A Reproducible Model of Cardiogenic Shock in the Dog

By S. LLUCH, M.D., H. C. MOGUILEVSKY, M.D., G. PIETRA, M.D., A. B. SHAFFER, M.D., L. J. HIRSCH, PH.D., AND A. P. FISHMAN, M.D.

SUMMARY

An animal model of cardiogenic shock has been developed in the intact unanesthetized dog. Selective embolization of the circumflex coronary artery with 0.2 ml of mercury produces infarction of the posterolateral wall of the left ventricle and a shocklike state in the dog which results in death of the animal in 5 to 48 hr. The syndrome of cardiogenic shock in the animal model simulates closely that observed in man. Systemic blood pressure falls sharply (25 to 30% of control) immediately after embolization, remains low for several hours, then slowly increases toward normal, but never reaches preinfarct levels. The left ventricular end-diastolic pressure (LVEDP) remains within normal limits (5 to 10 mm Hg) during the initial hypotensive state, but increases to values above 10 mm Hg during the period of rising systemic pressures. As left ventricular failure begins to develop as evidenced by the rise in LVEDP, the mean pulmonary artery pressure also rises above control values. The cardiac output falls to 40% of control levels following embolization and never recovers. Peripheral resistance rises to compensate for the reduction of cardiac output and remains above control levels. Electrocardiograms indicate an essentially normal sinus rhythm with short runs (5 to 15 beats) of ventricular tachycardia with A-V dissociation. The hypotensive state does not seem to be related to this arrhythmia. Death of the animal appears to be due to progressive failure of the left ventricular pump to maintain cardiac output and systemic pressures.

Additional Indexing Words:
Cardiac output Blood volume Pulmonary pressure Systemic pressure Peripheral vascular resistance Cardiogenic shock

Cardiogenic shock is an ominous complication of acute myocardial infarction. Indeed, during recent years, as methods for the detection and treatment of life-threatening arrhythmias have improved, cardiogenic shock has emerged as the leading cause of death in acute myocardial infarction.1, 2

Probably the most serious obstacle to the proper management of cardiogenic shock is the lack of clear understanding of the performance of the injured left ventricle. Only in very few instances have left ventricular or left atrial pressures been recorded in patients with acute myocardial infarction.3–5 Even in those cases, only spot measurements were possible because of the inaccessibility of the left side of the heart for direct puncture and the hazards of cardiac irritability in such gravely ill patients. Instead, recourse has usually been made to remote circulatory measurements (such as central venous pressure) or to indirect respiratory indices (such as the level of arterial oxygenation) to obtain some physiological guides for prognosis and treatment.

From the Cardiovascular Institute and the Departments of Medicine and Pathology, Michael Reese Hospital and Medical Center, Chicago, Illinois.

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The present study attempted to develop a suitable model of cardiogenic shock in animals so that hemodynamic events anywhere in the circulation could be systematically and serially examined. Others have also had this interest. But the previous animal models have only provided observations during anesthesia, and generally during thoracotomy. Both of these conditions are far removed from that of the patient with acute myocardial infarction since thoracotomy per se causes serious circulatory derangements, and anesthesia may depress the myocardium by a direct action. Also, if anesthesia is prolonged for hours, a changing state of the circulation and respiration ensues which not only complicates the appraisal of the hemodynamic features of cardiogenic shock but also modifies the neurohumoral mechanisms that may determine the pattern of circulatory adjustments to the severe myocardial injury.

Our observations on cardiogenic shock were made on intact, unanesthetized dogs. To produce cardiogenic shock, the circumflex branch of the left coronary artery was embolized with a single, minute dose of metallic mercury. The clinical syndrome of cardiogenic shock which resulted consisted of acute myocardial infarction, hypotension, tachycardia, depressed sensorium, severe oliguria to anuria, and death within 48 hr after the embolization. In all of these features, the animal model resembled the clinical picture of cardiogenic shock in man.

