 18 animals at the same time gave a mean figure of 38.7 ml./Kg./min. with a range of 67.7 to 17.3 ml./Kg./min. The ratio of RCCP flow to BSP flow was 1.05 with a range of 1.60 to 0.56. In only 6 instances of 18 did the ratio diverge more than 0.20 from unity. The mean disappearance half time in these animals was 1.6 minutes. This closely approximates Dobson’s figure of 1.5 minutes for half time of RCCP removal in dogs.7

In 10 animals, samples from an hepatic vein, obtained less than 5 minutes after the RCCP injection, were counted. Extraction ranged from 52 to 98 per cent. In 2 animals, bleeding produced no change of extraction percentage.

In response to a hemorrhage of 25 ml./Kg., 10 animals showed only a slight increase in half time from 1.6 to 1.9 minutes (table 2). Measured blood volume usually fell only about one half the total volume of shed blood. The hematocrit rose 5 per cent in response to these acute hemorrhages. The animals had not been splenectomized. Hence there was a small change of hepatic blood flow of from 42.3 to 35.4 ml./Kg./min. This change is not statistically significant.

In the 4 animals bled to a mean pressure of 40 mm Hg (35 ml./Kg.), half time increased from 1.4 to 2.4 minutes (table 3), and flow fell from 43.4 to 20.8 ml./Kg./min. In these animals, measured blood volume fell 70 per cent of the amount of shed blood. Hematocrit fell 2 per cent.

### Table 1.—Comparison of Hepatic Blood Flow Simultaneously Measured by BSP and RCCP Removal Methods in 18 Dogs

<table>
<thead>
<tr>
<th>Blood flow</th>
<th>Blood flow</th>
<th>Ratio, Cr Pm / CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half time (min.)</td>
<td>38.3</td>
<td>38.7</td>
</tr>
<tr>
<td>Range</td>
<td>52.8—25.2</td>
<td>67.7—17.3</td>
</tr>
</tbody>
</table>

### Table 2.—Response of HBF to Acute Hemorrhage in 10 Dogs

<table>
<thead>
<tr>
<th>Half time (min.)</th>
<th>Pre-bleeding</th>
<th>Post-bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.6</td>
<td>1.9</td>
</tr>
<tr>
<td>S.D.</td>
<td>±0.34</td>
<td>±0.34</td>
</tr>
<tr>
<td>Range</td>
<td>1.2—2.3</td>
<td>1.2—2.7</td>
</tr>
</tbody>
</table>

### Table 3.—Response to HBF to Severe Hemorrhage in 4 Dogs

<table>
<thead>
<tr>
<th>Half time (min.)</th>
<th>Pre-bleeding</th>
<th>Post-bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.4</td>
<td>2.4</td>
</tr>
<tr>
<td>S.D.</td>
<td>±0.23</td>
<td>±0.29</td>
</tr>
<tr>
<td>Range</td>
<td>1.2—1.8</td>
<td>2.0—2.8</td>
</tr>
</tbody>
</table>

### DISCUSSION

This study was undertaken to compare hepatic blood flow determined by BSP and radio colloidal removal rates. The figures of 38.7 ml./Kg./min. for BSP removal and 38.3 ml./Kg./min. for RCCP disappearance agree with each other and with already published data.2, 3, 7, 8 The great variation from animal to animal found in these experiments has been noted by all observers of hepatic hemodynamics, and is caused not only by the crudeness of the methods, but by the very real variations of hepatic blood flow which occur from moment to moment.9

The response of RCCP disappearance to hemorrhage was deliberately chosen to investigate the manner in which such curves responded to major physiologic changes before investigation of subtler phenomena was undertaken. The decrease of flow demonstrated by RCCP method in the first group of experiments was not as large as previously reported.2, 3 Dobson has also reported no change of half time or hence of removal constant in
response to hemorrhage. He points out that this is to be expected, since bleeding decreases blood volume in roughly the same proportion as it does flow, so that the fraction of colloid removed per minute remains the same. Hamrick and Myers have found a correlation between volume of blood shed and decrease of flow. This is a surprising observation, since, in other vascular beds, changes of flow in response to contraction of blood volume have been considered dependent upon vasomotion or selective shunting of effective circulating blood volume to or away from a given organ, rather than upon simple intravascular blood volume changes. Renal blood flow is notoriously sensitive to relatively small stimuli. The decrease of flow demonstrated in the second group of experiments is to about half of the control figure, which is of the order reported by other observers. In addition to the quantitative data that have indicated a decrease of HBF in response to hemorrhage, there is the qualitative observation that blood is obtained from the hepatic venous catheter with great difficulty and that the blood so obtained is grossly unsaturated for oxygen in the dog that has been bled. These observations suggest slowed hepatic perfusion.

