Surgical and Chemical Denervation of Abdominal Viscera in Irreversible Hemorrhagic Shock*

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HEMORRHAGIC SHOCK is characterized by hyperactivity of the sympathetic nervous system. Acute hemorrhage of significant magnitude is associated with a marked sympathetic response, and the resultant vasoconstriction is most pronounced in epinephrine-sensitive vascular beds such as abdominal viscera and skeletal muscle. The vasculature of the brain and the heart, however, constrict only minimally in response to sympathetic stimulation. By this selective compensatory vasoconstriction, blood flow to the abdominal viscera is reduced and the available blood supply is diverted to the brain and other vital structures that are extremely sensitive to lack of oxygen. As hypotension persists and abdominal viscera are perfused at minimal rates, hypoxia is excessive and the viscera suffer irreversible ischemic injuries.

Reduction of sympathetic activity by pretreatment with adrenergic blocking agents improves survival rates of animals exposed to hemorrhagic or endotoxic shock.[8, 11, 12] Staged total surgical sympathectomy,[9] bypass perfusion of the mesenteric circulation and excision of the major portion of the bowel all afford varying degrees of protection from irreversible shock.[6] These observations strongly implicate the abdominal sympathetic nervous system in the pathogenesis of experimental shock and point out the need to evaluate the possible protective action of regional sympathetic denervation.

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Material and Methods

Sixty adult mongrel dogs (10 to 15 Kg.) were premedicated with 1.5 mg./Kg. of morphine sulphate 1 hour prior to the experiment. The femoral artery and vein were cannulated with a glass cannula under sterile conditions and local procaine anesthesia. Heparin, 2.5 mg./Kg., was injected into the femoral vein and 30 mg. into the reservoir. Arterial pressure was monitored continuously with a mercury manometer. Fine's method of graded hemorrhage was employed to induce and maintain shock. The animals were bled from the femoral artery into a reservoir situated 40 cm. above the level of the right atrium and thereby a mean pressure of about 30 mm. of Hg. was maintained. All the blood in the reservoir was reinfused when 40 per cent of the maximal bleeding volume was taken up spontaneously or 6 hours after the onset of shock if the 40 per cent uptake was not completed by that time. Autopsies were performed on all animals whether they died or were sacrificed. Dogs alive 72 hours after the onset of the experiment were considered as permanent survivors.

The experiment was performed in two stages. In the first phase, 30 dogs were divided into three groups of ten animals.[4]

Group I (Control 1). The animals were shocked as described.

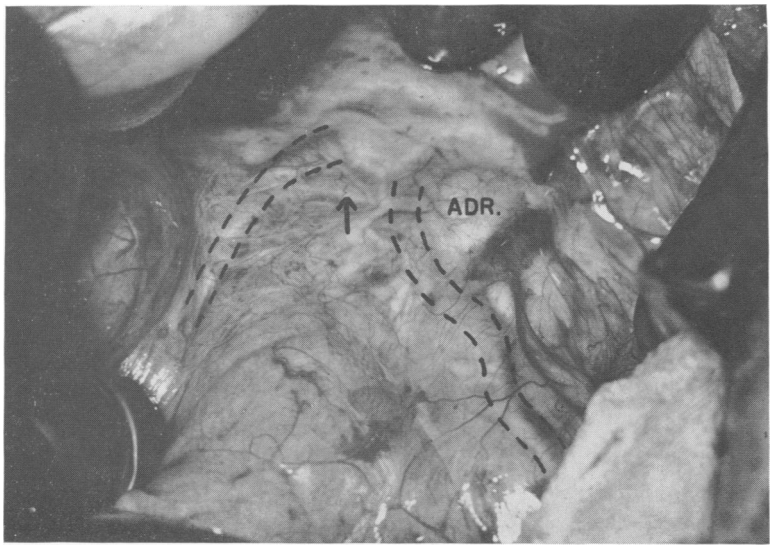

FIG. 1. Operative field is exposed. Posterior peritoneum is intact. Celiac axis and superior mesenteric artery are outlined by interrupted lines. Arrow points to interganglionic nerve fibers. Left adrenal gland is marked by ADR.

