LOAD REGULATION OF CARDIAC MUSCLE

G. COOPER

Cardiology Section of the Department of Medicine, and the Department of Physiology, Temple University School of Medicine, Philadelphia, Pennsylvania

The intent of this review is to discuss briefly the recent work, both in my laboratory and in the laboratories of my colleagues, which tends to suggest a primary role of hemodynamic load in the regulation of the structure, composition and function of adult mammalian myocardium. Taken as a whole, this body of work supports the concept that the initiation of normal cardiac growth and development, the maintenance of normal cardiac properties in the adult, and the transition from normal to abnormal heart muscle during sustained hemodynamic alterations are each directly related to the environment of systolic and diastolic stress and strain to which the cardiocytes comprising ventricular myocardium are exposed.

This postulated regulatory role of load in determining the basic properties of heart muscle is supported by the remarkable plasticity which adult mammalian heart muscle exhibits in response to the entire spectrum of potential cardiac loading conditions. Within broad limits with respect to the degree and duration of load alterations, the myocardial response to reversible increases and decreases in hemodynamic loading appears to be fully reversible. We would suggest that this cardiac plasticity in the face of hemodynamic alterations is a primary load response intrinsic to each cardiocyte, with other trophic factors having a largely supportive or modulatory role.

The data which tend to support these concepts have been derived from surgical models employing the cat right ventricle. In the first model, a reversible increase in load is produced by placing a biologically inert, removable band around the proximal pulmonary artery. In the second model, a reversible decrease in load is produced by severing and then re-attaching the chordae tendinae of a single papillary muscle at their junction with the tricuspid valve apparatus. The experimental techniques which have been used to

---

1Supported by Grants No. HL-07198, HL-29146, HL-29351 and HL-29718 from the National Institutes of Health.
Figure 1. Average right ventricular systolic pressures recorded serially from solid-state transducers in awake, unrestrained animals. The pulmonary artery bands were in place for the specified number of weeks after operation.

Study these models include an analysis of cardiac ultrastructure in perfusion-fixed tissue, an analysis of cardiac contractile and energetic function in isolated superfused papillary muscles, and an analysis of cardiac composition in terms of the major structural and functional proteins which comprise the cardiocytes and the myocardial interstitium.

CARDIAC OVERLOADING

Pressure overload

Our attempts to examine selectively the direct effects of an increased load on the heart began in 1979 (1). It had been suggested (2,3) that many of the effects observed before in the study of experimental cardiac hypertrophy...