Mechanism of Cardiogenic Shock

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The mechanism of shock following acute myocardial infarction is still controversial. Numerous investigators have applied techniques such as: (a) ligation of the different branches of the coronary arteries,¹-⁴ (b) chemical or traumatic methods to produce myocardial injury,⁵ and (c) introduction of embolizing particles into the coronary circulation.⁶ The results are conflicting, largely because the methods used to modify the coronary circulation necessitated either the direct approach of opening the chest for coronary ligation or embolization, or the indirect approach of injecting embolizing particles through an aortic catheter in the vicinity of the coronary ostia. Although the latter procedure may be performed in animals without opening the thorax, it not only lacks selectivity of distribution of the embolizing particles in the coronary vascular bed, but spills a considerable share of the emboli into the systemic circulation.

The method we have used in the present study circumvents previous difficulties because it permits us to catheterize selectively individual coronary arteries⁷ without opening the chest or interfering with perivascular nerves and to inject embolizing agents into specific coronary vascular beds.

Methods

We studied 24 adult mongrel dogs (20 to 25 Kg.), anesthetized with morphine (3 mg./Kg.) and 0.25 ml./Kg. of a combination of equal volumes of Dial-urethane solution (100 and 400 mg./ml., respectively) and of pentobarbital sodium (60 mg./ml.).

We placed a no. 7, 8, or 9 double lumen cardiac catheter in the right heart (via a jugular vein) for measurement of pulmonary arterial pressure and another in the left heart (via a femoral artery) for measurement of left ventricular and left atrial pressures. We measured cardiac output by injecting T 1584 dye into the pulmonary artery while measuring continuously, with a recording densitometer, the concentration of dye in blood withdrawn through a plastic tube in the aorta;¹⁰ the latter also served for measurement of systemic arterial blood pressure. We calculated total peripheral resistance by dividing mean aortic pressure in mm. Hg by the cardiac output in ml./min.

Based on the flowmeter records, we selected embolizing agents used were one per cent suspension (in saline) of lycopodium spores or of glass microspheres. The sizes of the lycopodium spores and glass microspheres ranged between 30 and 40 μ, as measured with an ocular micrometer under the microscope. The suspension was agitated before each injection to assure an even distribution of the particles. The dead space of the stopcock-catheter system (1 ml.) was first cleared of its heparinized saline solution and then 2 ml. of coronary arterial blood was drawn into a syringe. The syringe containing the emboli was emptied manually in a period of two to three seconds and the system immediately flushed with the 2 ml. of blood. In our early experiments, we used a radiopaque substance rather than blood to flush the injecting system. We were unable to see, by fluoroscopy and by cinematography, any reflux of the contrast substance during the injection, indicating that all or practically all of the embolizing material went into the heart and little or none into the systemic circulation. To minimize variation of responses, we confined embolization to the left anterior descending branch, using initial and subsequent doses of 0.2 ml. This amount was selected because previous experiments have shown...
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Acute hemodynamic effects following coronary embolization (initial injection) of lycopodium spores into the left anterior descending branch. The pulmonary artery pressure is electrically averaged. Cardiac output (from dye curves) is indicated on top of the tracings; the control value is 2.8 L/min. Each vertical line on the record represents 0.1 second. Note the decrease of the cardiac output to 0.8 L/min. by 30 seconds, the decrease in systemic blood pressure, and elevation of the pulmonary artery and left ventricular diastolic pressures following embolization. Also note the increase in heart rate (85 to 120) and the T-wave change. Partial recovery occurred five minutes later (cardiac output, 2.5 L/min.).

that this dose of a 1 per cent lycopodium spore suspension invariably resulted in systemic hypotension when injected into the left anterior descending coronary artery.9

Results

HEMODYNAMIC STUDIES

We observed the acute hemodynamic changes that resulted from coronary embolization in four groups of experimental animals: (1) 10 normal dogs embolized with lycopodium spores, (2) 4 normal dogs embolized with glass microspheres, (3) 4 vagotomized dogs embolized with lycopodium spores, and (4) 6 atropinized (0.1 mg./Kg.) dogs embolized with lycopodium spores.

