Oxygen Saturation of Hepatic Blood During Hemorrhagic Shock in the Dog

By James J. Smith, M.D., Ph.D., Donald A. Roth, Ph.D., M.D., and Robert A. Grace, M.S.

During experimental hemorrhagic shock there was a large fall in oxygen saturation of portal, hepatic venous and inferior vena caval blood. Saturation levels were restored to about 90 per cent of the control values after reinfusion of the drawn blood.

Since the work of Frank, Seligman and Fine and Shorr on the relationship of hepatic anoxia to the development of irreversible shock, increasing attention has been given to possible methods of further exploring this problem. A logical step would be to determine, if possible, just what degree of hepatic anoxia actually prevails during the shock state. This would enable a correlation of the oxygen lack in this organ with the circulatory and metabolic failure that develops.

To obtain accurate values for oxygen consumed by the liver, it is necessary to measure volume flow and oxygen gradients through both the portal vein and hepatic artery. Because of the technical difficulties involved in direct flow experiments it is necessary to study the problem fragmentally. Selkurt, Alexander and Patterson found that during hemorrhagic shock in the dog mesenteric venous flow fell very sharply to about one quarter of its previous value. Upon reinfusion the flow was rapidly restored to its pre-hemorrhagic level from whence it gradually declined.

Recently, other workers using the dye method have measured total hepatic blood flow and splanchnic oxygen consumption during hemorrhagic shock. Hamrick and co-workers reported that after a single massive hemorrhage and with the blood pressure at an experimental mean of 67 mm. Hg, total hepatic blood flow fell to about 40 per cent of its control value. There was an increase in arterial-hepatic venous oxygen gradient but large parallel falls in total oxygen consumption and splanchnic oxygen consumption.

The purpose of the present study was to measure blood oxygen gradients across the liver during and following a controlled hemorrhagic procedure in the dog in an attempt to obtain additional information on the state of oxygenation of the liver during shock.

**Method**

Mongrel dogs were anesthetized with sodium barbital (175 mg./kg.) given 30 minutes after a subcutaneous injection of morphine sulfate (3 mg./kg.). Two cardiac catheters were passed via the right jugular vein, one into an hepatic vein, the other into the inferior vena cava just below the level of the diaphragm. One femoral artery was connected for bleeding purposes to an inverted reservoir bottle containing anticoagulant.* Arterial pressure was recorded with a damped mercury manometer.

The abdomen was opened through a midline incision under clean but not sterile conditions. A polyethylene catheter of appropriate size was passed into the portal vein to the level of the liver hilum through a slightly curved thin walled 18 or 14 needle and tied into the vein wall. The catheter was led out through the midline incision and the abdominal wound closed tightly around the catheter in two layers. After a recovery period of one to two hours control blood samples were drawn and the animal bled into the reservoir at a rate of 50 cc. per minute. Wiggers' standard method of bleeding was modified as suggested by Glasser and Page. The blood pressure level was maintained at 60 mm. Hg for 90 minutes and for 40 mm Hg for 45 minutes as suggested by Selkurt (8). Following this, all the drawn blood was reinfused intra-arterially.

* Treburon (RO 3053) supplied through courtesy of Hoffman-LaRoche Co.
Table 1.—Survival Time of Animals in Hours post-Infusion

<table>
<thead>
<tr>
<th>No. of Animals</th>
<th>Hours Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>0 to 6</td>
</tr>
<tr>
<td>4</td>
<td>6 to 12</td>
</tr>
<tr>
<td>4</td>
<td>12 to 24</td>
</tr>
<tr>
<td>1</td>
<td>recovered</td>
</tr>
</tbody>
</table>

All glassware was siliconized.* Blood samples were taken from the femoral artery, portal vein, hepatic vein and inferior vena cava before, during and after the hemorrhaging. Blood was drawn into oiled syringes containing Treburon anticoagulant. Blood oxygen content was determined by the manometric method of Van Slyke and oxygen capacity by the method of Roughton et al. Duplicate determinations were run on each sample. All four blood samples were drawn as nearly simultaneously as possible before bleeding was begun, approximately midway in the 60 mm. bleeding period, approximately midway in the 40 mm. bleeding period, from one to two hours after reinfusion and approximately three to four hours after reinfusion. Animals were observed closely for at least six hours post-infusion.

