Chronic heart failure (molecular pathophysiology)

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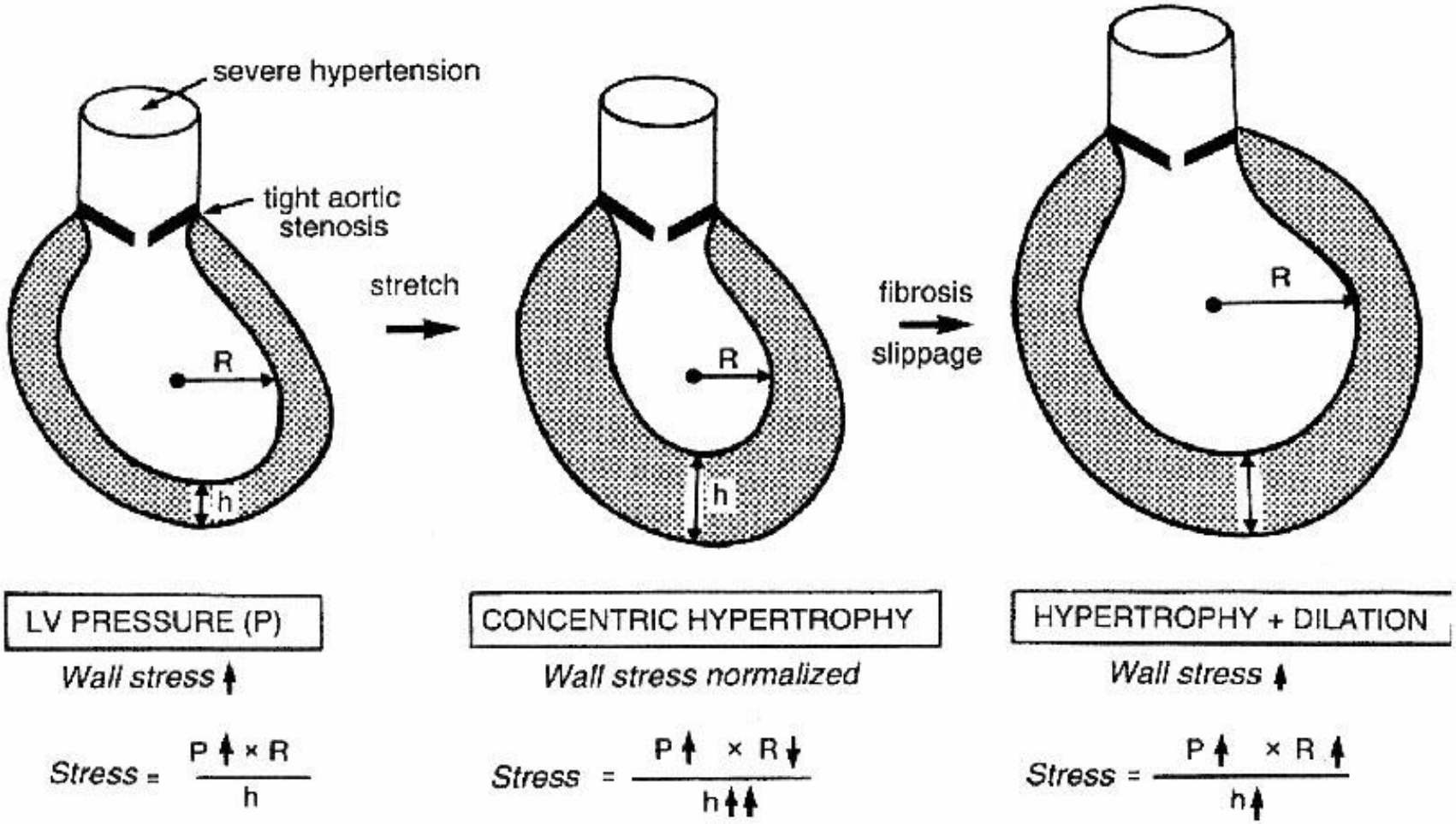
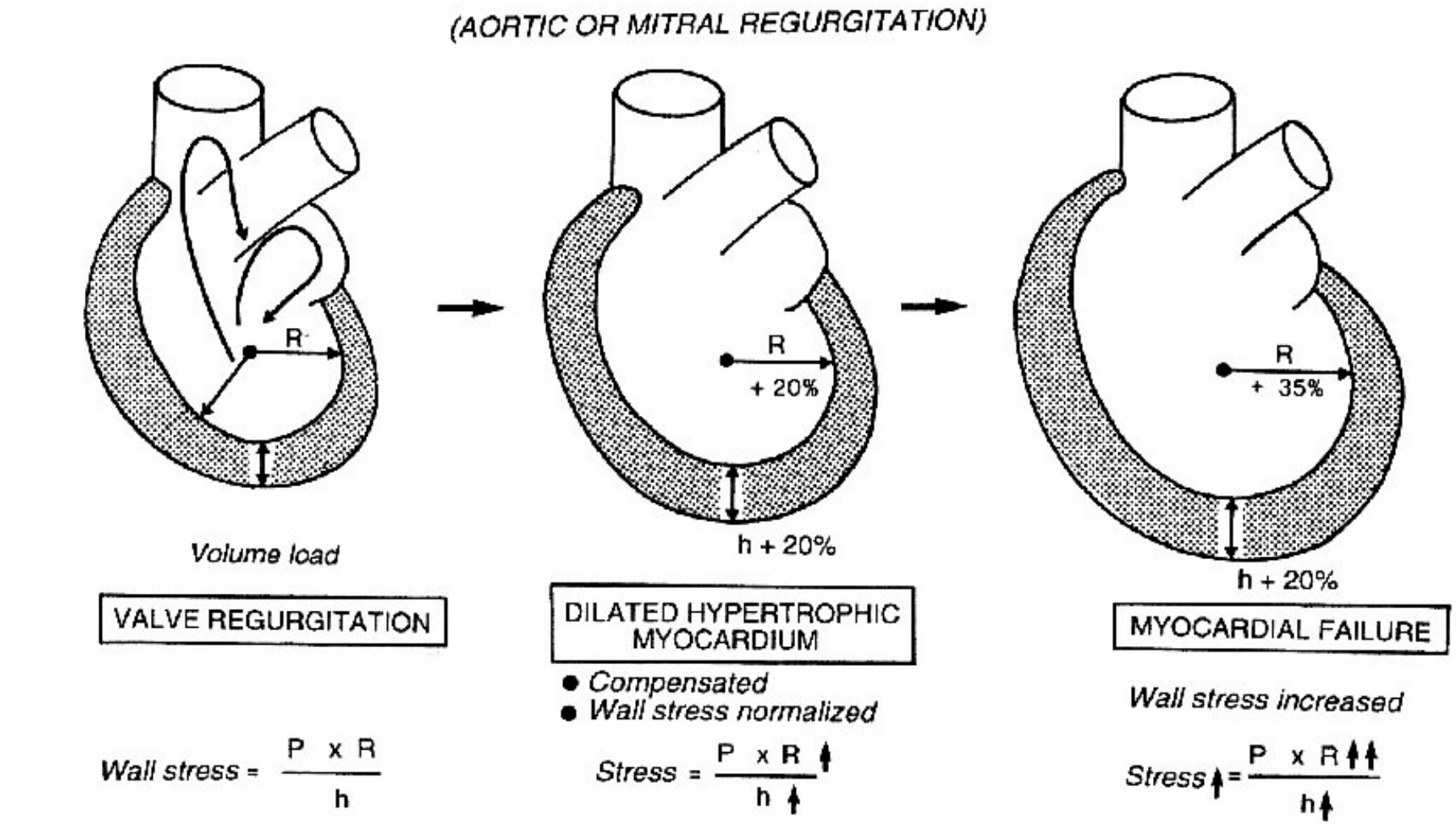
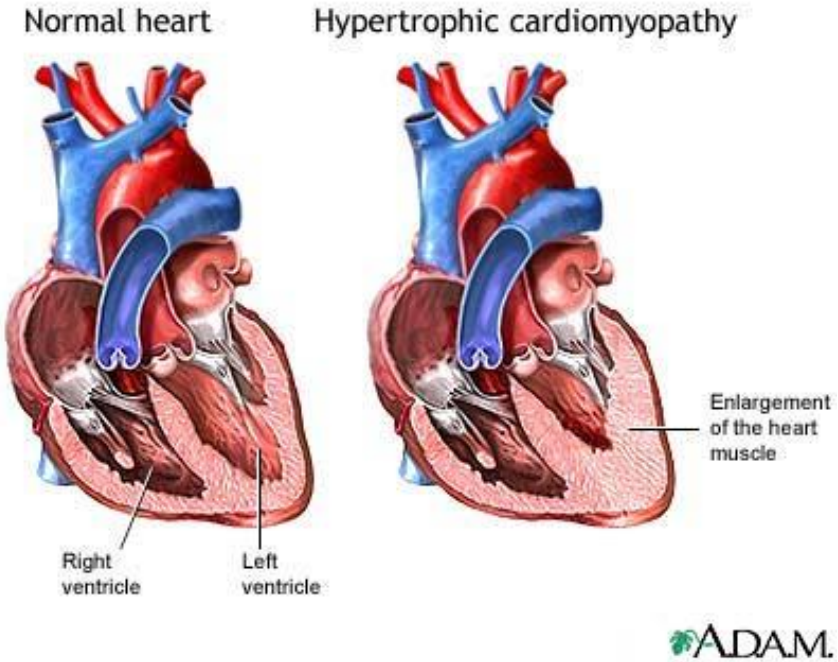
Pressure overload hypertrophy

