Effect of Tourniquet Shock and Acute Hemorrhage on the Circulation of Various Organs in the Rat

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Changes in cardiac output and the circulatory responses of certain organs to various forms of stagnant hypoxia (hemorrhage, shock, dehydration, etc.) have been studied by many investigators, including Wiggers,1 Gomori and Takács,2 and Sapirstein, Sapirstein, and Bredemeyer.3 It has been gradually accepted that blood flow in various organs does not change uniformly; compared to the limited change in coronary and cerebral blood flow, the renal blood flow is severely affected. In earlier experiments, Gomori et al., Takács, and Kállay have studied the cardiac output and circulatory response of the heart,4 kidneys,5-8 and of the extremities,9 in shock, dehydration, and arterial hypoxia in dogs. Having observed a similar shifting in the distribution of cardiac output (increase of the coronary fraction and decrease of the fractions of the kidneys and of the extremities), both in "hypovolemic" hypoxia (low cardiac output) and in "hypervolemic" (arterial) hypoxia with high cardiac output, we have assumed that the same factor, namely, hypoxia of the tissues, may be responsible for the changes involved.

Experimental methods used in the past were not suited for measuring the circulation of several organs simultaneously. In the above-mentioned states, most authors measured only the blood flow and vascular resistance of the organs and neglected the simultaneous determination of cardiac output. Thus, they failed to point out the changes in the distribution of reduced cardiac output.

Some years ago, Sapirstein10,11 described an "indicator fractionation" method using first K42 and later Rb86. This method offers a possibility of measuring simultaneously the fractionation of cardiac output among all organs except the brain,12 because the K42 and Rb86 extraction ratios of all organs other than the brain are virtually the same as those of the whole body during the period of the experiment. As the isotope injected is diluted in the total cardiac output, the quantity of the isotope accumulating in the various organs is proportional to their fraction of the cardiac output. Determination of cardiac output and blood pressure then makes possible the calculation of the blood flow and the vascular resistance of the organs.

Sapirstein investigated with K42 the circulation of rats after "mild" (10 ml./Kg.) and "moderate" (21 to 25 ml./Kg.) bleeding.13 After repeating Sapirstein's experiments with Rb86, we studied the effects of more severe hemorrhage and of tourniquet shock on the circulation in rats.14 Regarding the effect of moderate hemorrhage, our results with K4213 and Rb863 show close agreement with his.

Methods

Essentially, we followed Sapirstein's method.11 Seventy-one male rats, weighing 140 to 280 Gm. and fasted for 18 to 24 hours, were used. The animals were anesthetized with 40 mg./Kg. sodium pentobarbital intraperitoneally (I.P.), as we had found that this drug is better suited for the actual purpose in the rat than urethane or chloralose.15

Tourniquet shock was produced by ligation of both hind legs with a rubber band for three hours in unanesthetized rats. Circulatory studies were begun one to two-and-a-half hours after the removal of the ligation and after giving sodium-pentobarbital I.P.
Two bleeding groups were set up: from one group an average of 23 (20 to 26 ml./Kg.) and from the other an average of 32 ml./Kg. (27 to 39 ml./Kg.) blood were withdrawn through a catheter in the carotid artery. Measurements were taken 5 to 20 minutes after hemorrhage.

Blood pressure was measured in the carotid artery with membrane manometer, Vorsatz-Kállay. Coagulation of the blood was prevented by injecting 2.5 mg. heparin in 0.2 ml. of saline into the tail vein. Cardiac output was determined with Evans blue dilution: 0.5 ml. 1.5 per cent dye solution was injected into the femoral vein and blood samples were taken from the carotid artery with the Kállay-Vorsatz type fractionating blood collector at 0.66-second intervals from the controls and at one- and two-second intervals from the shocked and bled groups, respectively. Dye concentration was measured in 20 μl. blood diluted with physiological saline to 3.0 ml. A Beckman B spectrophotometer, set at 590 m/μ, was used.

The cardiac output fractions of the various organs were determined by the injection of 5 to 10 μc. Rb86 CI in 0.5 ml. physiological NaCl solution into the femoral vein. The animals were sacrificed after 70 to 80 seconds (those subjected to severe hemorrhage after 120 seconds) by injecting 0.5 ml. saturated KCl into the tail vein. The experiment thus proceeded as follows: anesthesia, measuring of blood pressure, administration of Rb86 Cl, and, after 5 to 60 seconds determination of cardiac output, sacrifice. The organs were then dissolved in a 20 per cent KOH solution, and the radioactivity of the samples was measured with a Geiger-Müller tube.

Having thus obtained values for the cardiac output and measured the weight of the organs, we calculated the blood flow of each organ. Circulatory resistance of the whole body and of the organs were calculated from the cardiac output or blood flow and arterial blood pressure (taking venous pressures as 0) and were expressed in dynes/sec./cm2. Flow and resistance values were calculated for 100-Gm. organ weight.