In dogs surviving this period, the position of the cardiac catheters were rechecked by fluoroscopy and the cardiac catheters removed. The portal catheter was then sealed and sewn into the subcutaneous tissue over the abdomen. The groin wounds were closed, 50 mg. protamine sulfate and 100,000 units penicillin injected intravenously, and the animal returned to its cage. Fourteen of the 20 animals died within six hours post-infusion and in all of these the position of the catheters was verified at autopsy. Those animals in which there was any question of positioning of the catheters or in which there were any unusual surgical or technical difficulties were eliminated from the analysis.

RESULTS

A summary of the results of oxygen saturation determinations is presented in table 2. Also included in this summary are the oxyhemoglobin capacities, mean arterial blood pressure and heart rate values. All of these determinations were grouped and averaged for the different periods of the shock experiment.

The arterial saturation showed a numerically small but significant fall during the 60 mm. period. Most marked, however, was the sharp drop in oxygen saturation of portal, hepatic venous and vena caval blood as soon as bleeding was begun. There was a small additional drop during the 40 mm. bleeding period and a rapid recovery after reinfusion. These mean values are depicted graphically against a time abscissa in figure 1. The running record of saturation values shown in figure 1 was the practically invariable pattern of all the experiments. In some animals the portal saturations were as low as six to eight per cent and the hepatic venous two to three per cent. The portal saturation was, however, always the greater. Analysis of individual experiments and correlation of each of these variables with survival revealed no significant statistical relationship. The dogs which showed the lowest portal and hepatic venous saturations often survived longer.

Table 3 presents a summary of the oxyhemoglobin saturation gradients of the liver. During the control periods the arterial-portal (A-P) gradients were approximately equal to the portal-hepatic venous (P-Hv) gradients; the former became much greater during the bleeding periods because of the relative stability of the arterial saturation level. Analysis of these gradients and survival times again failed to reveal any consistent association.

At post mortem all the animals except three showed moderate to marked hemorrhages into the mesentery, omentum and upper small intestine. In some the congestion and hemorrhagic areas were most marked on the serosal surface of the intestine, mesentery and omentum with minimal mucosal changes. In the majority however this was reversed and the outstanding changes were found on the mucosal surface of the duodenum with, in

* General Electric Co., Dri-Film SC-87.
HEPATIC BLOOD OXYGEN IN SHOCK

TABLE 2.—Mean Oxygen Saturation Values at Various Periods in Standard Hemorrhagic Shock

<table>
<thead>
<tr>
<th>Arterial Blood Pressure</th>
<th>Control Values</th>
<th>60 mm Hg Bleeding Period</th>
<th>40 mm Hg Bleeding Period</th>
<th>0 to 2 Hrs. Post-Infusion</th>
<th>2 to 6 Hrs. Post-Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>mm Hg</td>
<td></td>
<td>110.2 ± 14.2</td>
<td>90.</td>
<td>96.7 ± 19.7</td>
<td>86.2 ± 26.2</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>161. ± 33</td>
<td>179 ± 45</td>
<td>171. ± 33</td>
<td>176 ± 36</td>
<td>180 ± 28</td>
</tr>
<tr>
<td>Arterial Sat. (%)</td>
<td>89.5 ± 4.4</td>
<td>89.2 ± 4.0</td>
<td>85.2 ± 3.0</td>
<td>84.4 ± 12.0</td>
<td>92.6 ± 3.1</td>
</tr>
<tr>
<td>Portal Sat. (%)</td>
<td>71.6 ± 7.6</td>
<td>30.7 ± 18.1</td>
<td>26.4 ± 14.6</td>
<td>58.1 ± 22.2</td>
<td>64.5 ± 13.9</td>
</tr>
<tr>
<td>Hepatic Ven. Sat. (%)</td>
<td>55.9 ± 11.6</td>
<td>12.8 ± 11.0</td>
<td>6.4 ± 8.1</td>
<td>48.0 ± 22.8</td>
<td>32.4 ± 18.3</td>
</tr>
<tr>
<td>Inf. Vena Cava Sat. (%)</td>
<td>62.5 ± 12.9</td>
<td>19.4 ± 17.7</td>
<td>15.5 ± 13.5</td>
<td>55.8 ± 14.7</td>
<td>46.7 ± 12.4</td>
</tr>
<tr>
<td>HbO₂ Capa. (vol. %)</td>
<td>20.02 ± 3.27</td>
<td>17.92 ± 3.81</td>
<td>16.84 ± 4.04</td>
<td>17.57 ± 2.37</td>
<td>18.17 ± 2.76</td>
</tr>
</tbody>
</table>

