Reduction of left ventricular contractility during acute hemorrhagic shock

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MUCH EXPERIMENTAL EVIDENCE has accumulated from different species which suggests that hemorrhagic shock may be detrimental to cardiac contractility (6, 11, 12, 14, 15, 21). Some investigators have associated the onset of irreversible hemorrhagic shock with cardiac failure (1, 2). Others (13) have presented contradictory findings in dogs indicating that, at “oxygen debts” normally associated with irreversibility, left ventricular function is unimpaired. Furthermore, during early hemorrhagic oligemia ventricular contractility may be increased (13, 19). This can be abolished by beta-receptor blockade with propranolol, suggesting that it is an adrenergic response.

The inotropic influence of digitalis glycosides on normal hearts is still under discussion (5), and their therapeutic value for hearts in shock is controversial. Some workers (4) have suggested that digitalis enables animals to tolerate greater oxygen deficits before the onset of irreversible shock, and in that sense the cardiac glycosides were beneficial. This appears to be inconsistent with the findings of others, however (10).

The present study was designed to assess left ventricular contractile changes during sustained hemorrhagic shock, to evaluate the inotropic effects of digitalis on cardiac performance in shock, and to study the reversibility of myocardial depression. A preliminary report on these findings has appeared (23).

METHODS

Twenty-three adult mongrel cats were anesthetized with intraperitoneal sodium pentobarbital, 30 mg/kg, and prepared for measurement of left ventricular function. Following endotracheal intubation a midline thoracotomy was performed, and ventilation was maintained with a Harvard constant-volume positive-pressure pump. The left subclavian artery was cannulated and a polyethylene cannula was passed into the aortic arch for measurement of aortic pressure. Heparin, 10 mg/kg, was given intravenously. The thoracic aorta was cannulated and cardiac output (minus coronary flow) was measured with a Shipley-Wilson 800-ml rotameter (Fig. 1).

To provide data for the construction of ventricular function curves, cardiac output was temporarily varied by means of a pump-operated arteriovenous bypass which permitted blood to be pumped in progressive increments from the flowmeter circuit to the superior vena cava. Arterial blood pressure was regulated by means of a constant-pressure reservoir. The extracorporeal tubing, flowmeter, and reservoir were primed with freshly drawn heparinized (5 mg/100 ml) cat blood. Following insertion of the flowmeter circuit, the brachiocephalic artery was ligated to render the higher portions of the nervous system reflexly inactive.

The apex of the left ventricle was cannulated with a no. 15 needle secured with a purse-string suture. Left ventricular and aortic pressures were measured using Sanborn transducers. The first derivative of the rate of rise of left ventricular pressure (dP/dt max) was obtained using an R-C differentiating circuit with a time delay of 0.286 msec. These data were recorded on a Sanborn 358 direct-writing oscillograph. Heart rate was maintained constant by electrical pacing of the right atrium. Ventricular function curves relating stroke volume to left ventricular end-diastolic pressure at constant heart rate and aortic pressure were obtained as described previously (7). Blood temperature was maintained within a range of 37 ± 1°C in most experiments by
suitable heat exchangers (Fig. 1), as well as a variable-intensity heating pad, and monitored with a rectal thermistor probe and a Yellow-Springs telemeterometer. Arterial blood samples were drawn for measurement of pH, Po2, and Pco2 values following each ventricular function curve. These measurements were made immediately with an Instrumentation Laboratories (model 102) electrode system which incorporated a Radiometer pH electrode, a modified Clark oxygen electrode, and a Pco2 electrode.

The experiments were designed to measure left ventricular function prior to, and for a 2-hr period during hemorrhagic hypotension at arterial pressures of 30 ± 5 mm Hg. The degree of myocardial depression at each defined time interval was expressed as a percentage by dividing the SV10 (stroke volume at left ventricular end-diastolic pressure of 10 cm H2O) and left ventricular dP/dt max by the initial value (at the initiation of shock). Each animal in the shock group was compared at equal time intervals with those of a control normotensive group.

The 23 animals used in this study were divided into five groups. Group I (four animals) served as controls. The aortic pressure was maintained at 100 ± 5 mm Hg. To compare these with animals in other groups subjected to hemorrhagic shock, a similar time base was selected for the performance of ventricular function curves. Thus, curves were run at -20, -5, 0, 15, 30, 45, 60, 90, and 120 min. Time 0 corresponds to the point immediately following the rapid reduction of arterial pressure to 30 ± 5 mm Hg in the remaining groups of animals.