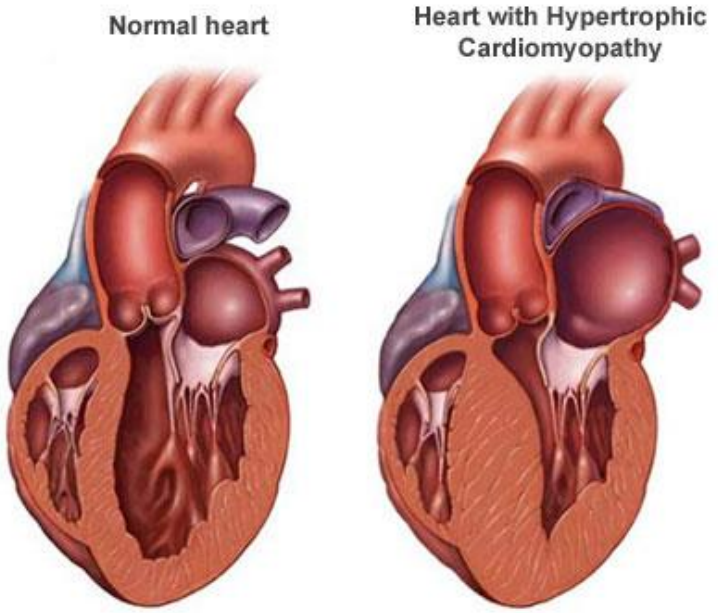


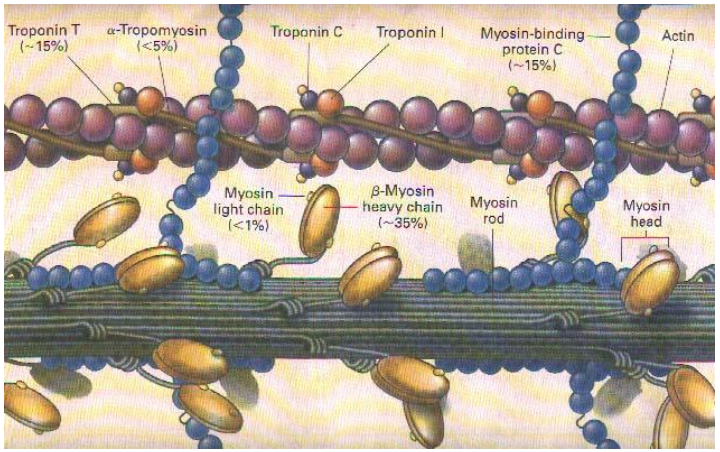
Volume overload hypertrophy

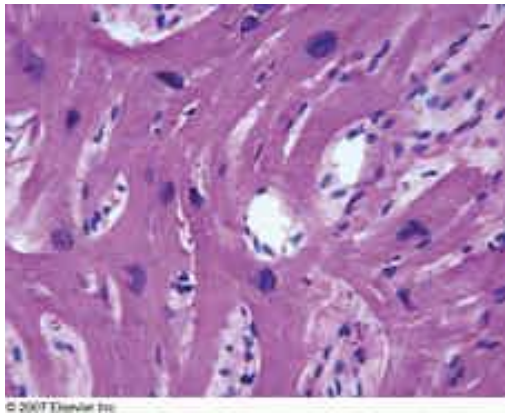


Hypertrophic cardiomyopathy

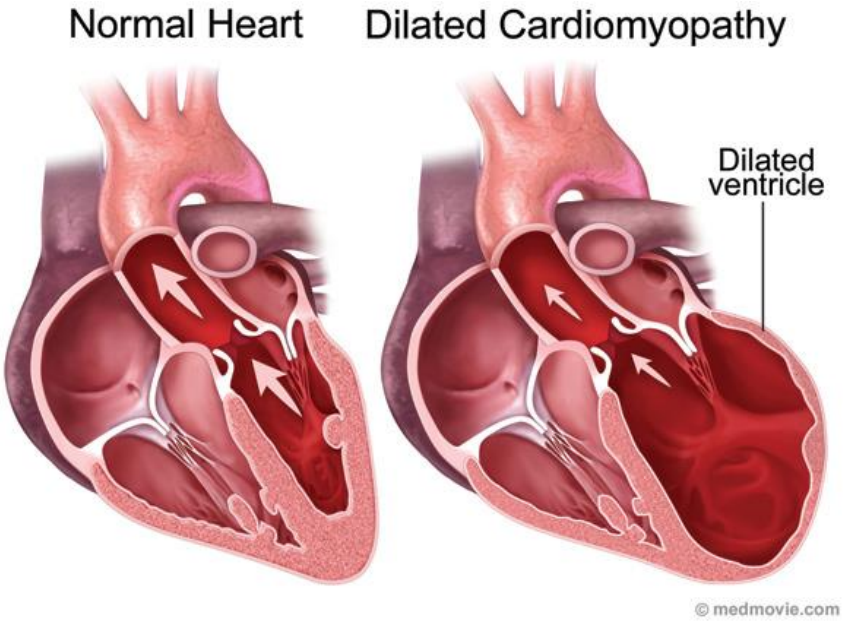