It has been commonly noted in experimental shock that the arterial saturation remains high until shortly before death when it decreases markedly along with the blood pressure. The smaller decrease in saturation during the critical stage of hemorrhagic shock may have been masked, however, by the recovery in arterial oxygen saturation which occurs after reinfusion. Although the decrease in arterial saturation during the 40 mm. period is relatively small, it occurs at a critical stage of very severe generalized anoxia.

The precipitous fall in portal and hepatic venous oxygen saturations during the bleeding periods of the shock procedure are of the same order of magnitude observed in the rat by Engel and coworkers⁹ and in the cat and the rabbit by McMichael.¹⁰ Both of these investigators observed a high correlation between arterial blood pressure and portal oxygen saturation.

Since the P-Hv gradient during the control and 40 mm. period were comparable and Selkurt³ using a similar experimental method found that the portal blood flow decreased to about one-fourth during the 40 mm. period, it would seem that in deep shock portal oxygen supply is reduced in proportion to blood flow. The elevated A-Hv gradient during this same

![Fig. 1. Oxygen saturation of hepatic blood during hemorrhagic shock.](image)

FIG. 1. Oxygen saturation of hepatic blood during hemorrhagic shock.

Many instances, bloody fluid in the lumen of the small intestine.

**DISCUSSION**

The mortality rate, bleeding volumes and pathological changes in the present group of animals are quite comparable to the findings of other investigators who have used Wiggers' method for the production of hemorrhagic shock.

The decrease in arterial oxygen saturation during the drastic 40 mm. hypotensive period from a mean value of 89.52 per cent to 85.15 per cent was statistically significant (p < 0.02).
period would seem to indicate a greatly increased dependence of the liver on hepatic arterial blood during the hypotensive period.

The equivalence of A-P and P-Hv gradients in the control period indicates that of the oxygen given up by the splanchnic arteries feeding the portal vein, about half goes to the liver and half to extra-hepatic tissue. The large increase of A-P gradient during the bleeding periods is undoubtedly due to the greatly diminished flow throughout the mesenteric bed. The consequence to the liver is, of course, severe temporary reduction of oxygen from the portal vein.

SUMMARY AND CONCLUSIONS

Nineteen of the 20 dogs submitted to standardized hemorrhagic shock died within 24 hours after reinfusion. All showed hemodynamic and pathological changes comparable to those found by other investigators who used this method of producing experimental shock.

Mean arterial-portal and portal-hepatic venous oxygen gradients were about equal during the control periods indicating about equal extraction of portal oxygen by the liver and extrahepatic splanchnic organs.

During the period of drastic hypotension, the reduction of blood flow through the splanchnic arteries results in an increased extraction of oxygen from the mesenteric blood by the extrahepatic abdominal organs as manifested by greatly increased arterial-portal oxygen saturation gradients. This results in a severe curtailment of the portal oxygen supply to the liver during the hypotensive periods of experimental hemorrhagic shock and an increasing dependence of the liver on hepatic arterial blood for its oxygen during this period.

REFERENCES

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