Comparison of Early Hemodynamic Phenomena in Three Forms of Shock in Dogs[1] (35320)

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Since shock was first formally described 300 years ago (1), it has proven to be an elusive subject of research. Despite efforts of generations of investigators, agreement is lacking about even the gross central and peripheral mechanisms of the various types of shock—a factor which has contributed to a succession of therapeutic "fads." Clinically, shock continues to be common, difficult to treat, and lethal.

Our object was to develop a relatively simple animal preparation that would allow comparison of early hemodynamic phenomena in the three major forms of shock: hemorrhagic, endotoxic, and cardiogenic shock. The study was designed to assess directly both inflow and outflow events in the heart, and to assess indirectly vascular events in the peripheral circulation.

Methods. Three series of experiments were performed, one for each type of shock. Each series consisted of experiments on 6 mongrel dogs of both sexes (15–20 kg). Animals were anesthetized with pentobarbital (30 mg/kg), supplemented as necessary in the preparatory and control periods. An open-chest preparation was consistently used, with ventilation maintained by a pump respirator at 4 liters/min. In the hemorrhagic and cardiogenic shock series, the chest was opened by a midline sternal incision. In the endotoxic shock series, an incision at the right fifth intercostal space was substituted. A 30-min control period then preceded the induction of shock in all experiments.

In the 6 dogs exposed to hemorrhagic shock, 30% of the calculated blood volume (2.5% of body wt) was rapidly removed by a cannula in the femoral artery; hemodynamic measurements (described below) were then recorded for 2 hr. The animals in endotoxic shock received an LD_{100} dose (1.2 mg/kg) of *Escherichia coli* lipopolysaccharide B (Difco), injected intravenously as a bolus, after which measurements were continued for 1 hr. In the 6 dogs in cardiogenic shock, a curved metal sound was passed through an incision in the left carotid artery to the aortic root, and through the left coronary ostium, to be positioned in the anterior descending branch of the left coronary artery. An infarcting agent (0.005 ml/kg of hexachlorotetrafluorobutane, Hexa) was injected as a bolus in the coronary artery and the sound was removed (2). In this group, measurements were taken for 2 hr.

During the 1- or 2-hr observation periods, continuous recordings were made of (a) systemic arterial pressure, (b) central venous pressure, (3) lead II of the electrocardiogram, (d) cardiac output, and (e) venous return. Systemic arterial pressure was measured with a strain-gauge transducer (Sanborn) connected to a femoral artery. Cardiac output (minus coronary artery flow) was measured by a noncannulating, electromagnetic blood-flow transducer of the gated, sine-wave type (Micron); this was placed snugly on the ascending aorta and connected to an amplifier (Biotronix). Venous return was determined by a similar blood-flow transducer placed in the inferior vena cava via a small incision in the right atrial appendage. The transducer was

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TABLE I. Comparison of Early Hemodynamic Phenomena in Three Forms of Shock.[a]

Shock group (min)	Systemic arterial pressure (mm Hg)	Cardiac output (ml/min)	Venous return (ml/min)	Total peripheral resistance (mm Hg/ml/min)
Hemorrhagic				
Control period	100 ± 3	2150 ± 116	1396 ± 149	0.047 ± 0.002
+5	53 ± 5[b]	931 ± 82[b]	534 ± 104[b]	0.058 ± 0.007
+60	68 ± 10[c]	1268 ± 145[b]	626 ± 139[b]	0.053 ± 0.007
+120	70 ± 8[b]	1013 ± 117[b]	502 ± 87[b]	0.075 ± 0.008[b]
Endotoxic				
Control period	96 ± 8	1862 ± 198	1390 ± 206	0.052 ± 0.006
+3	40 ± 3[b]	897 ± 118[b]	603 ± 84[b]	0.043 ± 0.005
+30	69 ± 5[c]	1648 ± 120[c]	1300 ± 130	0.040 ± 0.002[b]
+60	57 ± 3[c]	1507 ± 124[c]	1167 ± 107[c]	0.037 ± 0.002[b]
Cardiogenic				
Control period	130 ± 10	1880 ± 113	1451 ± 138	0.071 ± 0.009
+5	115 ± 13	1627 ± 141	1193 ± 188	0.075 ± 0.013
+60	108 ± 6[b]	1601 ± 112[b]	1173 ± 105[b]	0.069 ± 0.004
+120	89 ± 11[c]	1117 ± 81[c]	977 ± 107[b]	0.081 ± 0.010

[a] Values recorded are mean ± SE.