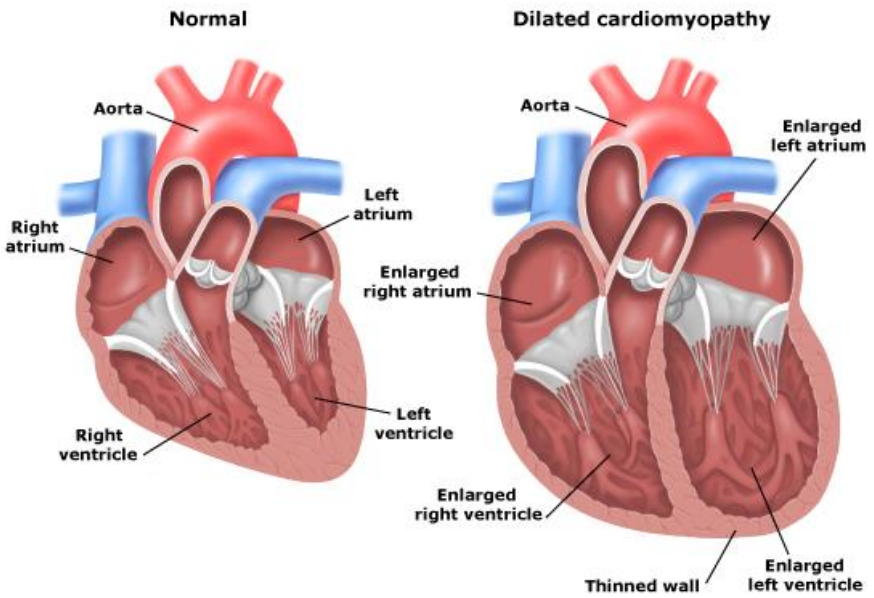


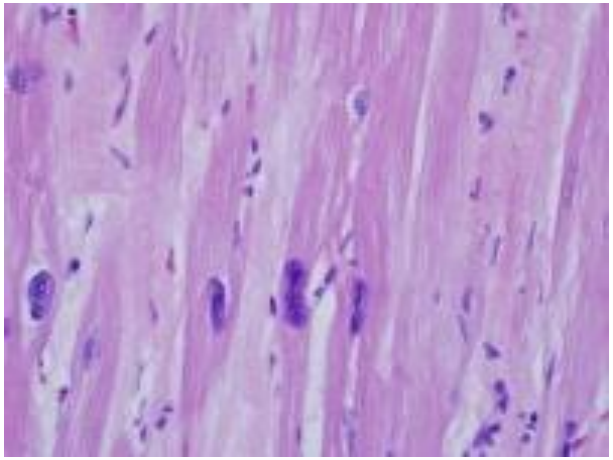


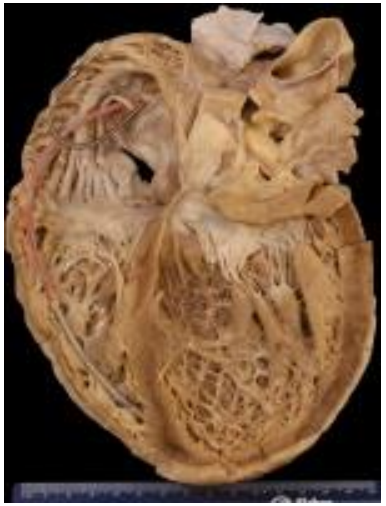


Dilated cardiomyopathy

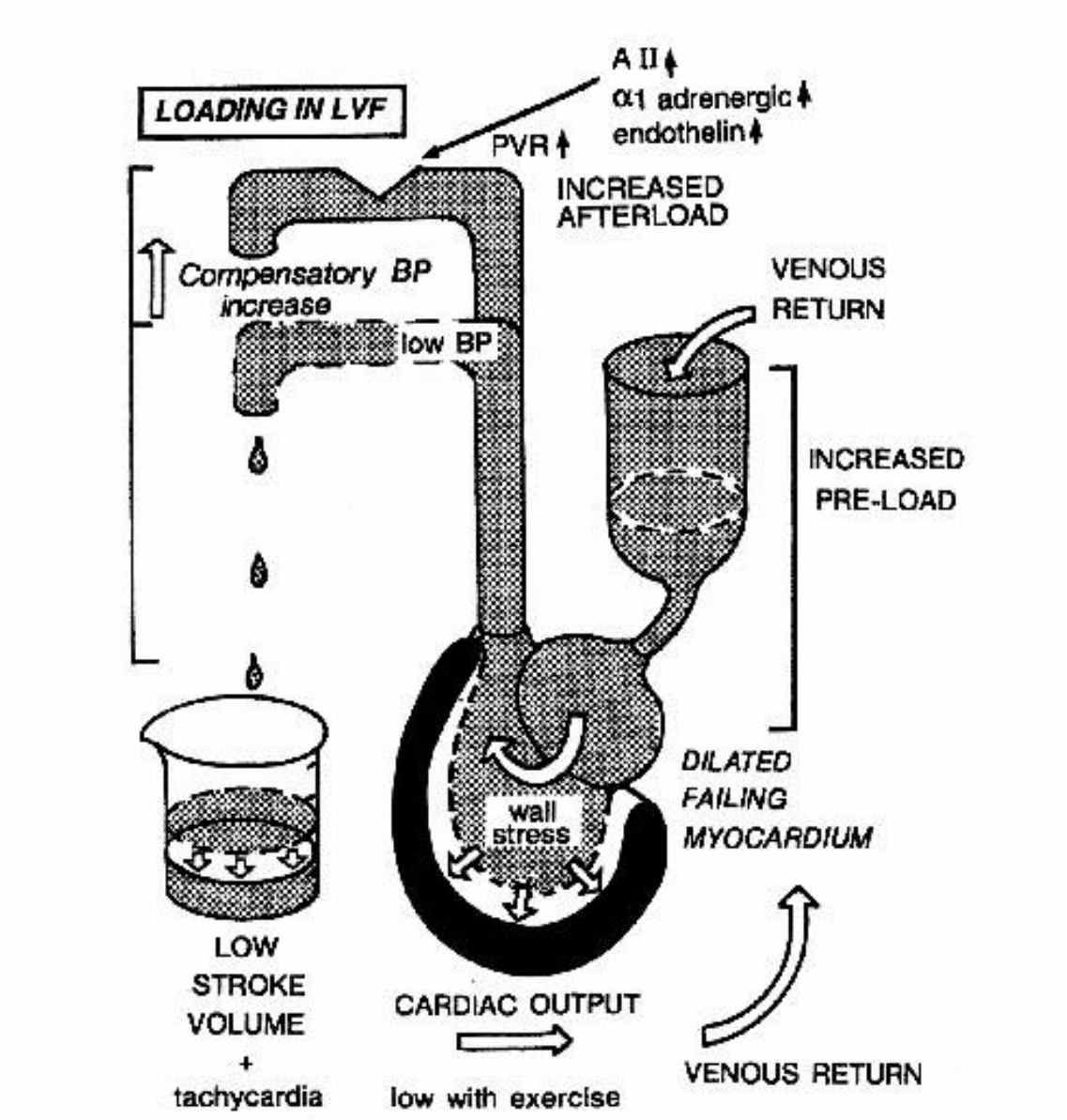




