Effects of Hemorrhagic, Endotoxin, and Catecholamine Shocks on Canine Gracilis Muscle Vasculature[1] (36029)

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The response of skeletal muscle vasculature to circulatory shock states appears to be variable. Skeletal muscle vascular resistance usually increases initially but then vascular resistance is reported either to wane toward control, or to plateau at some increased level, or to continue to further increase with time (1–4). These variable resistance responses are possibly attributable to differences in species, in shock types and severities, and in the particular skeletal muscle bed utilized as the test organ. In order to more clearly delineate these factors, the effect of different circulatory shock states on a single skeletal muscle bed was studied, the canine gracilis muscle. Furthermore, the severity of one form of shock was varied, hemorrhagic. The gracilis muscle was selected as the test organ because of its easy accessibility which reduces surgical manipulations, and because it is a mixed skeletal muscle bed whch makes it more representative of whole body skeletal muscle mass.

Methods. Mongrel dogs of either sex (anesthetized with sodium pentobarbital, weighing 15–20 kg) were utilized in this study. The gracilis muscle was surgically isolated except for the gracilis artery, vein, and nerves supplying the muscle. The tendons were tied to insure a collateral-free preparation. The animals were then well heparinized (10 mg/kg) to prevent clotting. Blood flow from the gracilis vein was drained via a catherized femoral vein (P. E. 320) into a saline filled reservoir kept at a constant volume by returning blood to the animal via a variable speed jump connected to a catherized jugular vein. Systemic pressure was monitored by inserting a catheter into the brachial or contralateral femoral artery. A catheter was inserted into a side branch of the gracilis vein to measure outflow pressure. The two pressure catheters were attached to Statham low volume displacement transducers; and pressures were recorded on a Sanborn direct writing recorder. Gracilis blood flow was measured by timed collections of the gracilis vein outflow. Total gracilis vascular resistance was calculated by dividing the arterial to venous pressure gradient (mm Hg) by the gracilis blood flow (ml/min). All responses were followed in all animals up to 4 hr. The average weight of the gracili used in this study was 60 g.

Hemorrhagic shock was induced by depleting estimated blood volume (8% of body wt) by 60%. Two groups of 6 animals were used in this part of the study. In the first group (rapid hemorrhage), the animals were bled until their systemic pressure fell to 30 mm Hg and again when their systemic pressure reached 50 mm Hg. This procedure was continued until 60% of the blood volume was removed (30–45 min). In the second group (slow hemorrhage), the animals were bled until their systemic pressure fell to 50 mm Hg and again when their systemic pressure reached 75 mm Hg, the average bleeding time was 105–120 min. Endotoxin shock ($n = 6$) was induced by infusing 5 mg/kg of purified *E. coli* endotoxin (Difco Labs) suspended in 20 ml of saline intravenously over a 10 min period. Catecholamine shock ($n = 6$) was induced by infusing 3 μg of norepinephrine base/kg/min iv for 4 hr. The volume of the infusate was 0.2 ml/min. The controls consisted of 6 animals prepared in an identical manner, and all variables were followed for a period of 4 hr. Student's t test was used

