THE APPLICATION of physiological monitoring techniques to the management of patients with acute myocardial infarction has brought the pathogenesis and therapy of this disorder under renewed scrutiny, and recent clinical studies on these problems have been summarized by Shillingford and Thomas in the current issue of Modern Concepts of Cardiovascular Disease.\(^1\) As monitoring techniques improve the outlook for patients with the arrhythmias that surround acute myocardial infarction, cardiogenic shock is emerging as a leading cause of early death. In their investigations, Shillingford and Thomas observed two general hemodynamic patterns associated with simple hypotension but without clinical signs of shock. One consisted of increased cardiac output and a low ratio of arterial pressure to cardiac output, a response postulated to result from activation of vasodilatory reflexes. The other was characterized by reduced cardiac output and an elevated ratio of arterial pressure to cardiac output, a pattern presumably the result of depressed cardiac function. However, when the clinical criteria for cardiogenic shock were present, that is clouded sensorium, cool and pallid skin, oliguria, and often pulmonary edema,\(^1\) the hemodynamic mechanisms seemed less well defined, and it was concluded that this syndrome continues to pose an important therapeutic challenge.

Analysis of the numerous experimental and clinical investigations concerned with cardiogenic shock supports the proposition that both peripheral and cardiac factors are of basic etiological importance. Thus, many studies, reviewed elsewhere,\(^2\) have indicated that peripheral vascular resistance often fails to increase substantially. Implicated in this response has been the activation of stretch or chemoreceptors within the left ventricular wall. The evidence for their role in experimental myocardial infarction with shock has been summarized and extended recently.\(^5\) Left ventricular failure also occurs in patients with cardiogenic shock, as indicated by low cardiac output and by the pulmonary edema or congestion frequently evident on the chest roentgenogram.\(^1\) While it is not certain whether cardiac failure or inadequate peripheral vasoconstriction initiates the shock state, it is evident that the impairment of coronary perfusion consequent to hypotension can perpetuate and further depress myocardial performance. This combination of inadequate peripheral vasoconstriction and cardiac failure poses a unique therapeutic dilemma and focuses on several mechanical characteristics of left ventricular contraction that have

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important bearing on the interplay between aortic pressure and ventricular function, and hence on the treatment of cardiogenic shock.

The afterload on the left ventricle is determined by the aortic pressure or impedance during ejection, but it is defined as the tension developed by the fibers of the myocardial wall in response to the imposed pressure load. Therefore, afterload is dependent upon ventricular geometry and, because of the La Place relation, a large ventricle must meet a higher afterload than a small ventricle at the same level of aortic pressure. Experimental studies in the intact heart have now shown that the level of afterload markedly influences the extent of shortening of the myocardial fibers and hence the stroke volume. When ventricular end-diastolic volume and contractility are held constant, increases in the afterload result in a decreased speed and extent of fiber shortening and a reduction of the stroke volume, while decreases in the afterload allow more rapid delivery of an increased stroke volume.\(^6\) As mentioned, a dilated ventricle must meet a higher afterload than a chamber of normal size, and the failing human left ventricle appears to be abnormally sensitive to alterations in the aortic pressure, the stroke volume being markedly diminished by an acutely induced elevation of the peripheral vascular resistance.\(^7\)

When the mean aortic pressure falls to shock levels, the coronary vascular bed becomes maximally dilated, and flow is then pressure-dependent. In addition, the vessels supplying viable myocardium often have narrowed areas due to atherosclerotic disease in which flow is particularly sensitive to alterations in the perfusion pressure. Hence, increased aortic pressure is essential for myocardial perfusion but necessarily must provide an unfavorable increase in the afterload on the failing left ventricle. The importance of this problem is emphasized by the fact that pure peripheral vasoconstrictors, such as methoxamine, further reduce the cardiac output in cardiogenic shock.\(^8\) In addition, the augmentation of myocardial wall tension and heart size induced by such pressor agents should increase myocardial oxygen requirements substantially. A more promising approach has been to augment both the mean aortic pressure and the contractility of the heart by administering positive inotropic pressor agents, such as norepinephrine.\(^2\) Clearly, it would be desirable to produce the least increase in afterload consistent with adequate coronary perfusion by using low doses of these compounds and to avoid an excessive inotropic effect, since myocardial oxygen requirements are increased by positive inotropic influences at a constant level of external ventricular work.\(^8,9\) Inotropic agents, such as isoproterenol and digitalis, may also increase the aortic pressure by improving the contractility and output of the failing ventricle.

It has been known since Starling's day that when the ventricular filling pressure is relatively normal or only moderately elevated, even a depressed ventricle can operate upon the ascending portion of its Starling curve, a situation that could well apply when ventricular filling is limited by peripheral factors during cardiogenic shock. Therefore, it would seem desirable to make optimum use of this intrinsic mechanism for augmenting the force and extent of fiber shortening, within the limits imposed by pulmonary edema. While infusion of whole blood alone has not appeared to alter survival,\(^10\) the recent successful use of low molecular weight dextran\(^9\) or large quantities of dextrose and water\(^11\) offer some support for this approach, and expansion of the blood volume during withdrawal of inotropic pressor agents has also proved beneficial.\(^12\) It is possible, however, that an important component of the effect of these substances may be a reduction of the blood viscosity and a consequent lowering of the impedance to left ventricular ejection and to coronary perfusion.

Perhaps the production of a balance between the coronary perfusion pressure and the ventricular afterloading through judicious use of inotropic agents, together with cautious elevation of the venous return or reduction of the blood viscosity, or both, will prove
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effective in some patients. Others may require more strenuous measures, such as mechanical counterpulsation, which may reduce ventricular afterloading while improving perfusion of the coronary circulation. In still others, extensive myocardial damage may prohibit successful therapy short of total cardiac replacement. As understanding of the physiological mechanisms that underlie cardiogenic shock increases, it may be hoped that an expanding therapeutic armamentarium will favorably alter the prognosis of patients with this now highly lethal syndrome.

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Left Ventricular Contraction and the Therapy of Cardiogenic Shock
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