[b] Significant ($p < .05$) difference from control value.

[c] Significant difference from both control value and value designated in footnote *b*.

lodged in position so that all flow in the vessel had to pass through the transducer (3). All measurements were recorded as mean values on a direct-writing polygraphic recorder (Sanborn). Total peripheral resistance was calculated as the product of the pressure drop from systemic arterial to central venous pressure and the reciprocal of aortic flow (mm Hg/ml/min).

Results were analyzed by Duncan's multiple range test (4).

Results. Hemorrhagic shock. During removal of blood from the dogs in hemorrhagic shock, arterial pressure, cardiac output, and venous return dropped abruptly. After the first hour, however, some recovery of pressure and flows occurred, although not to prehemorrhage values (Table I). Changes in heart rate among the 6 animals were inconsistent, and central venous pressure declined slightly over the 2-hr observation period. While calculated total peripheral resistance showed no significant change in the first hour after hemorrhage, it increased significantly during the second hour.

Endotoxic shock. Within 1 min after endotoxin injection, inferior vena cava blood flow decreased. Within the next 2 min, like decreases were observed in cardiac ouput and systemic arterial pressure (Table I). Total peripheral resistance changed inconsistently or not at all during this 3-min period. At 30 min after endotoxin injection, caval flow, cardiac output, and arterial pressure had recovered somewhat, but still remained below control values. Because cardiac output improved more than arterial pressure, the calculated value of total peripheral resistance was lower at 30 min than during the control period. At 60 min, venous return, cardiac output, and arterial pressure began to decline further, and total peripheral resistance remained significantly below control values. Inconsistent changes were observed in central venous pressure and heart rate.

Cardiogenic shock. In the 6 dogs reported in this series, intracoronary injection of Hexa produced electrocardiographic evidence of myocardial infarction without persistent ventricular arrhythmias (Fig. 1). (In another 6 animals, not included in the data reported here, Hexa caused persistent ventricular tachycardia and/or ventricular fibrillation.) After Hexa injection, cardiac output, venous