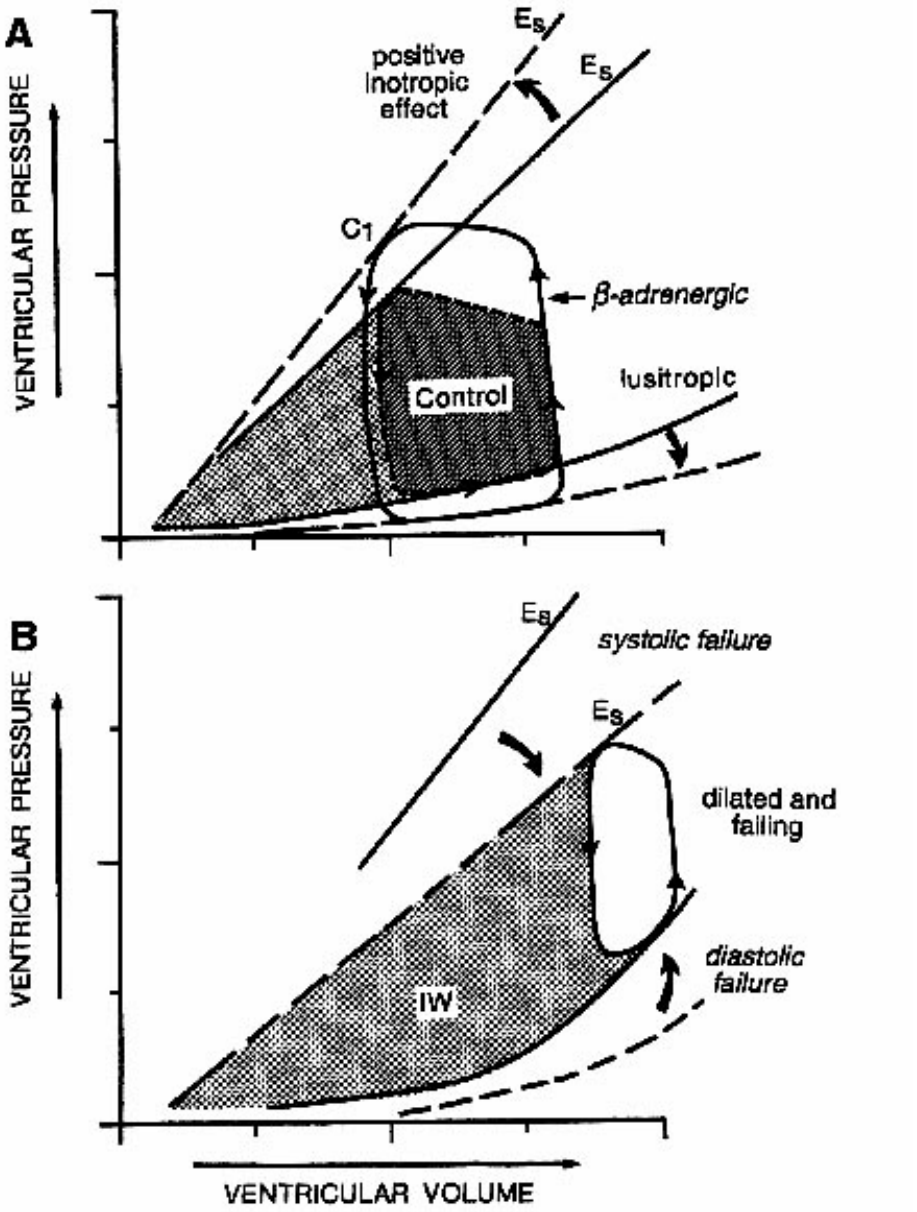




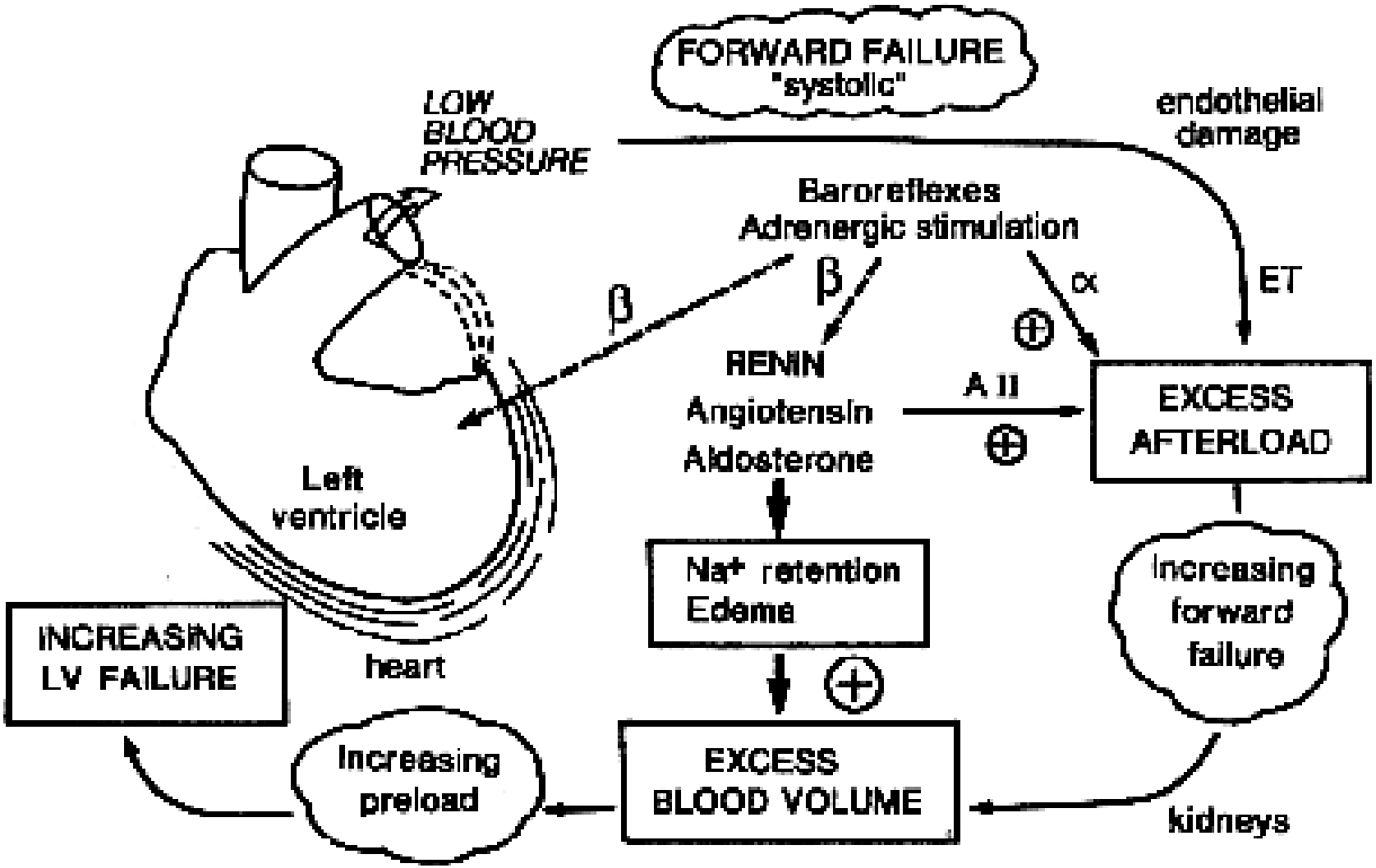
Haemodynamic changes during chronic heart failure



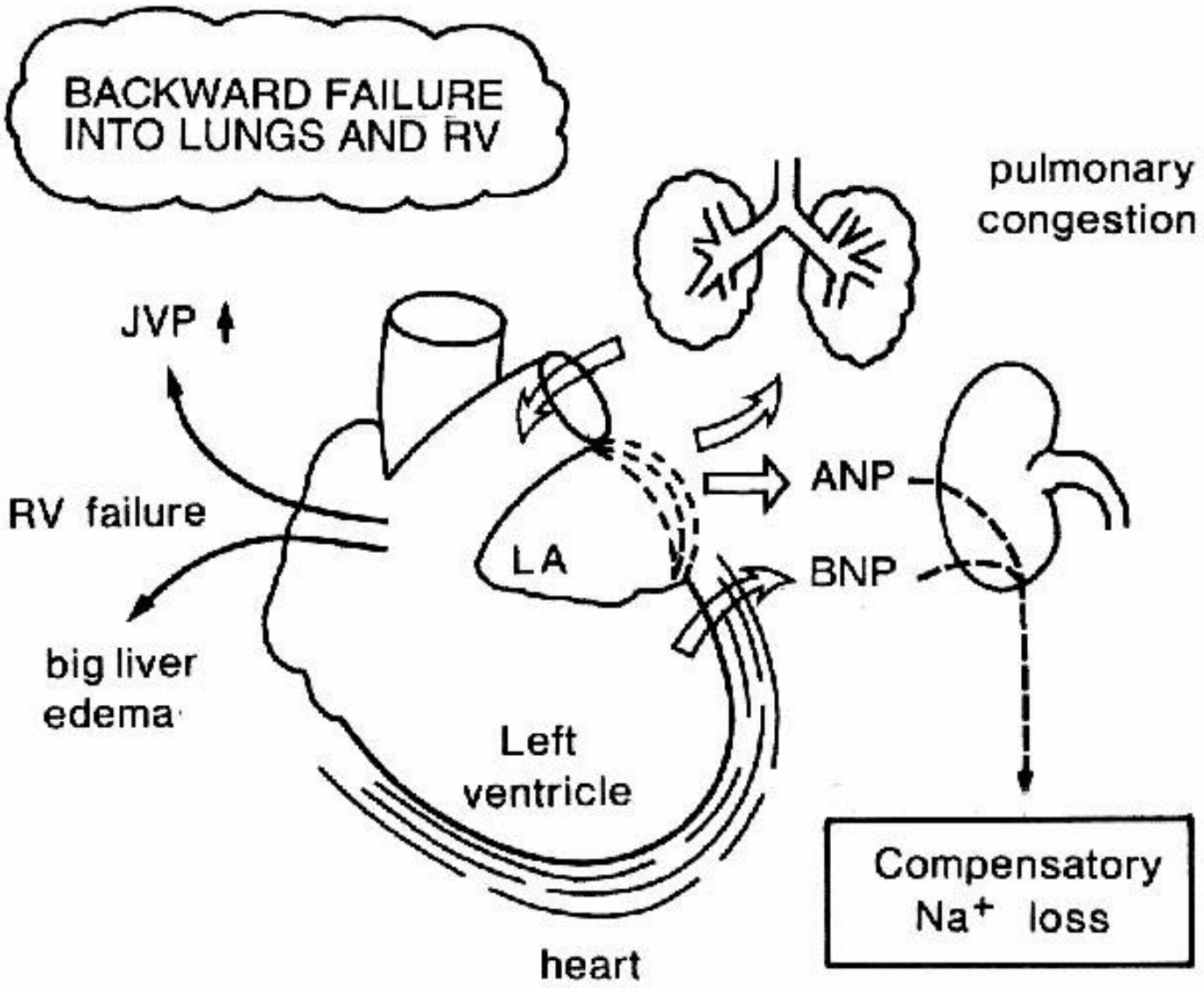
Healthy vs. failing myocardial energetics