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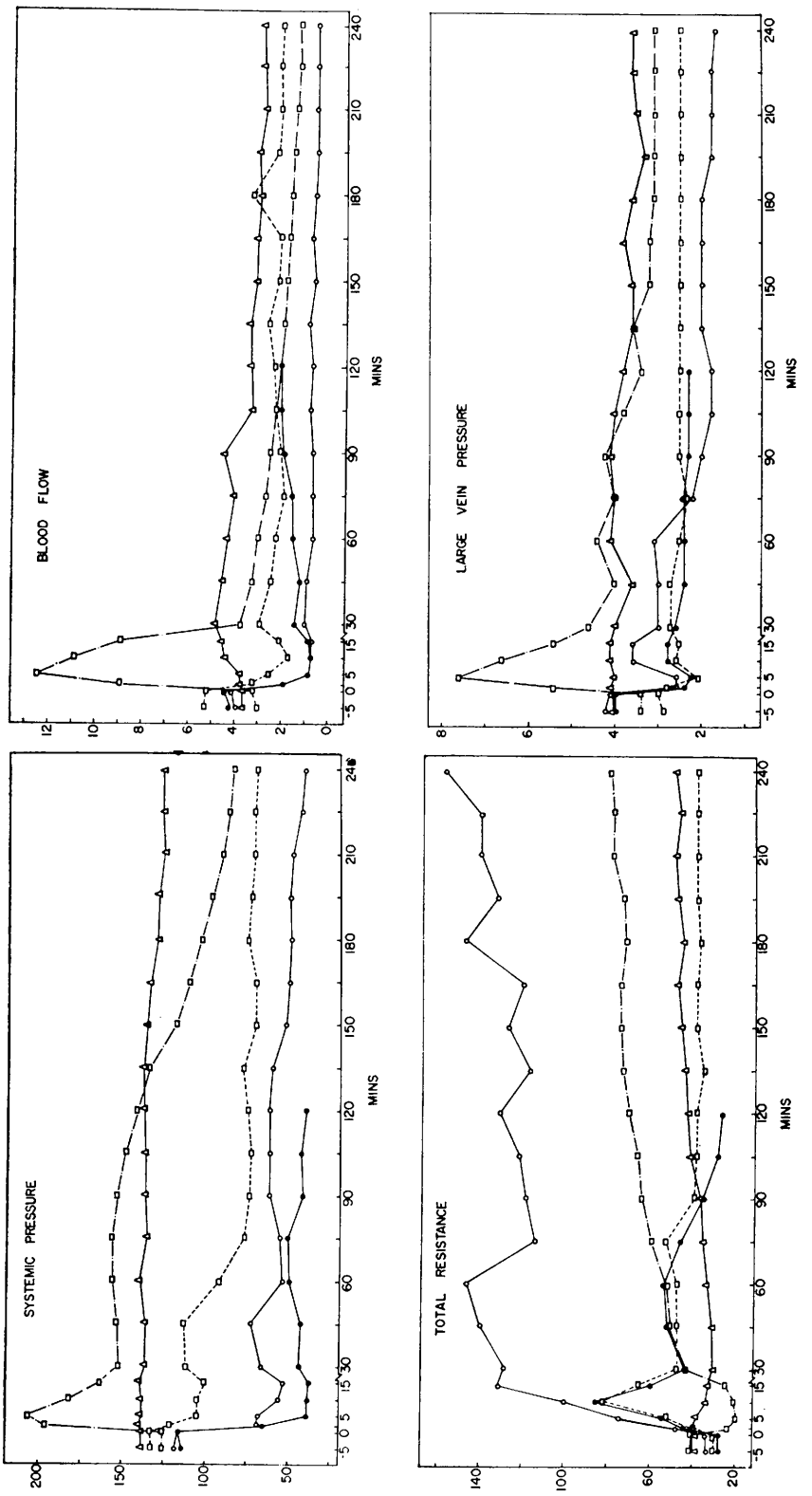

FIG. 1. Effects of hemorrhagic [rapid (●—) $n = 6$] [slow (○—) $n = 6$]; endotoxin (□ - -) $n = 6$; and catecholamine (□—•—) $n = 6$ shocks on systemic pressure (mm Hg) and gracilis muscle blood flow (ml/min), large vein pressure (mm Hg), and vascular resistance (mm Hg/ml/min). Responses in control animals ($n = 6$) (Δ—).

to compare data within each group.

Results. Hemorrhagic shock. Rapid hemorrhage produced significant decreases in systemic pressure ($p<.05$), and gracilis blood flow ($p<.05$) which remained significantly below prehemorrhage values until the animals died at min 120 (Fig. 1). Total gracilis resistance increased significantly until min ($p<.05$) after which time resistance steadily waned reaching prehemorrhage levels near min 105. The waning of gracilis muscle resistance was associated with an increasing blood flow from min 5 to 120, which was significant ($p<.05$). Most of these animals died after 2 hr of hypotension despite partial transfusions of the shed blood whenever systemic pressure fell below 30 mm Hg.