Methods

The experiments were carried out on 25 healthy mongrel dogs of both sexes, ranging in weight from 17 to 22 kg. The dogs were not trained, but care was taken to select docile animals that were easy to handle. A combination of a short-acting anesthetic and local anesthesia was used to place the catheters and to position them under fluoroscopic control. Thus, sodium thiopental (10 to 15 ml of a 2% solution in sodium chloride) was injected intravenously at the start of the experiment. The right carotid artery and jugular vein were exposed under sterile conditions after the areas around these vessels had been anesthetized by infiltration with lidocaine (Xylocaine, 2% solution). In nine of the dogs the left femoral artery and vein were also exposed under local anesthesia. Periodically, the area around the incision was re-infiltrated with lidocaine. Cournand catheters (no. 7) were guided, under fluoroscopic control, into the pulmonary artery and right ventricle through the jugular and femoral veins, respectively. A Sones catheter (no. 7) was also introduced via the left femoral artery into the left ventricle. A Ducor catheter (no. 8) was introduced into the ascending aorta by way of the right carotid artery; this catheter was used to embolize the circumflex coronary artery and to record the systemic arterial blood pressure. All catheters were connected to Statham pressure transducers (P23AA) and zeroed at the midsternal line. Cardiac output was measured in all the dogs by the indicator-dilution method following the injection of indocyanine green (2.5 mg) into the main pulmonary artery and sampling continuously from the root of the aorta. Blood was drawn through a Gilford 103 densitometer using a Harvard withdrawal-infusion pump.

In nine dogs plasma volume was determined by the injection of 5 ml of a 0.5% solution of Evans blue (T-1824) into the superior vena cava. Samples were then collected from the same site at 10, 20, and 30 min after the injection for extrapolation of dye at zero time as proposed by Erlanger. The plasma T-1824 content was measured with a Beckman Model DU spectrophotometer using a wavelength of 620 nm. The hematocrit was read in Wintrobe tubes centrifuged at 3,000 rpm for 30 min. Total blood volume was calculated from the plasma volume and the hematocrit of the blood samples. The oxygen content of blood from the aorta and pulmonary artery was analyzed by the manometric technique of Van Slyke and Neill. The blood drawn through the densitometer for the determinations of cardiac output was reinjected after calibration. The volumes of blood drawn for the determinations of blood volume and oxygen content were immediately replaced after sampling by equal volumes of saline. In seven dogs, the urinary output was determined by collection of urine from an indwelling Foley catheter (no. 8F). Blood pressures, cardiac output, and the electrocardiogram were recorded either on a Sanborn multichannel polygraph or an Electronics for Medicine photographic recorder.

Total peripheral resistance was calculated in arbitrary units as the mean aortic pressure (in mm Hg) minus the mean right atrial pressure (in mm Hg) divided by the cardiac output (in liters per minute).

Embolization Procedure

The catheter in the aorta was used for embolization of the circumflex coronary artery. After guiding the catheter under fluoroscopic control to the vicinity of the coronary ostia, small
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shortly after the embolization. Each animal rested on the floor, close by the table. The floor was padded to avoid loss of body heat. For the measurements, the dog was replaced on the table, so that the same transducer-body relationship could be maintained. Water was given ad libitum.

Results

Hemodynamic Data

The circumflex coronary artery was embolized in 25 dogs. Five developed ventricular fibrillation and died immediately after embolization; another survived for 11 days; the other 19 died within 48 hours following embolization. The average survival time for the 19 dogs was 19.5 hr (range, 5 to 48 hr).

Figure 2 illustrates the consecutive changes in aortic pressure, cardiac output, and lead II of the electrocardiogram in the dog shown in figure 1. Elevation of the S-T segment, inversion of the T wave, and later deep Q waves were present in all experiments. Before embolization, the mean aortic pressure was 145 mm Hg; immediately following embolization, it fell rapidly to approximately 65 mm Hg; a gradual increase occurred over the next 6 hr to 100 mm Hg, after which a gradual decline began, terminating in a pressure of 30 mm Hg at 24 hr, that is, 10 min before death. Coinciding with the decrease in mean aortic pressure during the 6 hr after embolization, urinary output decreased from 65 to 20 ml/hr; during the last 10 hr of the experiment no urine could be collected. Cardiac output remained low from the moment of embolization until the end of the experiment.
HEMODYNAMIC EFFECTS OF EMBOLIZATION

![Graph showing hemodynamic changes before and after embolization]

Typical hemodynamic response observed after embolization of circumflex artery with 0.2 ml of mercury. The electrocardiogram obtained 24 hr after embolization was recorded 10 min prior to death.