In group II (seven animals) initial ventricular function curves were obtained as in the control group. At time 0 the animals were rapidly bled into the reservoir and aortic pressure was stabilized at 30 mm Hg within 2-3 min. Ventricular function curves were performed at the time intervals indicated above, while the aortic pressure was maintained at this value.

The cardiac effects of digitalis (Cedilanid-D, Sandoz Pharmaceuticals) were studied in nine animals (including three from group II) which comprised group III. This group was studied and treated in the same fashion as group II. With the onset of severe myocardial depression, or serious cardiac arrhythmias, which often heralded impending ventricular fibrillation, Cedilanid-D was given. A total dosage of 0.04 mg/kg was administered intravenously in two divided doses, the second dose 5 min following the first. After full digitalization, ventricular function curves were done at 5, 15, 30, and 60 min.

Reversibility of myocardial depression was assessed in a group of four animals, including three from group II, subjected to hemorrhagic shock and treated in the same way as the other animals in group II. For clarity, these will be referred to as group IV. Following the 2-hr period of hypotension, the aortic pressure was reelevated to 100 mm Hg in these animals by infusion of blood from the reservoir. Once stability had been obtained, ventricular function curves were performed at this arterial pressure. A total of 10 curves was obtained on each animal in this group.

To provide further information on reversibility of myocardial depression, five animals (group V) were subjected to intermittent episodes of systemic pressure reelevation to 100 mm Hg. After the initial control studies, hemorrhagic shock was induced as in the four groups described above. After 30 min of hypotension a ventricular function curve was performed, following which the aortic pressure was immediately returned to 100 mm Hg by infusion of blood and a second curve was obtained. The aortic pressure was then returned to 30 mm Hg for another 30 min. This procedure was repeated 4 times throughout the course of the experiment so that the total duration of time in shock was the same as the preceding groups (120 min). The time required for pressure reelevation and performance of the ventricular function curves at normotensive levels did not exceed 5 min. Thirteen curves were obtained on each animal in this group.

RESULTS

Influence of time on ventricular performance in control animals—responses to digitalis (group I). Left ventricular contractility, as measured by stroke volume and dP/dt max at left ventricular end-diastolic pressure of 10 cm H2O, showed little change in the control group during 120 min at aortic pressure 100 ± 5 mm Hg (Table 1). At time 0 the mean control SV10 was 2.19 (± 0.21 SE) ml. This did not differ significantly from the mean values of two previous control curves obtained at -20 and -5 min. After 120 min the mean SV10 was 1.85 ± 0.08 ml, or 86 (± 7 SE)% of its initial value at 0 min, and the dP/dt max was 98 (± 7 SE)% of its initial value. Hence, after 120 min the control group manifested little spontaneous deterioration in left ventricular myocardial performance. The mean arterial pH fell slightly from 7.42 (± .09 SE) at time 0 to 7.32 (± .07 SE), and the arterial Po2 fell from 103 to 69 mm Hg (Table 1).

Following the 120-min ventricular function curves, the control animals were digitalized (Fig. 5). The mean SV10 increased from 86 to 98% (P < .05). The changes of dP/dt max from initial control values after digitalization were not significant, however. These data suggest that small positive inotropic responses to digitalis were demonstrable for 30 min after administration of the drug.

Cardiac function in hemorrhagic shock (group II). The animals...
TABLE 1. Comparison of normotensive with hypotensive animals at specified time intervals