Slow hemorrhage also produced significant decreases in systemic pressure ($p<.05$), gracilis vein pressure ($p<.05$), and gracilis blood flow ($p<.05$) which remained below prehemorrhage values throughout the 4 hr period. Unlike rapid hemorrhage, gracilis vascular resistance increased significantly ($p<.05$) and the increase was well maintained throughout the 4 hr period.

Endotoxin shock. E. coli endotoxin produced significant decreases in systemic pressure ($p<.05$), gracilis vein pressure ($p<.05$), and gracilis blood flow ($p<.05$) which remained significantly reduced throughout the 4 hr period. Total gracilis vascular resistance increased significantly until min 10($p<.05$) but then began to wane nearing preendotoxin values by the end of the 4 hr period.

Catecholamine shock. Norepinephrine produced transient but significant increases in systemic pressure ($p<.05$), gracilis vein pressure ($p<.05$), and gracilis blood flow ($p<.05$) but soon all three parameters began to wane, finally falling significantly below prenorepinephrine values ($p<.05$) by the end of the 4 hr period except for gracilis vein pressure which fell only to the predrug value. Total gracilis vascular resistance fell significantly until min 15 ($p<.05$) but then increased significantly ($p<.05$), and the increase was well maintained above predrug levels during the remainder of the 4 hr period.

Controls. Only slight changes were observed in the control animals during the 4 hr observation period, none of which were significant.

Discussion. The present data show that a particular skeletal muscle bed can indeed respond differently to different types of circulatory shock. The resistance responses to slow hemorrhage, administration of endotoxin, and infusion of catecholamines are clearly not the same. Additionally of interest is the divergent resistance responses to rapid and to slow hemorrhage. The bleeding volume was the same in both groups (60% of estimated blood volume), the bleeding time being the only difference. The increased gracilis vascular resistance was well maintained in response to slow hemorrhage. However, the increased gracilis vascular resistance soon waned in response to rapid hemorrhage, and resistance returned to prehemorrhage levels within 2 hr. The complete dissipation of the resistance response was accompanied by death in most animals after 2 hr. It is possible that these animals were unable to maintain vascular resistance at elevated levels owing to failure of the vasomoter center subsequent to more severe ischemia. This is supported by the observation that systemic pressure fell more with rapid hemorrhage than with slow hemorrhage. Thus, not only is the type of shock a determinant of the skeletal muscle vascular response to circulatory shock, but also the severity of a given type of circulatory shock.

These findings agree well with data obtained from the canine forelimb in which brachial outflow was used as an index of skeletal muscle blood flow and cephalic venous outflow was used as an index of skin blood flow (5–7). The resistance response pattern to slow hemorrhage (5) and to endotoxin (6) were identical in gracilis and in forelimb skeletal muscle. The effect of rapid hemorrhage was not investigated in the forelimb. The resistance response pattern of gracilis and forelimb skeletal muscle to norepinephrine (7) were identical from min 15–240, *i.e.*, sustained increases in skeletal muscle vascular resistance. From min 0–15 however, the results were divergent; resistance in the gracilis fell but resistance in forelimb skeletal muscle increased. The reason for this transient divergence is not clear. Perhaps the baroreceptor system was more sensitive in the former, since surgical

manipulation was reduced, as was surgery time. Nonetheless, these data indirectly strengthen the hypothesis that brachial venous outflow from the forelimb is a valid index of skeletal muscle drainage.

Summary. The effects of hemorrhagic, endotoxin, and catecholamine shocks on canine gracilis muscle vascular resistance were determined. Endotoxin produced a transient increase in vascular resistance followed by a steady decline toward preendotoxin values. Norepinephrine produced a transient decrease in vascular resistance followed by a sustained increase in resistance. Slow hemorrhage (60% blood volume depletion) produced sustained, marked increases in vascular resistance; whereas rapid hemorrhage (60% blood volume depletion) produced only transient increases in vascular resistance, which soon waned and fell to prehemorrhage levels. Most of the animals subjected to rapid hemorrhage died after 2 hr despite partial transfusion of the shed blood when systemic pressure fell below 30 mm Hg. Control animals displayed only minor alterations in the variables under study. These data demonstrate that the response of skeletal muscle vasculature to circulatory shock depends on the type of shock, and also on the severity of a given shock.

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