dogs showed an increase in heart rate (HR) and a considerable decrease in cardiac output (CO) and mean aortic pressure ($P_{Ao}$). The mean values for total peripheral resistance (TPR) and left ventricular end-diastolic pressure (LVEDP) increased, whereas the mean pulmonary artery pressure ($P_{PA}$) and right ventricular end-diastolic pressure (RVEDP) remained practically unchanged. The last three dogs in table 1 (dogs 18 to 20) did not exhibit the hemodynamic features of cardiogenic shock; in these dogs, the cardiac output, the mean aortic pressure, and the calculated peripheral resistance did not change appreciably until immediately before death. The mean pulmonary artery and left ventricular end-diastolic pressures increased slightly. Dogs 18 and 19 died 13 and 19 hr after embolization, respectively. On the other hand, dog 20 died 11 days after the embolization; frequent measurements during these 11 days revealed unchanged cardiac output and aortic pressures.

In 13 of the 17 dogs in cardiogenic shock, sequential hemodynamic measurements were made until the time of death. The consecutive changes in heart rate, cardiac output, mean aortic pressure, and calculated peripheral resistance are shown in figure 3. For the first 2 hr after embolization, the average heart rate of the 13 experiments was within normal limits; thereafter the heart rate increased and gradually leveled off at about 25% above control values. The cardiac output decreased to 30% less than the control values; it decreased further to 45% below control during the next 6 hr and subsequently remained at this level. The mean aortic pressure mirrored the changes in cardiac output; on the average, the difference from the control never exceeded 45%. The calculated peripheral resistance exceeded control value by 45% a few hours after embolization, gradually stabilizing at about 20% above control values by 16 hr.

Figure 4 shows the same kinds of measurements in the last three dogs of table 1, that is, in which the aortic pressure had stabilized at control levels before death. In these dogs, the cardiac output decreased promptly after embolization but not as much as in the other 17 dogs; in all three dogs, cardiac output had returned to control levels after 8 hr. Also, the changes in heart rate and in calculated peripheral resistance were initially similar to those in the hypotensive group but became normal by 8 hr after embolization. The one dog which survived for more than 1 day (dog 20 in table 1) was also the only one able to walk 4 hr after embolization even though its
### Table 1

**Hemodynamic Effects of Circumflex Coronary Embolization**

<table>
<thead>
<tr>
<th>Dog</th>
<th>HR (beats/min)</th>
<th>CO (ml/min)</th>
<th>$\text{P}_{AO}$ (mm Hg)</th>
<th>TPR (mm Hg/ml/min)</th>
<th>$\text{P}_{PA}$ (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>RVEDP (mm Hg)</th>
<th>Survival time (hr)</th>
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**Nonshock dogs**

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<th>CO (ml/min)</th>
<th>$\text{P}_{AO}$ (mm Hg)</th>
<th>TPR (mm Hg/ml/min)</th>
<th>$\text{P}_{PA}$ (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>RVEDP (mm Hg)</th>
<th>Survival time (hr)</th>
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<td>Mean</td>
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<td>2.7</td>
<td>2.6</td>
<td>117</td>
<td>108</td>
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<td>42</td>
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Abbreviations: HR = heart rate; CO = cardiac output; $\text{P}_{AO}$ = mean aortic pressure; TPR = total peripheral resistance; $\text{P}_{PA}$ = mean pulmonary artery pressure; LVEDP = left ventricular end-diastolic pressure; RVEDP = right ventricular end-diastolic pressure.

*After embolization = 1 to 3 hours before death.
ECG showed the same pattern of myocardial infarction, premature ventricular contractions, and A-V dissociation as the others. Because of his apparent good health, after making measurements in this animal for 24 hr, the catheters were removed. Subsequent measurements of systemic arterial pressure and cardiac output were made on the third and sixth days by needle puncture of the femoral artery and by the introduction of fine polyethylene tubing into the right atrium via the femoral vein for injection of the dye. As shown in figure 4, the cardiac output and mean aortic pressure were similar to the control on these days; the cardiac rhythm was also normal. X-rays taken on the fifth day showed the distribution of the mercury to be unchanged from the original film. This dog died 11 days after the embolization from cardiac tamponade as a consequence of the rupture of the superficial layers of the myocardium.

