A. Pathophysiologic Mechanisms of Chronic Heart Failure

The chronically failing heart has at its disposal specific compensatory mechanisms.

I. Frank-Starling Mechanism

In chronic congestive heart failure, the compensatory responses provided by the Frank-Starling mechanism are maximally utilized. The failing ventricle works with a maximal prestretched fiber length. Further augmentation is not possible for anatomic-myocardial reasons and is limited by the pericardium. A higher ejection performance, resulting from an increase in prestretching cannot be translated into increased inotropism due to cardiac insufficiency. Other peripheral auxillary regulatory mechanisms must be employed to improve cardiac function.

II. Sympathetic Adrenergic Stimulation

One of the consequences is stimulation of the sympathetic adrenergic system leading to an increased blood supply to the heart by venous constriction, associated with an increase in peripheral vascular resistance and mobilization of myocardial reserves in the form of positive inotropism. In the dilated heart, high end-diastolic pressures and a low stroke volume are mostly accompanied by elevated catecholamine serum levels (Lehmann and Keul 1982). Although venous and arterial vessels still respond to sympathetic mediators with an increase in vascular tone, the myocardium itself can no longer be adequately stimulated.

1. Reduction of Beta-Adrenergic Receptor Density

In a recently published study, Bristow et al. (1982) demonstrated that the hearts of patients undergoing cardiac transplantation had a 50 percent reduction in beta-adrenergic receptor density. Isoproterenolstimulation in these hearts was also reduced to 50 to 70 percent compared with intact ventricles. Similar findings were reported in vivo demonstrating that the administration of isoproterenol does not increase contractility in patients with severe heart failure (Bussmann 1974; Bussmann et al. 1977 a, b; 1978 a, b). The problem is, in which regions of the left ventricle is the beta-receptor density diminished? It would not be surprising to find that the regions affected are those that already show a loss in function as a result of either necrosis or fibrosis.
2. Decrease of Myocardial Norepinephrine Stores

The decrease in cardiac norepinephrine stores in patients with severe heart failure has been known for some time (Chidsey et al. 1964).

Whereas acute heart failure or myocardial ischemia are accompanied by an increase of beta-receptor density, the chronic condition is associated with a decrease of receptors. Consequently, this loss of receptors together with a reduced myocardial catecholamine content results in a diminished response to sympathetic stimulation. As a result, the failing heart is more and more uncoupled from the necessary adrenergic drive (Willerson 1982).

But since sympathetic adrenergic stimulation acts on the venous and arterial bed and is effective, the result is an increase in filling pressures by venoconstriction and a rise of peripheral resistance in the arterial bed. The failing heart reacts with particular sensitivity to this increase in resistance and as a consequence the ejection fraction decreases further.

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**Fig. 118.** a Regional distribution of cardiac output at rest (R) and during exercise (EX) in healthy volunteers (normal) and patients with congestive heart failure (CHF). The global cardiac output is represented, its distribution to the skeletal muscle (cross-hatched) and all other regions (dotted). There is a definite reduction in skeletal muscle perfusion in heart failure. b-d Distribution of cardiac output to various circulatory regions except skeletal muscle in healthy persons (b), in patients with mild to moderate heart failure (c), and in patients with severe heart failure (d). Blood flow to the heart is represented in black. The other circulatory regions rich in alpha receptors (kidney, skin, and splanchnic bed) are also graphically outlined. MAX EX: maximum exercise tolerance; SUB MAX EX: 67 percent of maximum exercise tolerance. (After Zelis and Flaim 1983)