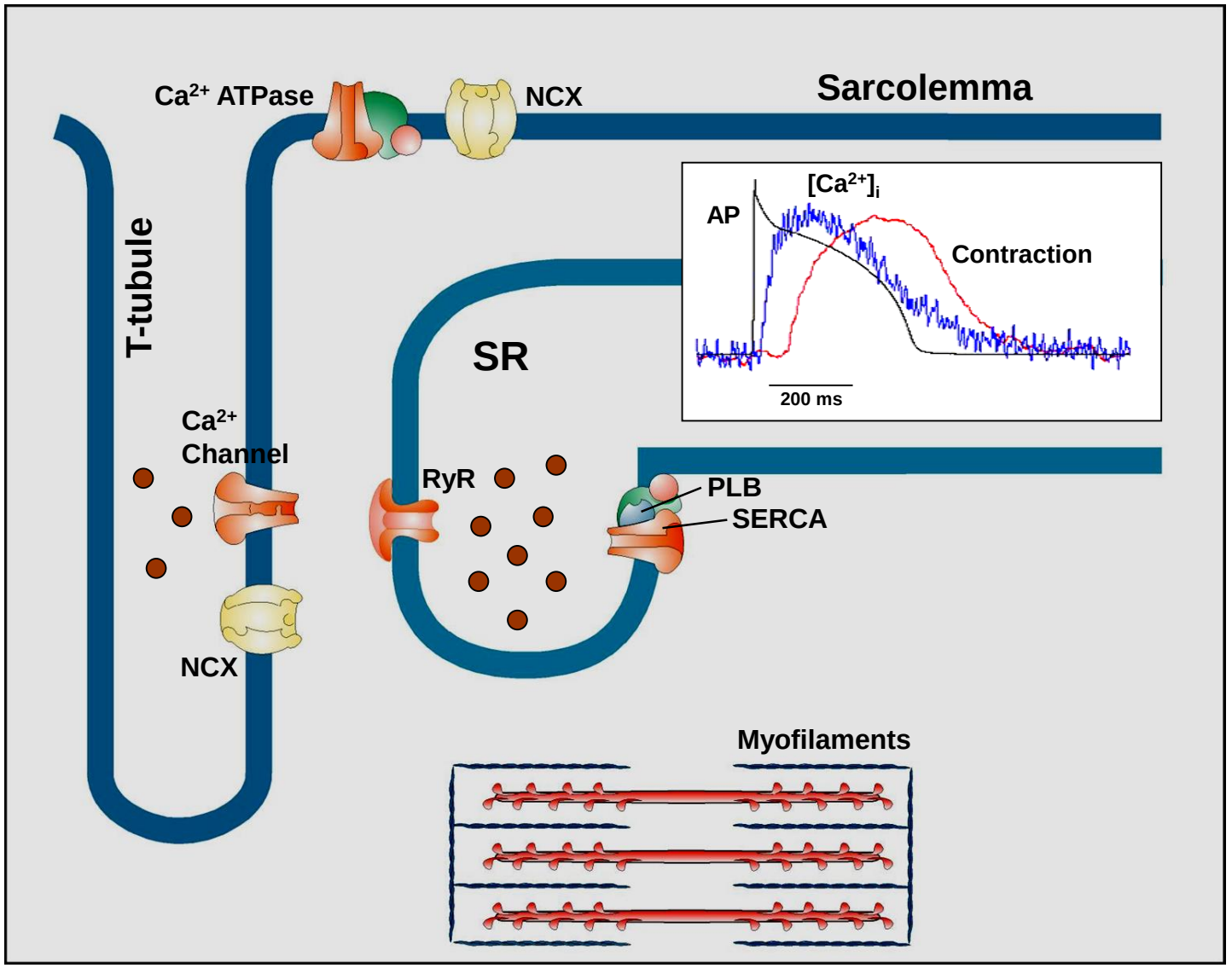
Forward left ventricular failure



Backward left ventricular failure

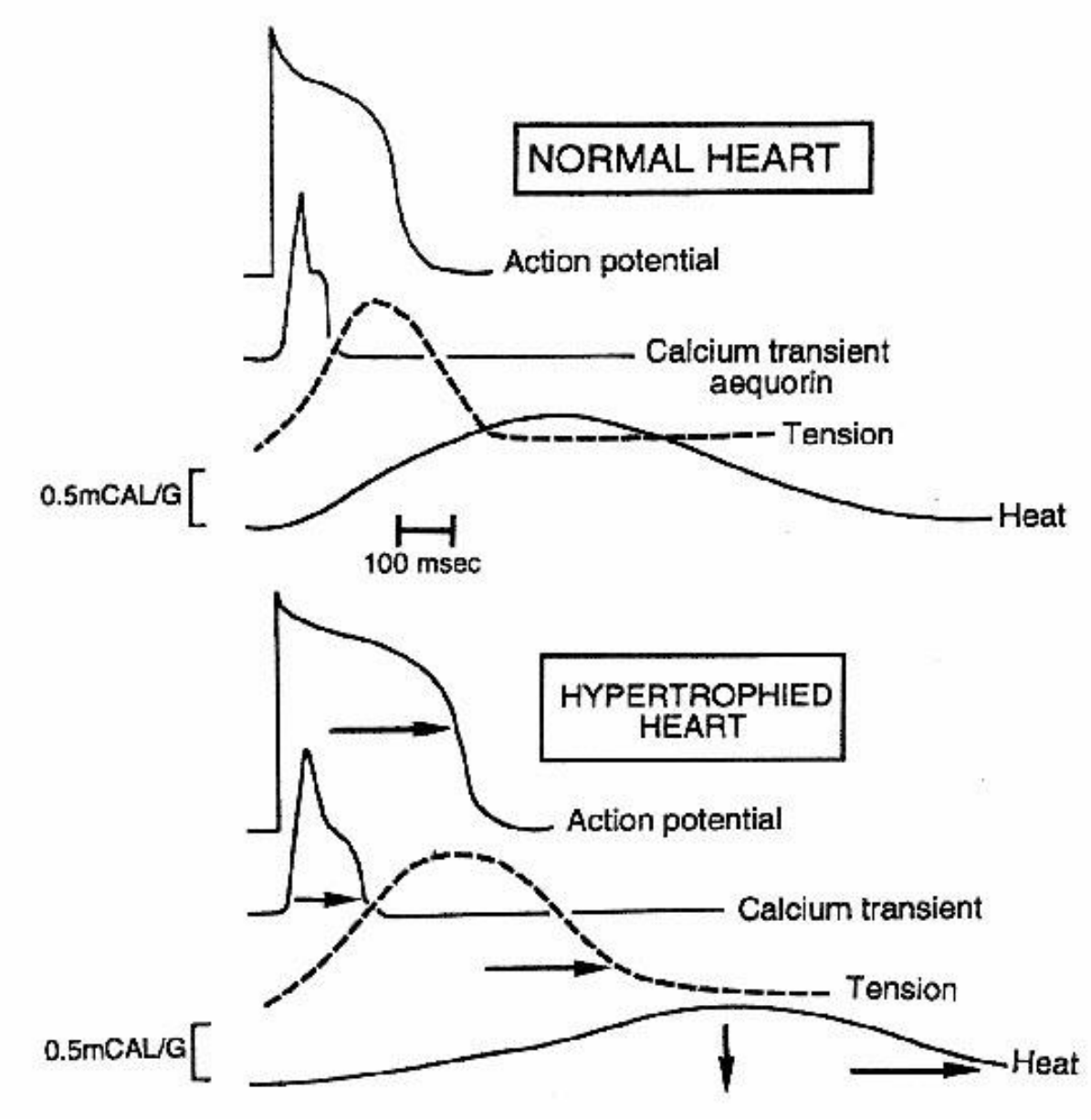


Ca^{2+} fluxes during excitation-contraction coupling