Group II (*Dibenzylene*). These animals were given 0.5 mg./Kg. of Dibenzylene 1 hour prior to the onset of hemorrhage.

Group III (*Sympathectomy 1*). Animals were subjected to abdominal postganglionic sympathectomy under nembutal anesthesia. The details of the procedure has been described.[13] In brief, the celiac, superior and inferior mesenteric ganglia were excised and the corresponding arteries were stripped of adventitia (Fig. 1, 2). Seven to 14 days after operation, the animals were subjected to hemorrhagic shock in a manner identical to the other two groups.

In the second phase of the experiment, 30 additional dogs were used and again divided into three groups of ten animals.

Group IV (*Control 2*). Because almost 1 year elapsed between the two parts of the experiments, we believed it was essential to reaffirm the data of the original control group.

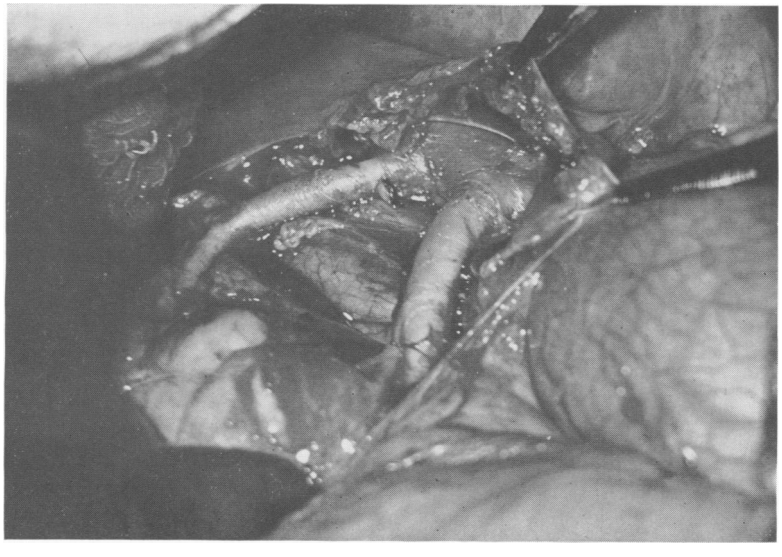

FIG. 2. Sympathectomy is completed. Stripped portions of the aorta, celiac axis and superior mesenteric artery are shown. Prevertebral ganglia and interganglionic nerve fibers have been excised.

TABLE 1. *Results*

Group	No. Dogs	Survivals	MBV (cc./Kg.)	MBT (min.)	UT (min.)
I					
Control 1	10	0	48	53	121
II					
Sympathectomy 1	10	2	40 ($P < .05$)	48	170 ($P < 0.01$)
III					
Dibenzylene	10	6	40 ($P < 0.5$)	105	219 ($P < 0.01$)
IV					
Control 2	10	0	55	47	116
V					
Sympathectomy 2	10	3	55	42	186 ($P < 0.01$)
VI					
Novocain block	10	0	50	33 ($P < 0.05$)	104

MBV Maximal Bleeding Volume (average); MBT Maximal Bleeding Time (average); UT Uptake Time (average).

Survival rates are significantly improved only by Dibenzylene pretreatment although sympathectomy appears to have a slight beneficial effect. Reduction of MBV was accomplished only by Dibenzylene pretreatment and in the first sympathectomy group. The bleeding time was favorably altered only with Dibenzylene while chemical blockage resulted in deterioration of this parameter. In the treated groups novacain block was the only modality that did not result in an improved uptake time.

Group V (Sympathectomy 2). The protocol employed in Group III was duplicated, except that the interval between sympathectomy and exposure to hemorrhagic shock was extended to six weeks.