In 10 normal dogs, initial embolization with lycopodium spore suspension resulted in an immediate and marked decrease in cardiac output, hypotension to shock level, elevation of left atrial, left ventricular end-diastolic, and pulmonary arterial pressures, and marked increase in total peripheral resistance (figs. 1 and 2). In 3 of the 10 dogs, death supervened two to five minutes following the initial embolization. In other animals, recovery, although not complete, occurred three to five minutes after the first embolization. Subsequent embolization resulted in a progressive and persistent decrease in cardiac output, hypotension and elevation of both left atrial
NORMAL DOGS (10)  ATROPINIZED DOGS (6)

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Graphs showing the mean changes in cardiac output, systemic blood pressure, and total peripheral resistance following initial embolization, in normal and in atropinized dogs. The vertical lines indicate 2 standard deviations of the values obtained in the first minute following coronary embolization. Note the profound cardiovascular changes that occurred in the normal dogs compared to those in the atropinized dogs. The normal dogs usually died after the second or third injection, while the atropinized dogs tolerated 8 to 12 injections before death.

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and pulmonary arterial pressures and total peripheral resistance; in these animals, death usually occurred after the second or third embolization.

In four normal dogs, we used glass microspheres (20 to 40 μ) as the embolizing agent to be sure that the response to the spores was not related to their specific chemical or physical characteristics. The hemodynamic response was essentially similar (fig. 3): two dogs developed irreversible hypotension following the first embolization; the other two required three embolizations before death occurred.

We performed similar hemodynamic studies in four dogs after bilateral vagotomy; embolization of the left anterior descending branch with lycopodium spores led to responses which were essentially similar to those in intact dogs. In contrast, however, animals with vagi intact, but injected with 0.1 mg. atropine/Kg., did not exhibit the marked changes in cardiac output and blood pressure observed in normal dogs (fig. 2). The decrease in cardiac output and systemic blood pressure was gradual; as a rule, 8 to 12 doses of lycopodium spores were needed before death occurred.

**ELECTROCARDIOGRAPHIC CHANGES**

The electrocardiographic changes following coronary embolization of the left anterior descending branch consisted of an initial S-T segment depression and slight T-wave inversion, followed later by a symmetrical peaking of the T wave and S-T segment elevation (figs. 1 and 3). These electrocardiographic findings were mostly localized in leads V₅ and V₆; occasionally, reciprocal ST-T wave changes were observed in leads II and aV₂.
In the animals that survived the first embolization with partial return of blood pressures to normal, electrocardiographic evidence of an acute myocardial injury persisted. The cardiac rhythm just before death was complete atrioventricular heart block with an idioventricular pacemaker in 20 of the 24 dogs and ventricular fibrillation in the remaining four.

**POSTMORTEM STUDIES**

Histological studies of the heart done in four normal dogs showed that the lycopodium spores were localized in the area supplied by the anterior descending branch. The spores were seen only in arterioles and appeared singly or as aggregates of 3 to 10 spores. The caliber of these arterioles ranged from 40 to 500 μ (fig. 4). In the two atropinized dogs studied, although the spores were located in vessels of arteriolar caliber (singly or in aggregates), the distribution was more widespread, appearing in both the areas supplied by anterior descending and left circumflex, probably as a result of the numerous injections of emboli.

**Discussion**

The shock-like state following acute myocardial infarction has been attributed to acute myocardial failure and/or peripheral circulatory collapse. Recently, Agress and Binder reappraised the problem of cardiogenic shock and described two types of hemodynamic responses following experimental coronary embolism: (a) severe fall in cardiac output (to 50 per cent of control value), associated with a well-maintained blood pressure owing to a rise in peripheral resistance, and (b) a similar fall in cardiac output, but...
a low mean arterial blood pressure (60 per cent of control). In this latter group, the total peripheral resistance showed no tendency to increase and so compensate for the failing cardiac output. They also demonstrated that shock may occur in the absence of congestive heart failure, that is, in the absence of a rise in central venous, pulmonary arterial, left atrial, or left ventricular diastolic pressures. They concluded that the abnormality in shock following coronary embolization is the failure of the total peripheral resistance to rise in the face of a failing heart.