**Statistical Analysis**

As the within-sample variances proved to be practically equal (Bartlett's test), the standard deviations were computed from the pooled sum-of-squares. Although in a few cases this pooling was not entirely legitimate, it was used in order to compile a uniform and synoptical table, as it did not materially affect the results. The data were tested by the Student's t.

**Results and Discussion**

The results are summarized in table 1.

The average cardiac output of control animals was 28.6 ml./100 Gm., which is somewhat higher than Sapirstein's value (23.1). The mean value of blood pressure was 120 mm. Hg; mean resistance was 336 × 103 dynes/sec./cm2.

The mean value of cardiac output in tourniquet shock was 10.1 ml./100 Gm., while blood pressure decreased to an average level of 50 mm. Hg. The corresponding mean resistance was 407 × 103 dynes/sec./cm2.

The mean value of cardiac output in the moderately bled group (23 ml./Kg.) was very low, not more than 6.0 ml./100 Gm. with a blood pressure of 47 mm. Hg, while resistance rose to 709 × 103 dynes/sec./cm2. After more severe hemorrhage (32 ml./Kg.) mean blood pressure was only 18 mm. Hg.

**Tourniquet Shock**

The blood flow showed the following pattern: there was a reduced blood flow in all of the organs. The smallest decrease was found in the heart, i.e., to 58 per cent of the control; the greatest changes were found in the kidney (to 26 per cent) and in the skin (to 23 per cent). While in the controls, renal blood supply was nearly twice the coronary (calculated for 100 Gm. weight of organ); in shock, coronary blood flow was greater than renal.

There was a significant increase in the vascular resistance of the skin and of the "carcass" (skeleton, muscles, and endocrine organs). Due to the great standard deviation, there was no change in the blood flow of the other organs which would be statistically significant, although the differences between some of the means were fairly large. Thus there was an average increase in renal resistance from 29 to 71 (the difference is near the significance level, P—0.05), while the circulatory resistance of the intestines increased from 136 to 183. The resistance of the "lungs" (bronchial circulation) showed a minor but significant decrease.

Considerable changes were observed in the distribution of the cardiac output: the coronary fraction increased definitely from 2.8 to 4.7 per cent, and the fractions in the "lungs" and liver to a lesser degree. The
### TABLE 1

Effect of Tourniquet-Shock or Hemorrhage on the Circulation in the Rat

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Control</th>
<th>Tourniquet-shock</th>
<th>Hemorrhage</th>
<th>Within-sample standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>22-30</td>
<td>19-20</td>
</tr>
<tr>
<td><strong>Mean values</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total body:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac output</td>
<td>22.6</td>
<td>10.1 ±</td>
<td>6.0 ±</td>
<td>6.6 ±</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>120.0</td>
<td>50.5 ±</td>
<td>47.3 ±</td>
<td>18.0 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>526.1</td>
<td>407.0 ±</td>
<td>708.0 ±</td>
<td>219.9 ±</td>
</tr>
<tr>
<td><strong>Heart:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>97.7</td>
<td>49.6 ±</td>
<td>37.2 ±</td>
<td>32.3 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>123.5</td>
<td>105.6 *</td>
<td>156.5 ±</td>
<td>44.7 ±</td>
</tr>
<tr>
<td>Fraction</td>
<td>2.8</td>
<td>4.1 ±</td>
<td>4.8 ±</td>
<td>7.1 ±</td>
</tr>
<tr>
<td><strong>Kidney:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>14.5</td>
<td>9.8 ±</td>
<td>6.4 ±</td>
<td>3.3 ±</td>
</tr>
<tr>
<td><strong>Lung:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>67.2</td>
<td>31.4 ±</td>
<td>15.4 ±</td>
<td>19.9 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>170.4</td>
<td>150.4 ±</td>
<td>104.8 ±</td>
<td>140.2 ±</td>
</tr>
<tr>
<td><strong>Liver:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>75.8</td>
<td>34.8 ±</td>
<td>15.6 ±</td>
<td>27.8 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>135.8</td>
<td>122.2 ±</td>
<td>290.0 ±</td>
<td>119.2 ±</td>
</tr>
<tr>
<td>Fraction</td>
<td>17.0</td>
<td>10.1 ±</td>
<td>15.2 ±</td>
<td>14.6 ±</td>
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<tr>
<td><strong>Intestine:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>25.6</td>
<td>30.4 ±</td>
<td>22.2 ±</td>
<td>21.4 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>86.8</td>
<td>113.4 ±</td>
<td>7.0 ±</td>
<td>6.8 *</td>
</tr>
<tr>
<td>Fraction</td>
<td>19.6</td>
<td>6.5 ±</td>
<td>4.9 ±</td>
<td>4.6 ±</td>
</tr>
<tr>
<td><strong>Splanchnic bed</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Blood flow</td>
<td>964.6</td>
<td>2423.3 ±</td>
<td>3496.1 ±</td>
<td>2120.3 ±</td>
</tr>
<tr>
<td>Resistance</td>
<td>8.8</td>
<td>5.6 ±</td>
<td>5.4 ±</td>
<td>2.5 ±</td>
</tr>
<tr>
<td>Fraction</td>
<td>45.8</td>
<td>45.2 ±</td>
<td>55.1 ±</td>
<td>53.3 ±</td>
</tr>
</tbody>
</table>

The mean values from experimental groups were compared with the mean values of the control group. The differences were statistically evaluated with the following results:

*P < 0.05.