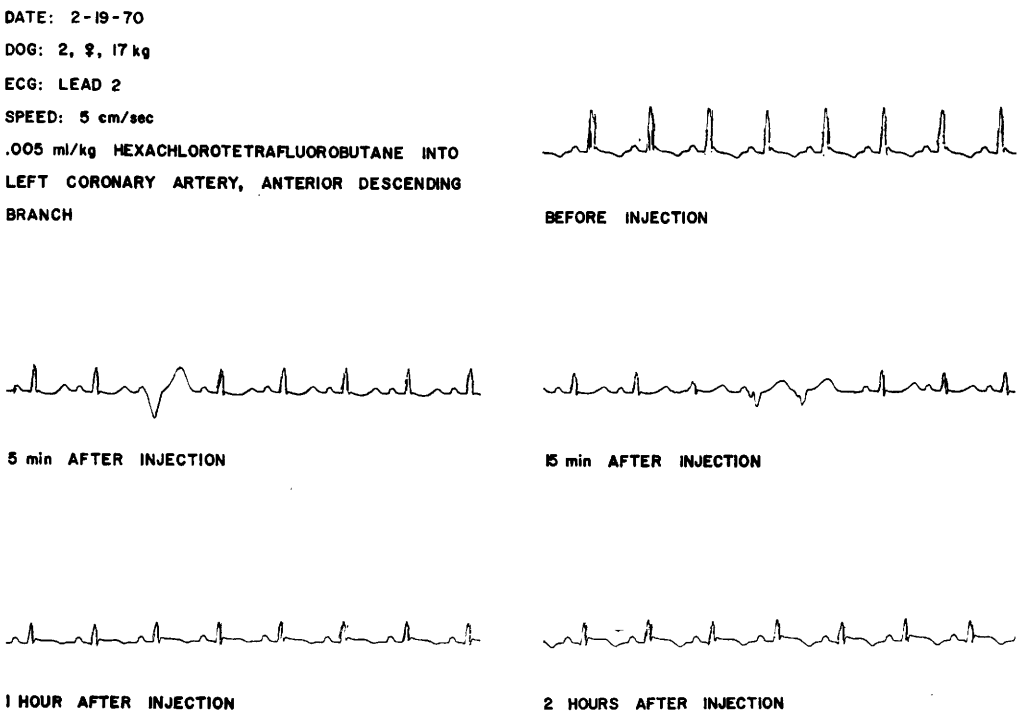

FIG. 1. Successive ECG tracings from a dog showing effect of intracoronary injection of Hexa. By 2 hours after injection the decreased amplitude of R waves and the ST segment elevation attest to myocardial damage.

return, and systemic arterial pressure declined gradually and progressively, the decreases being significantly different from control values at both 1 and 2 hr (Table I). Total peripheral resistance, heart rate, and central venous pressure changed inconsistently or not at all.

Discussion. All three shock models—hemorrhagic, endotoxic, and cardiogenic—were characterized by significant decreases in cardiac output, venous return, and arterial pressure. The three models are different, however, in that blood volume is reduced in hemorrhagic shock, blood is sequestered (*i.e.*, "effective" blood volume reduced) in endotoxic shock, and blood volume remains normal in cardiogenic shock. We found that total peripheral resistance increased in hemorrhagic shock, decreased in endotoxic shock, and showed no consistent changes in cardiogenic shock. Cardiac output, venous return, and arterial pressure were most profoundly depressed by hemorrhage. Although endotoxin diminished these parameters within 3 min, some recovery occurred during the first 0.5 hr, followed by a more gradual, persistent decline. Intracoronary injection of Hexa produced a gradual decline in pressure and flows over 2 hr. Thus, comparison of these early events indicates that the three lethal forms of shock do not exhibit the same basic hemodynamic phenomena. The dissimilar patterns of total peripheral resistance in the three shock states provide no support for the concept that a common mechanism is responsible for death in all forms of shock.

Hemorrhage has been shown to evoke generalized arteriolar constriction (5). Consistent with this concept, cardiac output fell more than arterial pressure in the dogs subjected to hemorrhage, and total peripheral resistance increased. In the endotoxic shock series, however, total peripheral resistance decreased, a result which conflicts with the postulated arteriolar constriction in this form of shock (6–10).

As previously reported by others (3, 11), intracoronary injection of Hexa in the dog

produced electrocardiographic changes indicative of myocardial infarction, transient arrhythmias, and shock. However, our animals showed no evidence of activation of a Jahrisch-Bezold type reflex in the first hour. This can probably be attributed to the use of an open-chest preparation (12, 13) and the exclusion of animals who developed persistent ventricular tachycardia and/or ventricular fibrillation.

The relative failure of reflex arteriolar constriction after myocardial infarction has been noted previously (1, 14–16). Inconsistent changes in calculated total peripheral resistance in our series confirms previous reports and suggests that some deleterious events in shock following myocardial infarction may be secondary to autonomic nervous influences on peripheral arterioles as well as to cardiac damage.

Summary. Response patterns of arterial pressure, cardiac output, venous return, and total peripheral resistance were determined in 3 lethal shock states. Hemorrhagic shock decreased pressure and flows most profoundly and most persistently but increased resistance. Endotoxic shock caused an initial transient decrease in pressure and flows, followed by a later depression of these measurements and also decreased total peripheral resistance. Cardiogenic shock gradually decreased pressure and flows and did not change resistance. The concept of a single early circulatory derangement as the primary cause of irreversibility in shock is not supported by our findings.

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