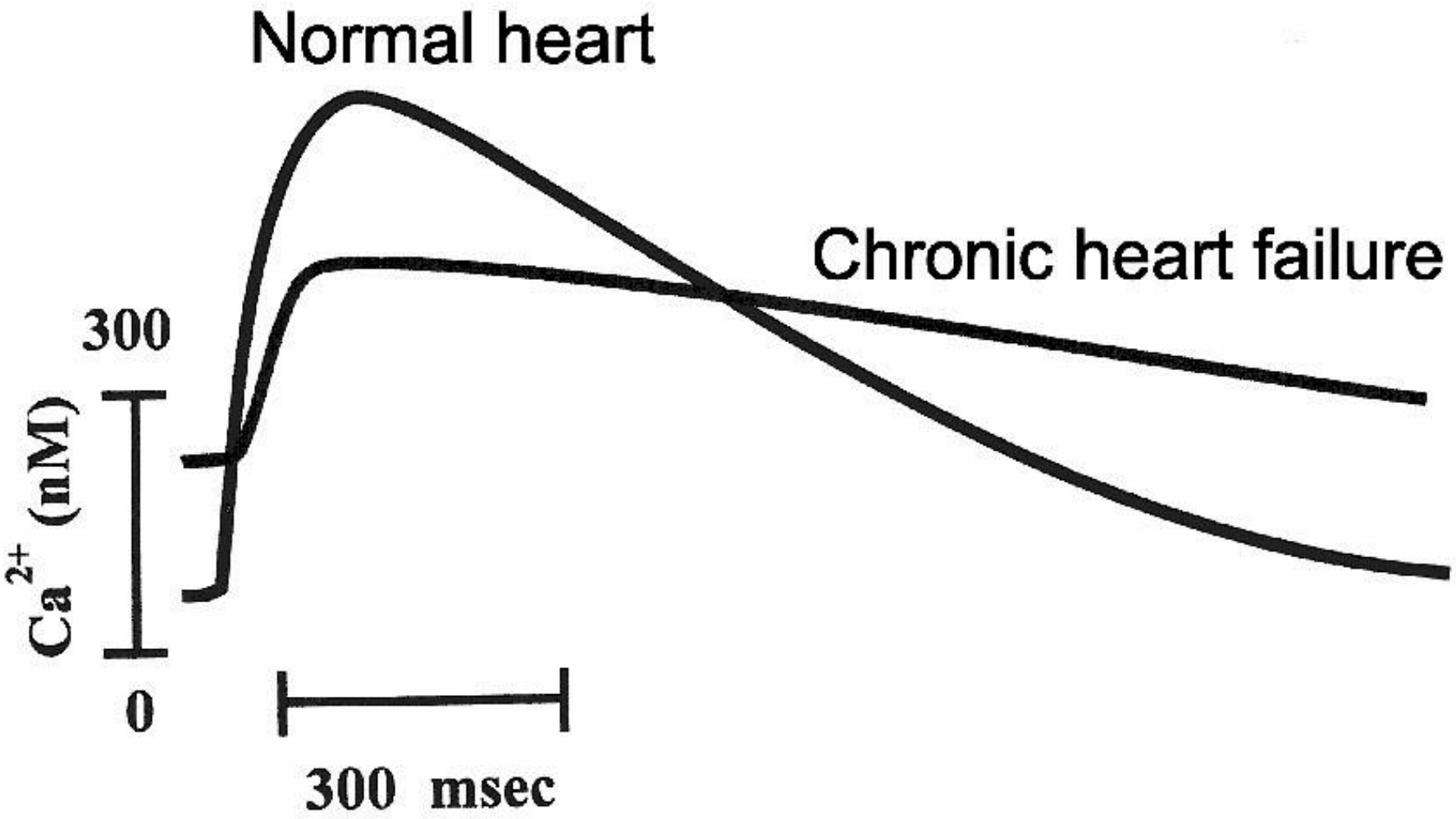


Adapted from Sjaastad et al., 2003

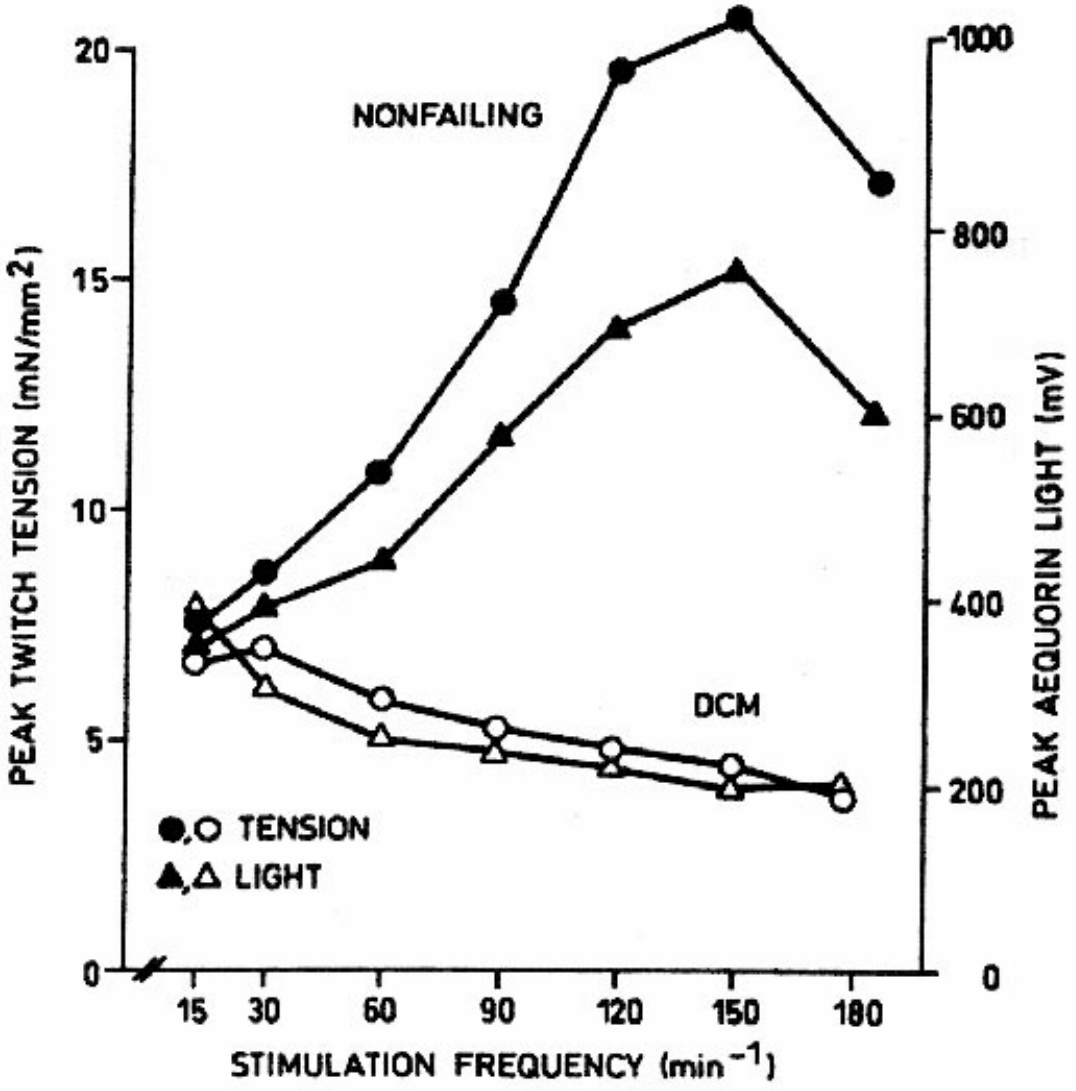
Cellular determinants of contractility during chronic heart failure