Escape of the colloid into the hepatic vein because of failure of extraction or because of rapid shunting of blood through large vascular channels cannot be assumed to be the reason behind the small alterations of RCCP disappearance curves in response to hemorrhage. Such escape would result in a less steep slope rather than in an unexpectedly steep one. Brauer has demonstrated decreased extraction of colloid by the slowly perfused liver, which he has implied is a consequence of selective shunting of blood through the liver. Knisely has demonstrated such selective shunting. No explanation for the lack of change of RCCP disappearance rates is apparent, save that advanced by Dobson. Another possibility is that, although closely related to hepatic blood flow, RCCP disappearance rates are not solely dependent upon this. The avidity of littoral cells for the material may be so great that removal, although largely dependent upon blood flow, certainly as far as upper limits go, may vary independently of it.

Summary

Hepatic blood flow simultaneously determined by the bromsulfalein removal method of Bradley and the radioactive colloidal chromic phosphate disappearance method of Dobson in 18 anesthetized dogs averaged 38.7 and 38.3 ml/Kg/min, respectively. The mean half time for radioactive colloidal chromic phosphate disappearance slope was 1.6 min.

In response to an acute hemorrhage of 25 ml/Kg., hepatic blood fell from 42.3 to 35.4 ml/Kg/min. by the radioactive colloidal chromic phosphate method in a group of 10 dogs. This change is not statistically significant. Half time increased from 1.6 to 1.9 min. in these animals.

Arterial hypotension at a level of 40 mm. Hg for 30 min. induced by hemorrhage (mean 33 ml/Kg.) was followed by a decrease of hepatic blood flow from 43.4 to 20.8 ml/Kg/min. by the radioactive colloidal chromic phosphate method in 4 dogs. Half time increased from 1.4 to 2.4 min.

Radiocolloidal disappearance rates may depend upon other variables than hepatic blood flow.

Acknowledgment

These data could not have been collected without the technical assistance of James Holler, Newton Brackett, and Anna Chrisanthis.

Summary in Interlingua

Le fluxo de sanguine hepatic in dece-octo canes in stato anesthesiate, determinate simul- tanemente secundo le metodo a elimination bromsulfaleina de Bradley e secundo le meth- odo a elimination de radioactive phosphato chromic colloidal de Dobson, amontava al valores medie de 38.7 e 38.3 ml/kg/min, respectivamente. Le valor medie pro le periodo de medie valor del inclination in le curva de disparition de radioactive phosphato chromic colloidal esseva 1,6 min.

In responsa a un acute hemorrhagia de 25 ml/kg, le fluxo de sanguine hepatic descende- va ab 42,3 a 35,4 ml/kg/min, secundo le me-
EFFECT OF HEMORRHAGE ON HEPATIC BLOOD FLOW

thodo a radioactive phosphato chromic colloidal in un experimento con un grupo de dece canes. Le periodo de medie valor ascendeva in iste animales ab 1,6 a 1,9 min.

Hypotension arterial al nivello de 40 mm de Hg, inducite per hemorrhagia (amontante a un valor medie de 33 ml/kg) e mantenite durante 30 min, esseva sequite per un reduction del fluxo de sanguine hepatic ab 43,4 a 20,8 ml/kg/min, secundo le metodo a phosphato chromic colloidal in un experimento con quatro canes. Le periodo de medie valor mon-tava ab 1,4 a 2,4 min.

Il es possibile que le valores obtenite in observationes del disparition radiocolloidal depende de variables altere que le fluxo de sanguine hepatic.

REFERENCES

Effect of Hemorrhage on Hepatic Blood Flow Determined by Radioactive Colloidal Chromic Phosphate Removal
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