In our experiments, the hemodynamic changes consisted of systemic arterial hypotension associated with a decrease in cardiac output and a marked rise in systemic total peripheral resistance. These were accompanied by increase in left ventricular end-diastolic, left atrial, and pulmonary arterial pressures. The differences between the type of response in our dogs and that obtained by Agress may be due to the different techniques used for embolization. The "critical caliber" of coronary vessel blocked in their experiments was between 220 to 350 μ (average, 290 μ)² ; in our studies, vessels between 40 and 500 μ were blocked (the larger vessels by aggregates of emboli). In their studies, the mean pressure in the aorta during the period of embolization was 200 to 250 mm. Hg; in our studies, it was normal. The emboli in Agress' studies went into both the right and left coronary arteries, whereas ours went only to the
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distribution of the left anterior descending coronary artery. Finally, almost 50 per cent of their emboli went to vessels in the skin or muscles where they may have produced mechanical block or reflex changes in vascular caliber. In our experiments, the embolizing particles were introduced directly into the left anterior descending branch and radiological observations indicated that none of the injected material spilled into the systemic circulation.

Atropine modified the hemodynamic response following coronary embolization. One possible explanation relates to the known blocking effects of atropine on the parasympathetic nervous system; if embolization of one branch of a coronary artery leads to vagally mediated vasocostriction in other branches, atropine could block such vasocostriction. This would mean that shock and death would occur in the atropinized dogs only after much of the total coronary circulation was mechanically blocked by reflux of emboli from the branch into which the particles were directed. In the nonatropinized dogs, spores and spheres were found only in the distribution of the injected vessels, while in the atropinized dogs, spores were found in both branches of the left coronary artery. However, the dogs did not benefit from bilateral vagotomy; this means that if reflexes were in fact involved, they could not be mediated through either the afferent or efferent cervical vagus fibers. This leaves us with the possibility that a local axone or intercoronary reflex is involved which might be blocked by atropine but not by cervical vagotomy. It is of course possible that an action of atropine other than its postganglionic parasympathetic blocking effect is involved; atropine may block certain cells in autonomic ganglia, although our understanding of this effect is limited.

The coronary chemoreflex does not appear to be involved in the production of hypotension. Activation of it by emboli (or by blood clots forming about emboli) should lead to bradycardia and systemic vasodilatation; neither was observed. It would be of interest to determine whether the cat (a species in which the coronary chemoreflex is activated powerfully by minute doses of serotonin) behaves differently in this respect from the dog (in which serotonin fails to elicit this response).

CLINICAL CONSIDERATIONS

We believe that it is unwise to transfer data obtained by a specific type of selective coronary artery embolization in anesthetized dogs to a variety of types of coronary insufficiency in unanesthetized man in whom atheroslerotic obstruction, thrombi, or emboli might be the critical etiological factor. However, we do wish to emphasize certain of our findings in the hope that they may stimulate further clinical investigations.

1. The hypotension was caused by a decrease in cardiac output, and the latter appeared to be out of proportion to the amount of coronary vascular bed selectively blocked. This suggests that either reflex coronary vasocostriction occurred or that myocardial contractility was inhibited. Coronary angiographic studies, to be reported separately, suggest that embolization of one branch of a coronary artery does in fact produce at least temporary narrowing of other nonembolized coronary vascular beds. Even if this caused or contributed to systemic hypotension only briefly, serious damage to the myocardium in general might occur in this period. For this reason, the use of agents capable of blocking reflexes should be considered.

2. Le Roy et al. noted that the incidence of ventricular fibrillation following ligation of the left anterior descending coronary artery was diminished considerably following atropinization. They suggested that ligation of a coronary artery induced a reflex vasocostriction of the unaffected coronary artery, leading to fatal ventricular fibrillation. Our studies in the dog suggest that atropine does have some action which minimizes the cardiovascular changes following embolization. We believe that the use of atropine in myocardial infarction in man deserves further cautious study, especially if it can be given as soon
as a diagnosis is established, and before shock has occurred.

Summary
The acute hemodynamic changes that result from coronary embolization were studied in the intact dog. Coronary embolization with lycopodium spore suspension resulted in an immediate and marked decrease in cardiac output, hypotension to shock level, elevation of pulmonary arterial and left atrial pressures, and marked increase in total peripheral resistance. These profound hemodynamic responses were partially blocked in dogs previously atropinized. The therapeutic implications of the results were discussed.

Acknowledgment
We wish to express our gratitude to Dr. Julius H. Comroe, Jr. for his advice and encouragement in this work, and to Dr. Robert Wright of the Department of Pathology for doing the postmortem studies of the heart.

References
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Circ Res. 1962;10:746-752
doi: 10.1161/01.RES.10.5.746

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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