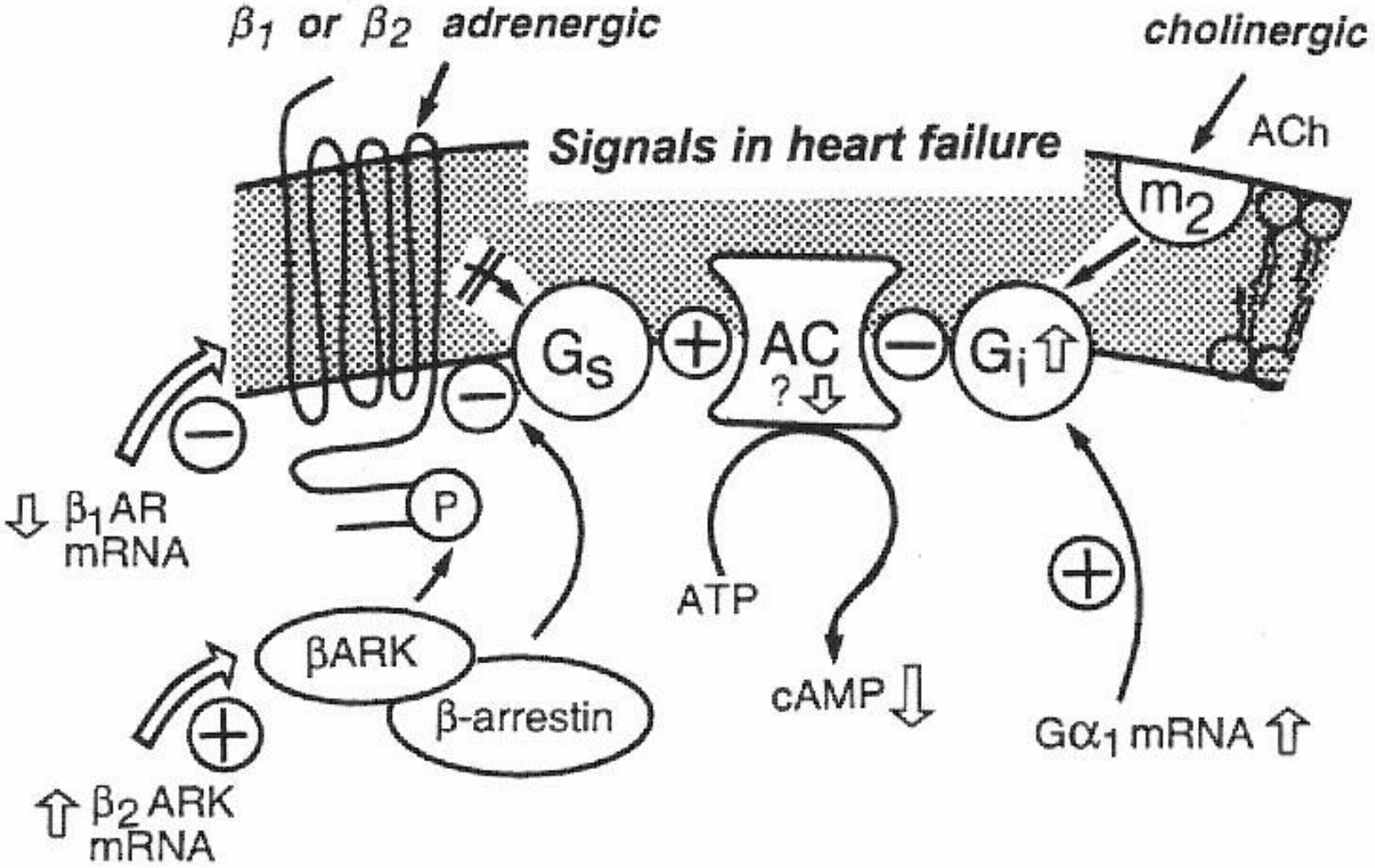
Ca^{2+}-transients during chronic heart failure



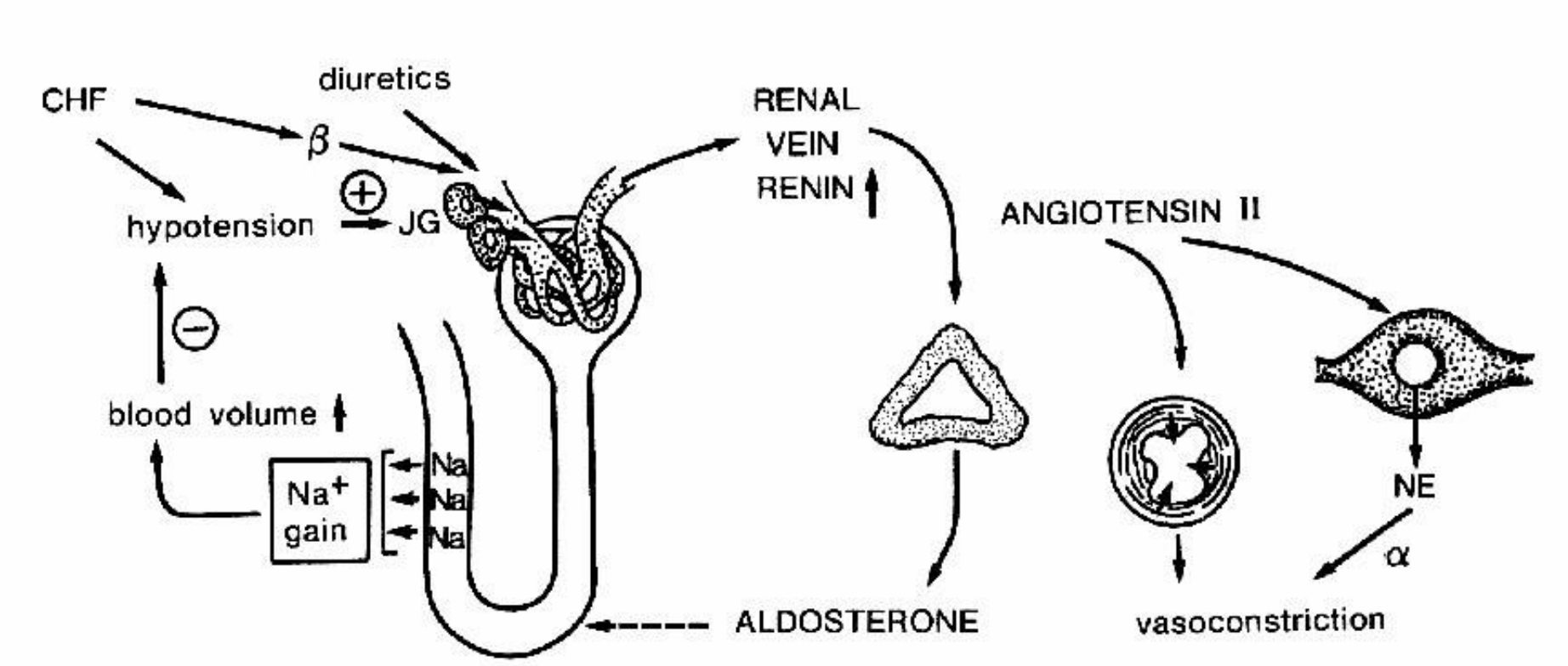
Blunted force-frequency relationship during chronic heart failure