†P < 0.01.

‡P < 0.001.

No symbol, P > 0.05.
fraction in the splanchnic bed (liver + intestines) rose from 25.6 per cent to 30.4 per cent. A significant decrease occurred in the fractions distributed in the kidney and the skin.

HEMORRHAGE

As cardiac output was not measured in more severe hemorrhage, blood flow and vascular resistance in hemorrhage were calculated in the moderately bled groups only. The blood flow of all organs decreased considerably. Coronary circulation suffered the least; nevertheless it reached only 35 per cent of the controls. Renal and cutaneous circulations were the most severely affected, the blood flow being not more than 12 to 13 per cent of the controls. The vascular resistance of the organs except coronary and bronchial vessels increased significantly.

Compared to the controls, the distribution of cardiac output showed a considerable change both in moderate and severe hemorrhage. Changes were in the same direction in both groups, although generally greater in severe hemorrhage. Increases in the fractions of the heart and the "lungs" were considerable and approximately of the same order. At both hemorrhage levels, the fraction of the "carcass" was significantly greater, i.e., 55.1 and 53.3 per cent, respectively, than the 45.8 per cent of the controls. Renal and cutaneous fractions showed considerably lower values. Fractions of the liver and intestines were somewhat lower in both groups, but this change only becomes significant in severe hemorrhage for the liver fraction. The total splanchnic fraction of the cardiac output dropped in hemorrhage from 25.6 per cent to 22.2 and 21.4 per cent, respectively. These changes considered separately were not significant, but when the two groups were pooled they reached the limit of significance (P < 0.05).

Regarding the moderately bled group, our data are in complete agreement with Sapirstein's results.3

Thus, we found in the rat some essentially common circulatory features, developing in 20 minutes after hemorrhage and which appear a few hours after the ligation of the extremities (tourniquet shock). In both cases, blood flow in all organs decreases and vasoconstriction appears in all the organs observed except the heart and the "lungs." Increase in the coronary fraction of cardiac output and decrease of the renal and cutaneous fractions represent a further common characteristic feature. Similar changes in renal circulation in hemorrhage, tourniquet shock, and in dehydration have been demonstrated by a corrosion method in dogs.18

In these states, there is a circulatory shifting by which the myocardium is favored at the expense of the kidney and the skin. The basic facts of circulatory redistribution observed in the rat are similar to those which others and we ourselves have earlier observed in dogs and men.

In tourniquet shock and moderate hemorrhage, blood pressure was more or less the same, but there was a more pronounced decrease in cardiac output and in the blood flow of all organs after hemorrhage, that is to say, hemorrhage caused a greater rise in vascular resistance. We did not study the cause of this difference, but it may be assumed that at an identical reduction in blood pressure there is a greater decrease in the circulating blood volume after hemorrhage.

It is rather surprising that in both bleeding groups we found increased "carcass" (bone and muscle) fractions. Sapirstein et al.3 reports the same observation after moderate hemorrhage. The reason for this phenomenon is not yet clear.

Summary

Cardiac output, blood pressure, and organ fractions of cardiac output, except the brain, were determined in rats subjected to tourniquet shock and to hemorrhage. Bleeding involved the withdrawal of 23 and 32 ml./kg. blood, respectively, and determinations were carried out 5 to 20 minutes after bleeding. Sapirstein's "indicator fractionation" method with Rb186 was used for the determination of the cardiac output fractions. Blood flow and circulatory resistance of the organs were calculated from the experimental data. Cardiac
output was not measured after severe (32 ml./Kg.) hemorrhage. In tourniquet shock at 50 mm. Hg blood pressure, the cardiac output and the blood flow in all organs decrease while vascular resistance of the skin and of the "carcass" (skeleton, muscles, endocrine organs) increases. The heart, "lung," and the liver fractions of cardiac output increase, renal and skin fractions decrease. After moderate hemorrhage at 47 mm. Hg blood pressure, cardiac output and the blood flow of the organs are low. Vascular resistance of all organs other than the heart and the "lung" rises. Cardiac output fractions of the heart, "lung," and "carcass" increase; renal and cutaneous fractions decrease. In severe hemorrhage, the redistribution of cardiac output has a similar tendency but is usually more pronounced.

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References
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