<table>
<thead>
<tr>
<th>Time, min</th>
<th>0</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I (controls)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV1</td>
<td>2.19 ± .21</td>
<td>102 ± 1</td>
<td>104 ± 4</td>
<td>103 ± 7</td>
<td>108 ± 2</td>
<td>99 ± 7</td>
<td>86 ± 6</td>
</tr>
<tr>
<td>dP/dt</td>
<td>3,470 ± 400</td>
<td>106 ± 4</td>
<td>108 ± 4</td>
<td>109 ± 7</td>
<td>108 ± 7</td>
<td>120 ± 6</td>
<td>98 ± 7</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 ± .09</td>
<td>7.40 ± .09</td>
<td>7.43 ± .05</td>
<td>7.33 ± .04</td>
<td>7.35 ± .04</td>
<td>7.36 ± .06</td>
<td>7.32 ± .07</td>
</tr>
<tr>
<td>Po2</td>
<td>103 ± 11</td>
<td>92 ± 5</td>
<td>85 ± 6</td>
<td>78 ± 5</td>
<td>75 ± 7</td>
<td>83 ± 4</td>
<td>69 ± 11</td>
</tr>
<tr>
<td>Group II (shock)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV1</td>
<td>2.25 ± .16</td>
<td>88 ± 4</td>
<td>77 ± 4</td>
<td>70 ± 4</td>
<td>63 ± 4</td>
<td>55 ± 4</td>
<td>46 ± 4</td>
</tr>
<tr>
<td>dP/dt</td>
<td>1,980 ± 300</td>
<td>80 ± 7</td>
<td>69 ± 7</td>
<td>65 ± 7</td>
<td>69 ± 5</td>
<td>69 ± 7</td>
<td>62 ± 7</td>
</tr>
<tr>
<td>pH</td>
<td>7.44 ± .03</td>
<td>7.41 ± .01</td>
<td>7.28 ± .05</td>
<td>7.22 ± .04</td>
<td>7.11 ± .05</td>
<td>7.04 ± .04</td>
<td>6.93 ± .05</td>
</tr>
<tr>
<td>Po2</td>
<td>110 ± 8</td>
<td>108 ± 5</td>
<td>102 ± 6</td>
<td>92 ± 10</td>
<td>104 ± 5</td>
<td>100 ± 14</td>
<td>99 ± 11</td>
</tr>
</tbody>
</table>

Values are means ±SEM. Normotensive animals: AP 100 mm Hg. Hypotensive animals: AP 30 mm Hg. Initial values (time 0) are given or SV1, in ml, and for dP/dt max, in mm Hg/sec. Other values are percent of initial. Po2 = mm Hg.

FIG. 2. Sanborn oscillograph tracings demonstrating falling cardiac output (CO) and rising left ventricular end-diastolic pressure with increasing time in shock at aortic pressure (AP) 30 ± 5 mm Hg. Note

in group II which were subjected to hemorrhagic shock underwent a gradually progressive decrease in left ventricular contractility (Figs. 2 and 3, Table 1). The initial control values obtained 20 and 5 min before initiation of shock in this group of seven animals were the same as those in the control series. The mean SV1 values of the first shock curves at 0 min did not differ from the 20 minute control period, indicating no mechanical effect of aortic pressure reduction on the SV1 measurement. As would be expected, dP/dt max fell immediately from approximately 3,400 to 2,000 mm Hg/sec as a mechanical consequence of lowering the aortic diastolic pressure (25).

After 30 min at aortic pressures of 30 mm Hg, there was only slight decrease in maximum rate of rise (dP/dt mm Hg/sec) of left ventricular pressure (LVP) between 60 and 120 min. LVEDP = left ventricular end-diastolic pressure. Chart speed = 100 mm/sec.

a significant reduction in the mean SV1 compared with the control series (P < .05). After 60 min the mean SV1 fell from 2.25 (± 0.16 SE) ml at 0 min to 1.39 (± .18 SE) ml, or to 63 (± 5 SE)% at 120 min the mean SV1 was 1.04 (± .14 SE) ml, or 46 (± 4 SE)% of the control series. These changes are significant at P < .01, and P < .001, respectively. During the first 30 min of shock the mean dP/dt max fell from 80 to 69%, but no further reduction was observed (Table 1 and Fig. 2).

Although the rate of reduction of left ventricular contractility varied from one animal to another, it was observed that the longer an animal was in shock the greater was the reduction in the SV1 value. With the exception of the
15-min point, the mean SV₁₀ values during shock were always significantly less than those of the control animals (Fig. 4).

Both control and shock animals had comparable mean arterial pH values at 0 min. No significant change occurred in the control series following 120 min of observation. However, a gradual and progressive acidosis developed in each shock animal (Table 1). The mean pH in this group fell from 7.44 (± 0.03 SE) to 6.93 (± 0.05 SE). A modest reduction of mean arterial PO₂ occurred over the 120-min period in group I (Table 1). On the average, the PO₂ was somewhat higher in the shock group than in the control series (Fig. 4).

Various other manifestations of ventricular depression, including pulse alternans, inability to follow pacing, and irregular ventricular pressure-wave forms, occurred in animals subjected to hemorrhagic shock. The most frequent event was ventricular fibrillation (7 of 13 animals in groups II and III). This was usually associated with a very rapid fall of contractility with increasing time. Under these circumstances, if the LVEDP increased to values greater than 12 cm H₂O, ventricular fibrillation usually occurred. If these signs of incipient fibrillation appeared, it could be avoided by a transient increase of arterial pressure to 50 mm Hg (less than 1 min).