Figure 5 summarizes the simultaneous end-diastolic pressures in both ventricles (LVEDP and RVEDP, respectively) as well as the mean pulmonary arterial pressure, cardiac output, and pulmonary vascular resistance in seven of the 17 dogs that developed cardiogenic shock. As the cardiac output fell, the left ventricular end-diastolic pressure increased and remained high until death. The end-diastolic pressure in the right ventricle followed the same general pattern, but the changes were less marked and remained within normal limits. Despite the sustained decrease in cardiac output and rise in left ventricular end-diastolic pressure, the pulmonary artery pressure remained relatively stable during the first 4 hr. However,
TABLE 2

Changes in Total Blood Volume in Shock and Nonshock Dogs after Embolization

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Nonshock dogs

<table>
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<tr>
<th>Dog</th>
<th>Before embolization (ml)</th>
<th>After embolization (ml)</th>
</tr>
</thead>
<tbody>
<tr>
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As the left ventricular end-diastolic pressure reached levels considered to be indicative of left ventricular failure, the pulmonary artery pressure began to rise and remained elevated during the course of the experiments. The calculated pulmonary vascular resistance closely followed the alteration in pulmonary artery pressure.

The changes in total blood volumes in seven of the dogs with cardiogenic shock and in two nonshock dogs are shown in table 2. Although there was a decrease in total blood volume in each of the hypotensive dogs after the embolization, the difference between the mean values averaged only 10%. This difference was, however, statistically significant (P < 0.05). In the two nonshock animals, total blood volume was virtually unchanged from control in one and was slightly decreased in the other.

The control oxygen content of the arterial blood averaged 17.2 ml/100 ml of blood (range, 15.2 to 22.5) for the 17 dogs in cardiogenic shock. The corresponding oxygen content of mixed venous blood was 12.0 (range, 9.9 to 13.2). After the induction of shock, the arterial oxygen content averaged 17.5 (range, 13.0 to 21.1) and the average mixed venous oxygen content was 9.8 ml/100 ml (range, 5.8 to 13.4). The last three dogs of table 1 (nonshock dogs), in which cardiac output and aortic pressure remained normal throughout the experiment, had an average arterial oxygen content of 19.0 ml/100 ml (range, 18.6 to 20.0); the corresponding mixed venous value was 13.5 ml/100 ml (range, 12.5 to 15.0). These values showed little change during the course of the experiments: the arterial blood O2 content ranged from 17.0 to 18.4 ml/100 ml after embolization whereas the mixed venous values ranged from 9.0 to 11.8.

Pathology

Gross Findings

Macroscopically the infarcts were identified as early as 7 hr following embolization, by a cyanotic discoloration of the myocardium in the vicinity of the embolized coronary artery. Constantly involved were the posterolateral wall of the left ventricle including the posterior papillary muscle, the posterior wall of the right ventricle, and the posterior half or third of the septum. In this area, scattered

Figure 6

Infarct, 22 hr old. External view of the posterolateral wall of the left ventricle. Mercury is present in the distal part of the circumflex artery and its finer branches. The black area in the picture is a subepicardial hemorrhage which indicates the site of an acute infarct. Arrows indicate presence of mercury in peripheral branches of circumflex artery.
perivascular hemorrhages were visible underneath the epicardium. Older infarcts appeared as mottled pale brown-red areas (fig. 6). On section, the infarcted myocardium was hemorrhagic, swollen, and pale brown. As seen in figures 6 and 7, mercury was present in the peripheral branches of the left circumflex artery and within intramural arteries. In the larger arterial branches the mercury was freely movable, even in the dog that died 11 days after embolization. The infarcts resulted from the confluence of numerous perivascular areas of necrosis generally centered around an embolized artery. On occasion, however, embolized small arteries were found in apparently normal areas of the myocardium. Infarcts were present in both ventricles and atria. They were generally of similar size and involved the entire thickness of the myocardium. Microscopically, infarcts were found in both atria in three dogs, in the left atrium of three additional dogs, and in the right atrium of another dog. Pericarditis was present only in the dog which survived for 11 days.

The lungs appeared grossly normal in all except two dogs in which patchy areas of atelectasis were present in the dependent portions. One of the two dogs (dog 17) had been in shock for 6 hr prior to death; the other (dog 13) died 21 hr after embolization. No frank pulmonary edema was observed. In addition, there was widespread hemorrhage of the duodenal and jejunal mucosa and of the adrenal cortex and medulla.