Group VI (Novocaine Block). Hemorrhagic shock was instituted as in the controls. Thirty minutes after the onset of shock, the abdomen was prepared, draped and infiltrated with 15 cc. of 1 per cent novocain. A midline abdominal incision was made and the celiac and superior mesenteric ganglia with their respective arteries were exposed and infiltrated with 10 cc. of 1 per cent novocain. Following this, the abdominal incision was closed in layers and the experiment was continued as in the controls.

Results

The results were analyzed in terms of survival of animals, bowel changes, maximal bleeding volume, maximal bleeding time and total uptake time (Table 1). Maximal bleeding volume (MBV) is defined as the maximal amount of blood shed by the animal into the reservoir. Maximal bleeding time (MBT) is the interval between onset of the hemorrhage and attainment of MBV. Uptake time (UT) represents the period between the time MBV was reached and retransfusion was instituted.

Pretreatment with Dibenzylene resulted in survival of 6 of 10 animals compared to a mortality of all ten in the control group. The amount of blood shed into the reservoir (MBV) was reduced, as was the rate of bleeding (MBT) and the rate of uptake (UT). Smaller bleeding volume and reduced rate of bleeding suggest that sympathetic vasoconstrictive response to hemorrhage was lessened in the early stages of shock, while prolongation of uptake time reflects a moderate degree of preservation in vascular tone during advanced phases of hypotension.

Animals that were shocked 7 to 14 days after sympathectomy demonstrated a slightly higher, but statistically not signifi-

cant, survival rates than the control group. A reduction in MBV was observed, but the bleeding time was not significantly changed. As in the Dibenzylene-treated group, uptake time was prolonged. Extension of the interval between denervation and hemorrhage to 6 weeks did not alter survival rates. The only hemodynamic change of note consisted of an increased uptake time. Chemical blockage of the mesenteric sympathetics after the onset of shock resulted in death of all animals. In addition, overall deterioration of the hemodynamic parameters were observed—presumably a result of added trauma of laparotomy during the hypotensive state.

Discussion

Evidence for sympathetic hyperactivity during shock is ample. The cold, clammy extremities and dilated pupils of the patient in shock are unmistakable signs of an epinephrine response. Rise in catecholamine levels have been demonstrated to parallel the onset of traumatic shock. The differential sensitivity of the vasculature of each organ to sympathetic impulses results in a regional redistribution of available blood flow. By this mechanism, blood is shunted away from organs with a relatively high tolerance to lack of oxygen to vital structures which survive only very brief periods of hypoxia. Frank[5] observed increased flow of blood to the heart, brain and adrenal gland, while Anderson[1] found a reduction in blood supply to the abdominal viscera during hemorrhagic shock. Pronounced vasoconstriction in the mesenteric bed has been shown to result in a marked reduction in blood flow to abdominal viscera.[13] As long as blood flow is adequate to maintain minimal metabolic needs of the tissues, constriction of blood vessels is sustained. Once flow becomes inadequate, the vessels sustain anoxic injuries and become toneless—presumably a result of local action of toxic metabolic products.

In the intestinal tract, ischemic vascular injury is manifested by pooling of blood in dilated vessels and hemorrhagic necrosis of the mucosa. The latter lesion is uniformly found in experimental shock and is implicated as the major cause of irreversibility. In man, we have noted similar changes in patients dying of congestive heart failure.[2] If the bowel is the site of lethal changes, then the very physiologic defense that preserves the organism in the early phases of shock is responsible for demise as hypotension persists.