Effects of digitalis on cardiac performance in hemorrhagic shock (group III). The protocol was designed so that these animals were given digitalis at variable times (average, 78 min of hypotension), but at fairly comparable levels of ventricular depression (from 50 to 70% of the initial SV₁₀ at 0 min). The data from group III animals are shown in Table 2, and the contractile changes before and after giving digitalis are compared with those of the group I controls in Fig. 5. Seven of the nine animals in group III had positive inotropic responses to digitalis. There was an increase of mean SV₁₀ from 1.12 (± 0.13 SE) to 1.36 (± 0.11 SE) at 5 min, and 1.38 (± 0.10 SE) at 15 min. Thirty minutes after digitalis the mean SV₁₀ was reduced below the 15-min value, and within

### TABLE 2. Group III—responses to digitalis in shock

<table>
<thead>
<tr>
<th>Time After Digitalis, min</th>
<th>5</th>
<th>15</th>
<th>30</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV₁₀</td>
<td>57 ± 7</td>
<td>72 ± 5</td>
<td>76 ± 7</td>
<td>65 ± 6</td>
</tr>
<tr>
<td>p</td>
<td>&lt; .01</td>
<td>&lt; .01</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>dP/dt</td>
<td>73 ± 7</td>
<td>86 ± 8</td>
<td>89 ± 12</td>
<td>70 ± 7</td>
</tr>
<tr>
<td>pH</td>
<td>7.05 ± .05</td>
<td>7.07 ± .05</td>
<td>7.06 ± .05</td>
<td>7.07 ± .08</td>
</tr>
<tr>
<td>PO₂</td>
<td>79 ± 8</td>
<td>89 ± 6</td>
<td>85 ± 4</td>
<td>80 ± 3</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± sem. SV₁₀ and dP/dt expressed as percent of initial control values. PO₂ = mm Hg.
60 min was below the predigitalis level (Fig. 5). A similar pattern was observed for ventricular dP/dt max (Table 2). The responses of the shock group were similar to the controls. The onset was discernible at 5 min, with a maximum effect between 5 and 30 min in both groups. The effect was transitory and appeared to be virtually gone after 60 min.

The animals in group III developed a significant acidosis (mean pH 7.05) after 78 min of hypotension. This is comparable to that of the group II animals which was 6.93 after 120 min. After digitalis there was no significant change in pH or Po2 in either group.

Responses to reelevation of aortic pressure following sustained hemorrhagic shock (group IV). The effect of reelevation of the aortic pressure to 100 mm Hg following 120 min of sustained hemorrhagic shock was evaluated in four animals. Shock was induced in the same manner as the previous groups. Shock in this series resulted in high LVEDP values (10-15 cm H2O) even though cardiac output was still markedly reduced. Some hearts would not tolerate aortic pressure of 100 mm Hg and it had to be maintained at 75 mm Hg for 5-10 min, then gradually increased to 100 mm Hg. As the time at 100 mm Hg increased, the LVEDP values fell to a range of 6-9 cm H2O, but cardiac output was still reduced. In one animal the LVEDP did not rise strikingly following pressure reelevation. The time required to achieve stability of the aortic pressure and LVEDP in a range where ventricular function curves could be carried out varied from 5 to 20 min, with a mean time of 15 min (R point in Fig. 6).

Ventricular function curves obtained at aortic pressure of 100 mm Hg showed severe depression of SV10 in the three animals that had initially high LVEDP values on pressure reelevation. In one animal the SV10 returned to a level of 2.32 (79% of its initial 0-min value) from a level of 1.24 (49% of its initial 0-min value). The mean SV10 following aortic pressure reelevation was 1.16 (± 0.40 se) or 47 (± 11 se)% of the value at 0 min. This was not statistically greater than the value after 120 min of shock. Similarly, dP/dt max failed to increase with reelevation of aortic pressure (Table 3) to values comparable to control (group I) animals.

As with other shock groups, a progressive acidosis developed (pH 6.92). Following pressure reelevation there was no significant improvement. The mean arterial Po2 values showed little change, and were comparable to the Po2 levels obtained in other shock groups, and in the controls (Table 3).