**Microscopic Observations**

The hearts were cut into 12 to 15 blocks; sections were stained with hematoxylin and eosin, Van Gieson-elastin stain for collagen, phosphotungstic acid-hematoxylin for cross striations and periodic-acid-Schiff with diastase for glycogen. The histological changes and their evolution during the first few days following embolization did not differ from the pattern that has been reported for both human and experimental infarcts. The earliest available pathological observations were in dog 9 which died 5 hr following embolization. This dog showed free mercury in both extramyocardial and intramyocardial arteries with no evidence of damage of the surrounding vascular wall. During histological preparation the mercury was dislodged, leaving in its place an optically empty space in the distended small arteries. The myocardium revealed small areas of coagulation necrosis and hemorrhages. Periodic acid-Schiff positive material was present only in the subendocardial areas which were not infarcted.

Seven hours following embolization, the coagulative necrosis and the eosinophilia with loss of cross-striation of the myofibers were more pronounced. The small arteries showed

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**Figure 7**

Five cross sections of the same general area of the heart from five dogs dying between 20 and 48 hr after embolization of the coronary artery. The infarcted myocardium appears in various shades of gray and black in the picture. The posterior wall of the heart is in the upper half of the sections. The infarcts are of similar sizes and involve similar areas of the myocardium. They result from the confluence of numerous perivascular areas of necrosis. Mercury droplets can be recognized within the lumen of intramural arteries. The left posterior papillary muscle is consistently infarcted. Arrow indicates mercury in intramural branches of circumflex branch of left coronary artery.
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Figure 8

Infarct, 7 hr old. An intramural branch of the circumflex artery contains mercury droplets (black in the illustration) and a recent thrombus. While the intramural arteries are frequently thrombosed, the larger branches of the coronary artery are always free of thrombi and without microscopic evidence of endothelial damage. H and E; reduced from × 200.

pyknosis of endothelial nuclei and occasional thrombosis (fig. 8).

Twelve hours after embolization the small arteries contained fibrin and platelet thrombi; the myocardium showed more pronounced changes and infiltration with polymorphonuclear leukocytes. Eighteen to 24 hr after embolization, the ischemic changes of the myocardium were marked, manifested by coagulation necrosis, eosinophilia, loss of striation, and marked infiltration of neutrophils (figs. 9 and 10). There were also hemorrhages and edema. The periodic acid-Schiff stain was strongly positive in leukocytes and myofibers at the periphery of the necrotic areas. Striking changes were noted in the intramyocardial arteries. Their lumina contained droplets of mercury surrounded by recent thrombi. In addition, there was necrosis of the arterial walls and marked leukocytic infiltration (fig. 10). During the following 24 hr the changes just mentioned increased in severity.

In dog 20, which died 11 days after embolization, the left ventricle contained a large area of necrosis in the posterolateral wall. This had left a large area of the heart devoid of epicardium and of the outer layer of the myocardium. The eroded myocardium was oozing blood and mercury which had collected in the pericardial sac. Freely movable mercury was found in the peripheral branches of the left circumflex artery. Grossly, the pericardium appeared dull because of fibrinous deposits and infiltration with leukocytes. The infarct involved the posterolateral wall of the left ventricle, including the base of the papillary muscle. The septum and right ventricle, however, were only focally involved.

Figure 9

Twenty-hour old infarct. There is extensive necrosis of myocardial fibers, hemorrhage and infiltration of neutrophils. There is also associated necrosis of the intramural arteries. H and E; reduced from × 200.
Microscopically, the infarcted areas were undergoing repair with young fibroblasts and newly formed capillaries. However, the reparative process appeared delayed, with persistence of large areas of necrosis and infiltration with polymorphonuclear leukocytes and macrophages. In addition, numerous intramural arteries were completely necrotic and appeared as empty spaces surrounded by fragments of arterial wall.

In seven dogs, microscopic examination of the lungs showed various degrees of patchy atelectasis, marked congestion of the arteries, capillaries, and veins of the dependent portions of the lungs, and focal peri-arterial and alveolar hemorrhages (fig. 11). These changes appeared more severe the longer the shock had lasted. There was marked congestion of centrolobular veins, sinusoids, and portal veins of the liver in three dogs, with focal necrosis of liver cells throughout the liver lobules.