Modification of the generalized epinephrine activity, either by pretreatment with adrenergic blocking agents or by staged surgical sympathectomy, has been found to protect against experimental shock.[1-4] Furthermore, exclusion of the intestinal tract through excision or bypass perfusion of the mesenteric circulatoin also provides varying degrees of benefit. It seemed to us that local sympathetic denervation of the abdominal viscera may prove to be another effective method of protection from the lethal changes in the bowel. We employed a postganglionic mesenteric sympathectomy for another study and applied the experimental model to the first phase of the present experiment. The results showed hemodynamic changes that resembled the protective effects of Dibenzylene pretreatment and a slight increase in survival rates.[4]

Fine[10] and his group reported that in their laboratory the denervation procedure provided striking protection from hemorrhagic and endotoxic shock, in terms of both survival rates and hemodynamic parameters. In discussing our failure to obtain similar results, Fine questioned the completeness of the denervation procedure in our hands. He further objected to our experimental protocol by suggesting that the interval between the denervation operation and shocking was too short to permit full recovery of the animal from the catabolic effects of a major surgical procedure.

We have standardized our experimental model and found a direct correlation between functional response of the bowel and anatomic completeness of the denervation procedure.[3] A good functional result was therefore accepted as evidence for total denervation and consequently only animals that exhibited the overt manifestation of mesenteric sympathectomy, such as diarrhea and tenesmus, were included in the present study.

Since the effectiveness of sympathectomy reaches a peak at 10 to 14 days, we elected to shock the animals during this period with full awareness of the ill effects of the diarrhea that is invariably exhibited. In order to meet Fine's objection, the second phase of the present experiment was designed and a group of animals in which the interval between denervation and institution of shock was extended either to 6 weeks or to the time when the animals were well and regained preoperative weights.

In the group with extended interval between sympathectomy and shock, hemodynamic data gave evidence of a lesser degree of protection than was seen in Group III. One explanation is resumption of sympathetic activity through regeneration of nerve fibers. Disappearance of the functional gastrointestinal effects of the sympathectomy supports this supposition. However, persistence of partial protection against shock gives evidence of residual effects from denervation.

Chemical blockage of abdominal sympathetic nerves after onset of shock resulted in rapid deterioration of the animals. In the absence of a significant degree of protection from the procedure, an increased resistance to shock could not be expected, for the animals in this group suffered the additional trauma of a surgical procedure. Furthermore, results obtained from this group parallels the findings with systemic sympatholytic agents in that protection is afforded only if the drug is given prior to the institution of shock, but it is of no benefit if given after the onset of hypotension. This part of the experiment casts serious doubts on the effectiveness of regional sympathetic block in human shock since, by necessity, treatment would have to be applied after the onset of the hypotensive state.

In hemorrhagic shock, postganglionic mesenteric sympathectomy produced hemodynamic changes similar to those provided by pretreatment with Dibenzylene. However, reduction of regional sympathetic activity does not provide the same degree of protection as obtained by total body denervation, either chemical or surgical. It seems that in the advanced stages of experimental shock sympathetic hyperactivity plays a major role in producing an irreversible state. The abdominal viscera are a substantial but not the only site for ensuing lethal pathologic processes. Therefore, reduction of mesenteric sympathetic impulses provides only partial protection from persistent shock. This beneficial effect appears to be restricted to pretreatment of animals and is not operative if applied after the onset of shock.

Summary

The role of the mesenteric sympathetic nervous system in experimental hemorrhagic shock was studied. Two groups of dogs were subjected to a postganglionic mesenteric sympathectomy and exposed to hemorrhagic shock 2 and 6 weeks after denervation. In another group of dogs, the same structures were infiltrated with 1 per cent novocain 30 to 45 minutes after the onset of the hemorrhagic shock. The survival rates and hemodynamic parameters were compared with a control group and with another series of animals that were pretreated with Dibenzylene.

The denervation procedure provided protection similar to that of Dibenzylene except to a much lesser degree. Chemical blockage of the mesenteric sympathetic nerves after the onset of shock afforded no

benefit at all. There is the suggestion that denervation of the mesenteric sympathetic system is effective only if performed prior to the onset of shock.

Acknowledgment

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