Cardiac function in hemorrhagic shock with periodic reelevation of aortic pressure (group V). When hemorrhagic shock was intermittent two series of points were produced as shown in Fig. 7. The closed triangles represent mean SV10 values obtained while aortic pressure was 30 mm Hg. The pattern of myocardial depression in shock was similar to those of the other shock groups. The degree of depression was significant after 60 min (P < 0.05). After a total duration of hypotension of 120 min the mean SV10 had fallen to 57% of its initial value of 2.08, (P < 0.01) and the dP/dt max to 63% (Table 3). This was not different from group II after the same duration of hypotension. A significant degree of acidosis developed (pH 7.01). The arterial Po2 was comparable to other groups. At each time interval studied, the myocardial depression was readily reversed by reelevation of the aortic pressure to 100 mm Hg. The increments in SV10 and...
TABLE 3. Comparison of intermittent with late reelevation of aortic pressure

<table>
<thead>
<tr>
<th>Time, min</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group IV—late reelevation</td>
<td></td>
<td></td>
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<tr>
<td>SV₁₀</td>
<td>2.26 ± 0.32</td>
<td>72 ± 4</td>
<td>60 ± 6</td>
<td>54 ± 6</td>
<td>45 ± 7</td>
<td>47 ± 11</td>
</tr>
<tr>
<td>dP/dt</td>
<td>1.770 ± 380</td>
<td>81 ± 4</td>
<td>78 ± 9</td>
<td>81 ± 13</td>
<td>70 ± 9</td>
<td>64 ± 9</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 ± 0.09</td>
<td>7.21 ± 0.08</td>
<td>7.10 ± 0.08</td>
<td>7.04 ± 0.05</td>
<td>6.92 ± 0.03</td>
<td>6.94 ± 0.03</td>
</tr>
<tr>
<td>PO₂</td>
<td>89 ± 4</td>
<td>98 ± 8</td>
<td>86 ± 7</td>
<td>87 ± 13</td>
<td>63 ± 13</td>
<td>87 ± 11</td>
</tr>
<tr>
<td>Group V—intermittent reelevation</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>SV₁₀</td>
<td>2.08 ± 0.16</td>
<td>80 ± 2</td>
<td>73 ± 4</td>
<td>63 ± 4</td>
<td>57 ± 4</td>
<td>78 ± 3</td>
</tr>
<tr>
<td>dP/dt</td>
<td>2.410 ± 400</td>
<td>83 ± 4</td>
<td>74 ± 10</td>
<td>69 ± 8</td>
<td>63 ± 4</td>
<td>74 ± 7</td>
</tr>
<tr>
<td>pH</td>
<td>7.47 ± 0.06</td>
<td>7.50 ± 0.05</td>
<td>7.21 ± 0.07</td>
<td>7.16 ± 0.07</td>
<td>7.08 ± 0.07</td>
<td>7.01 ± 0.08</td>
</tr>
<tr>
<td>PO₂</td>
<td>89 ± 4</td>
<td>91 ± 4</td>
<td>88 ± 3</td>
<td>81 ± 3</td>
<td>75 ± 7</td>
<td>73 ± 4</td>
</tr>
</tbody>
</table>

Values are means ±SEM. Initial values (time 0) are given for SV₁₀, in ml, and for dP/dt max in mm Hg/sec. Other values are percent of initial. PO₂ = mm Hg. R = values following reelevation of aortic pressure to 100 mm Hg compared with initial control values at 100 mm Hg. Other values obtained at aortic pressure 30 mm Hg.

DISCUSSION

The present investigations were undertaken to determine if sustained hemorrhagic shock is detrimental to myocardial contractility, and to assess the possible contribution that this factor may make to the irreversibility of this process. The findings reported herein clearly establish that, under carefully controlled hemodynamic conditions, measurements of cardiac performance which reflect myocardial contractility progressively diminish with increasing duration of hemorrhagic shock. Furthermore, after 2 hr of sustained shock, reelevation of the aortic pressure failed to reverse the cardiac depression in most animals. These findings are consistent with the implications of earlier studies (1, 2, 6). In the absence of appropriate measurements, however, it is difficult to interpret which mechanism may be responsible for reduced cardiac performance. That is, inability of the heart to maintain an adequate circulation can result from a variety of causes, one of which may be reduced myocardial contractility.