Microscopic changes in the kidneys generally consisted of moderate congestion of the glomeruli and of the medullary veins. In dog 13 there was extensive necrosis of the tubular epithelium and the interstitial space was infiltrated with neutrophils.

The adrenals of dog 13 also showed extensive hemorrhages, necrosis, and leukocytic infiltration of the zona reticularis, and hemorrhages of the medulla. In the remaining organs, the changes consisted of congestion and perivascular hemorrhage. No dog had necrosis of the intestinal mucosa.

Discussion

Cardiogenic shock continues to be a troublesome complication of acute myocardial infarction. One of the major problems in its management is the unavailability of a standard therapeutic program based on a full understanding of its pathophysiology. The present study was undertaken in the attempt to produce a standard experimental model of cardiogenic shock. After many preliminary trials, a standard procedure was developed in which embolization of the circumflex coronary artery by metallic mercury in the intact dog produced a characteristic myocardial infarction (the posterolateral wall of the left ventricle, the posterior papillary muscle, the posterior wall of the right ventricle, and the posterior portion of the septum), regularly followed by a clinical syndrome consisting of hypotension, tachycardia, depressed sensorium, severe oliguria or anuria, and death within 48 hours after embolization. The clinical picture was remarkably consistent in all 19 dogs and, because of the lack of anesthesia and of thoracotomy, provided the opportunity for examining the hemodynamic changes under near-natural conditions.

Experimental Preparation

The use of metallic mercury in this way to damage the heart is not new. Piša and Hammer produced myocardial infarction by injecting metallic mercury into the coronary arteries of anesthetized dogs using a technique.
which had previously been described by Herrmann and Decherd in 1934.18 But their experiments required several injections of mercury to produce severe hypotension—which probably accounted for the inordinate incidence of ventricular fibrillation in their experiments19—and their observations lasted for only 30 min. In contrast, the present studies required only a single minute dose of mercury to produce not only a characteristic myocardial infarct but also the subsequent syndrome of cardiogenic shock. Moreover, the dogs with cardiogenic shock survived, on the average, for approximately 20 hr, allowing adequate time for serial hemodynamic measurements. Finally, since the dogs were unanesthetized as the cardiogenic shock developed, and neurohumoral mechanisms were intact, the experimental situation was quite comparable to the sequence observed in man after acute myocardial infarction.

It should be emphasized that the aim of the present study was to produce a reproducible state of cardiogenic shock after myocardial infarction rather than myocardial infarction per se. The amount of mercury injected for this purpose appeared to be critical. Thus, in the present study, 19 of 20 dogs whose circumflex coronary arteries were embolized with a bolus of 0.2 ml of mercury developed the syndrome of cardiogenic shock. On the other hand, in preliminary trials with 10 dogs of the same size, using smaller amounts (0.1 to 0.15 ml of mercury), the dogs either did not develop a hypotensive state, or recovered within 48 hr; six of the dogs died between 2

Figure 11

Sections of lung from an animal which died 20 hr following embolization. (A) Section is taken from a grossly normal area. There is marked congestion but no changes in the alveolar septa. The air spaces are empty. H and E; reduced from × 490. (B) Section was taken from an atelectatic area of the lung. There is collapse of the air spaces. Again no morphological evidence of edema. H and E; reduced from × 200.
and 6 mo after the embolization, and four others are still alive, 9 mo after the embolization. Invariably, larger doses of mercury (0.3 to 0.4 ml) produced ventricular fibrillation within 10 min of embolization in 10 other dogs of the same size. One of the dogs that had received 0.2 ml of mercury lived for 11 days before the myocardium ruptured. Why this dog lived so long after embolization is unclear.

Once placed into the circumflex coronary, the mercury appears to be massaged by the beat of the heart not only into the finer radicles of the circumflex artery but also into small, superficial collateral vessels from the adjacent coronary arteries. At autopsy, these collaterals are visible as fine threadlike channels from which mercury may be milked into the other major coronary arteries. However, the mercury appears to remain within the coronary arterial tree since it was undetectable by x-rays in the kidneys, liver, lungs, brain, or muscle, and more than 90% of the injected dose was recovered at autopsy from three hearts in which the muscle mass had been digested by 24 hr of immersion in a concentrated solution of potassium hydroxide.