There is a growing body of evidence from studies with intact hearts (6, 22), as well as isolated papillary muscle preparations (14, 15), that supports the conclusion that hemorrhagic shock of sufficient duration may seriously reduce the ability of the contractile elements of the myocardium to develop force and shorten. Although a myocardial depressant factor has been described (14), and reports of an “intestinal factor” (17, 18) possibly leading to release of endotoxins into the circulation which can diminish myocardial contractility (24) must be considered, reduced oxygen delivery to the myocardium associated with diminished coronary blood flow (22) and the development of metabolic acidosis may prove to be more important factors.

Crowell and Smith (4) demonstrated that when the total accumulated oxygen debt of animals in hemorrhagic shock exceeded 120 ml/kg the shock was irreversible by reinfusion of blood. Although vasoactive drugs were without effect, the administration of digitalis generally prevented irreversibility at this level of oxygen debt, implying that cardiac failure was a major factor under these conditions. Interpretation of these findings is rendered difficult, however, by the recent report of Rothe (21), which indicates that total...
accumulated oxygen debt is poorly correlated with survival in hemorrhagic shock.

It is not possible to establish with certainty from the present study the extent to which diminished oxygen delivery to the myocardium may have contributed to the reduced contractility. It is of interest that briefly reelevating the arterial pressure at 30-min intervals completely abolished the myocardial depression and, even though subjected to an accumulated time of 2 hr of shock, when at normotensive pressures the animals were indistinguishable from controls (Fig. 7). It may be that briefly increasing the coronary blood flow provided sufficient oxygen delivery to prevent permanent impairment of high-energy phosphate production (3). Similar experiments, but with less severe hypotension (AP 40–50 mm Hg), have failed to demonstrate diminished myocardial concentrations of ATP or creatine phosphate, however (16).

All of the animals in the present studies subjected to hemorrhagic shock developed severe metabolic acidosis. This is in contrast with the control animals in which the arterial pH remained within or near normal values. This of course raises the possibility that metabolic acidemia may have contributed substantially to the observed reduction in myocardial contractility. It is of particular interest to note that those animals subjected to intermittent pressure re-elevation developed metabolic acidemia of nearly the same severity ('Table 3'). Nevertheless, re-elevation of arterial pressure reversed the cardiac depression without alteration of the pH. Previous observations on normotensive cats have demonstrated that, with adequate oxygenation, reduction of the arterial pH to values as low as 6.8 by lactic or hydrochloric acid infusion fails to diminish cardiac performance (8). If, on the other hand, there is coexisting hypoxemia the addition of acidemia seriously reduces ventricular performance (9). Although a satisfactory explanation for this potentiation effect has not been established, it suggests the possibility that acidemia may contribute to the depression of cardiac function in shock where there is likely to be coexisting hypoxia of the myocardial tissues. This possibility has yet to be established, however.

The animals in the present study were deprived of most centrally mediated reflex activity by ligation of the cephalic blood supply (9). This may in large measure account for the somewhat different observations reported by Goodyer (13) and by Regan, et al. (19). The latter group reported finding severe depression of cardiac contractility after several hours of hemorrhagic shock, but during the first 90–120 min contractility was enhanced over preshock values. Similarly, Goodyer (13) found an elevated left ventricular contractility during the earlier phases of hemorrhage, but with beta-receptor blockade a comparable duration of hypotension produced substantial reduction of contractility. The importance of the sympathoadrenal system for the preservation of cardiac contractility in hemorrhagic shock is also supported by the studies of Glaviano, et al. (11, 12). These workers demonstrated a decreased cardiac norepinephrine concentration and progressive reduction of cardiac responsiveness to stellate ganglion stimulation as the duration of hemorrhagic shock increased. It is also important to note that animals in which adrenergic influences on the heart have been removed by beta-receptor blockade are highly sensitive to metabolic acidemia (20). If sympathoadrenal function should fail over the course of many hours of hemorrhagic shock, metabolic acidemia would then be expected to contribute importantly to the deterioration of cardiac function.

Although it has been reported (4) that digitalis affords an impressive degree of protection against irreversibility in hemorrhagic shock, presumably by its cardiotonic action (2), the precise explanation is not certain. Glasser and Page (10) were able to demonstrate minimal and inconstant effects in a large series of dogs. In the present study only a modest improvement in myocardial contractility could be demonstrated following digitalization of the shock group, and this was not greater than that observed in control animals followed for the same length of time (Fig. 5). Further studies on the efficacy of pharmacological agents that may be useful in improving myocardial contractility in hemorrhagic shock are clearly necessary.

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