**Hemodynamic Features**

There were two distinctive features to the cardiogenic shock produced in the present study: (1) cardiac output fell promptly after embolization and remained low throughout the experiment, and (2) the end-diastolic pressure in the left ventricle became abnormally high. Other changes were less impressive or consistent. For example, systemic hypotension was consistently mild until shortly before death; the same situation occurs in human cardiogenic shock and has been responsible for confusion concerning a proper definition of cardiogenic shock. The right ventricular end-diastolic pressure also increased, on the average, by 2 to 3 mm Hg, presumably as a consequence of its own intrinsic damage; in the dogs in which it was measured serially, the central venous pressure barely changed during the entire course, that is, an average increase from 0 to 1 mm Hg.

The change in right ventricular filling pressure was much less dramatic than in left ventricular filling pressure, particularly since the aortic blood pressure tended to be somewhat low. The pulmonary arterial pressure remained at near-normal levels during the early hours following embolization, even though the cardiac output was low. Finally, the total blood volume was only slightly reduced as has been reported previously in human cardiogenic shock. The lack of severe systemic hypotension or hypovolemia stands in marked contrast to hemorrhagic shock and to endotoxemic shock. Indeed, it would appear from these results that one of the most important physiological derangements in cardiogenic shock is acute left ventricular failure from myocardial injury with a concomitant reduction in cardiac output, rather than peripheral circulatory collapse, and that the "shocklike" features are secondary to the failure of the left ventricular pump.

Sustained arrhythmias following embolization, which themselves could produce a "shocklike" state, did not occur. However, arrhythmias of short duration were present (4 to 15 beats) but did not appear to contribute significantly to the hypotension which developed. The most common of the arrhythmias was ventricular tachycardia with A-V dissociation (fig. 12).

Even during ventricular tachycardia, the heart rate was not appreciably different from the sinus rate which obtained during the control period. Similar transient arrhythmias occur in human subjects after acute myocardial

**22 HOURS AFTER CORONARY EMBOLIZATION**

![Figure 12](image)

*Figure 12*

*A short run of ventricular tachycardia with A-V dissociation 22 hr after embolization. The rate during the tachycardia is the same as during the sinus rhythm.*

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infarction28-31 and in dogs with long-standing ligation of a major coronary artery.32

It seems clear that the present studies have not only provided a model of experimental cardiogenic shock in the dog but also have provided one which has considerable relevance to the syndrome of cardiogenic shock in man. This model may be useful for uncovering some of the pathophysiological features of cardiogenic shock and for developing rational therapeutic approaches to the disorder.

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300 Years Ago
Paradoxical Pulse

The wife of a certain citizen of London, aged 30, healthy and active enough previously, became very dejected and melancholy during the last three years of her life, suffered from breathlessness on the least exertion, had a small and often an intermittent pulse, and complained almost continuously of attacks of pain and of great physical discomfort [p. 100] in the precordium. . . . we discovered a pathological condition of the heart, to which we may rightly attribute the cause of all her troubles. The thorax was opened and the lungs were healthy enough; the pericardium, however, had become closely attached all over to the whole surface of the heart, so that it could only with difficulty be separated from it. Further, this membrane had become thick, opaque, and hard, instead of being thin and transparent, as it should naturally have been. Hence, as there was no space for the free movement of the heart, and no fluid for moistening its surface, it is little wonder that she complained all the time of these ills. Further, as the diaphragm is always attached to the pericardium in man, when the heart itself was also united to [p. 101] the pericardium, the diaphragm must of necessity have carried the heart down with it at every inspiration, and during that time must have held up and suppressed its movement. So the observed intermission of the pulse succeeded regularly at every inspiration.—Richard Lower: Tractatus de Corde item de Motu & Colore Sanguinis et Chyli in eum Transitu. (1669) Translated by K. J. Franklin. In: R. T. Gunther: Early Science in Oxford, vol. 9, Oxford, University Press, 1932, ch. 2.
A Reproducible Model of Cardiogenic Shock in the Dog
S. LLUCH, H. C. MOGUILEVSKY, G. PIETRA, A. B. SHAFFER, L. J. HIRSCH and A. P. FISHMAN

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