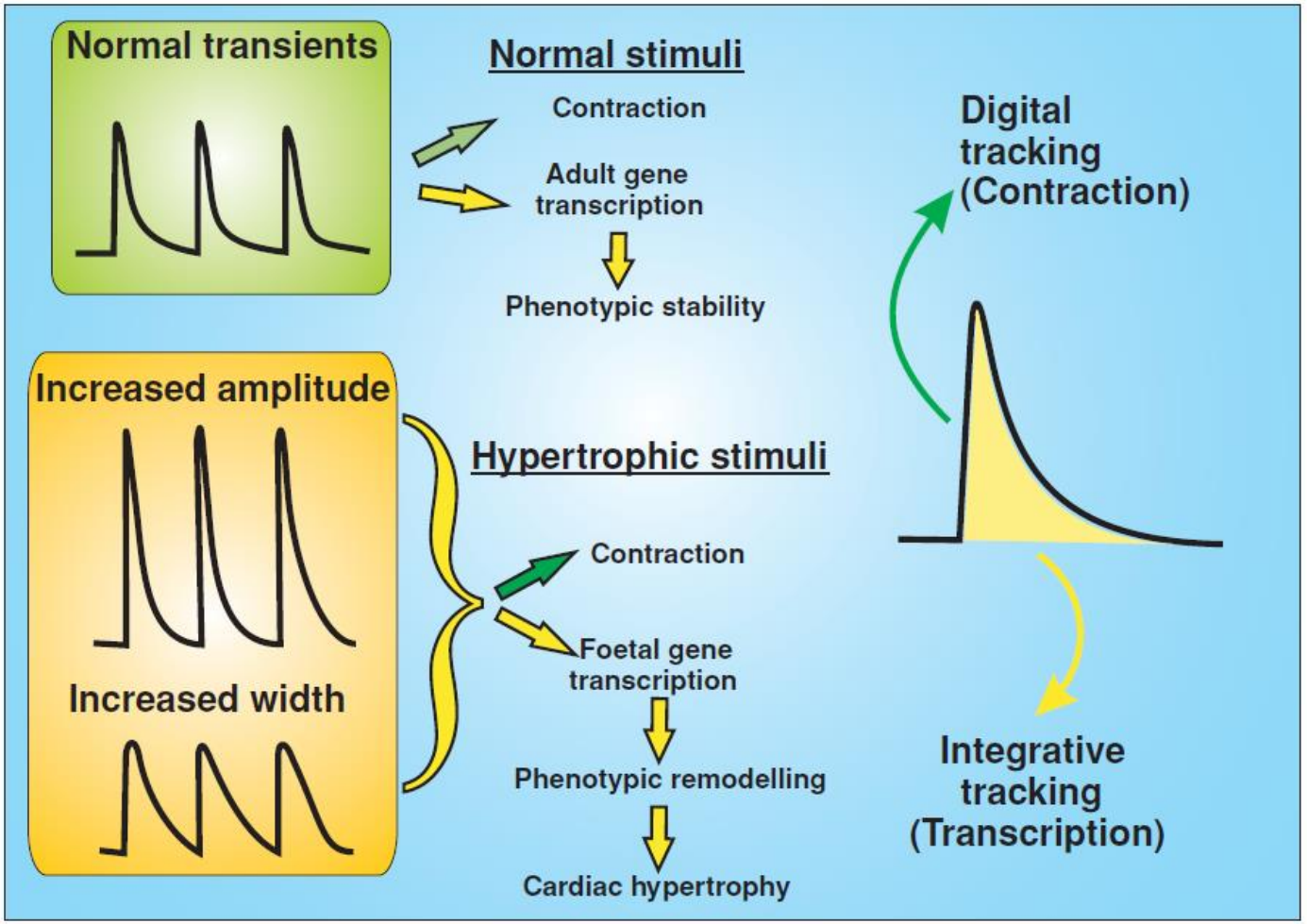
The β - adrenergic system during chronic heart failure



Renin-angiotensin system activation during chronic heart failure

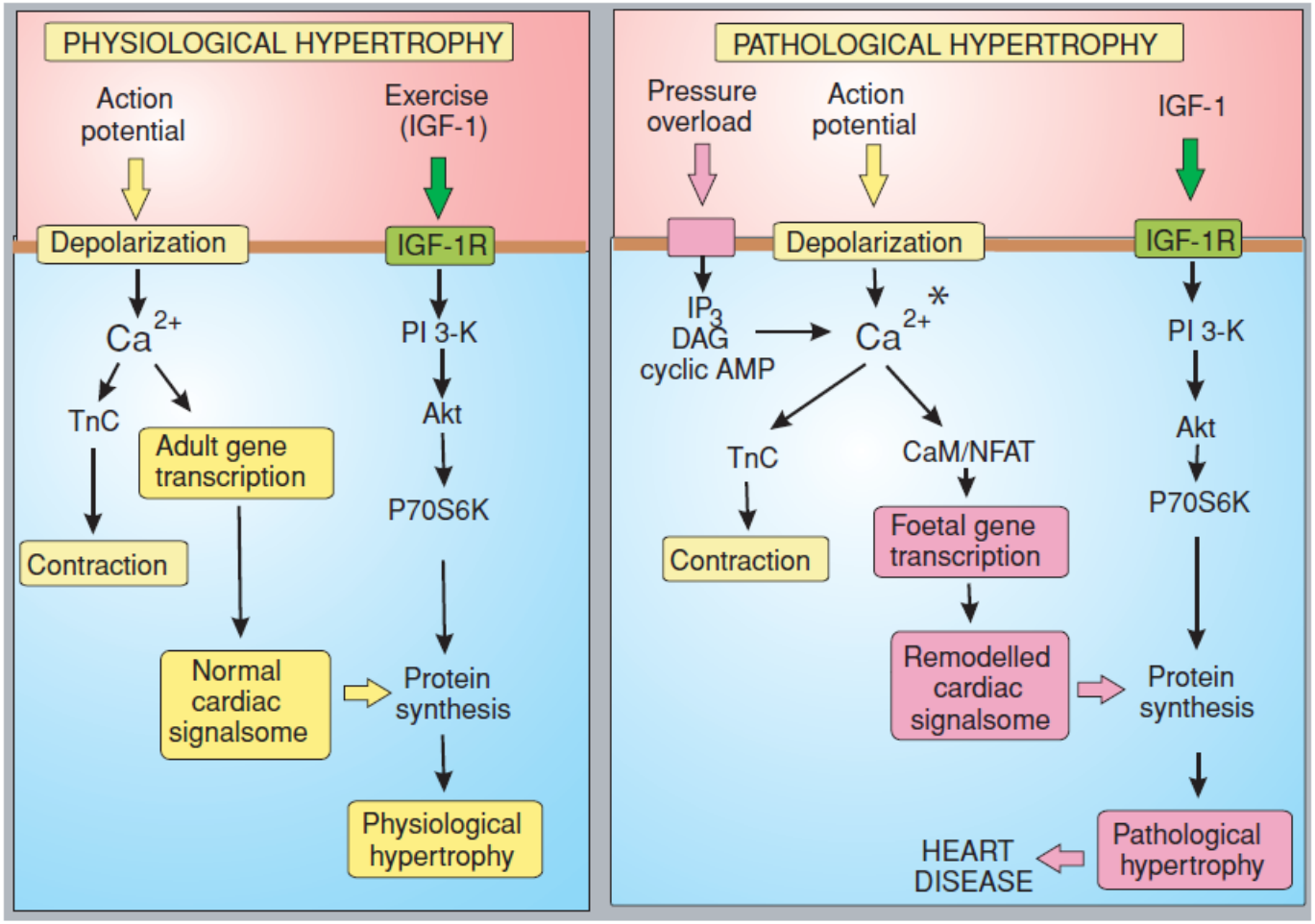


Hypothetical explanation for the hypertrophic process



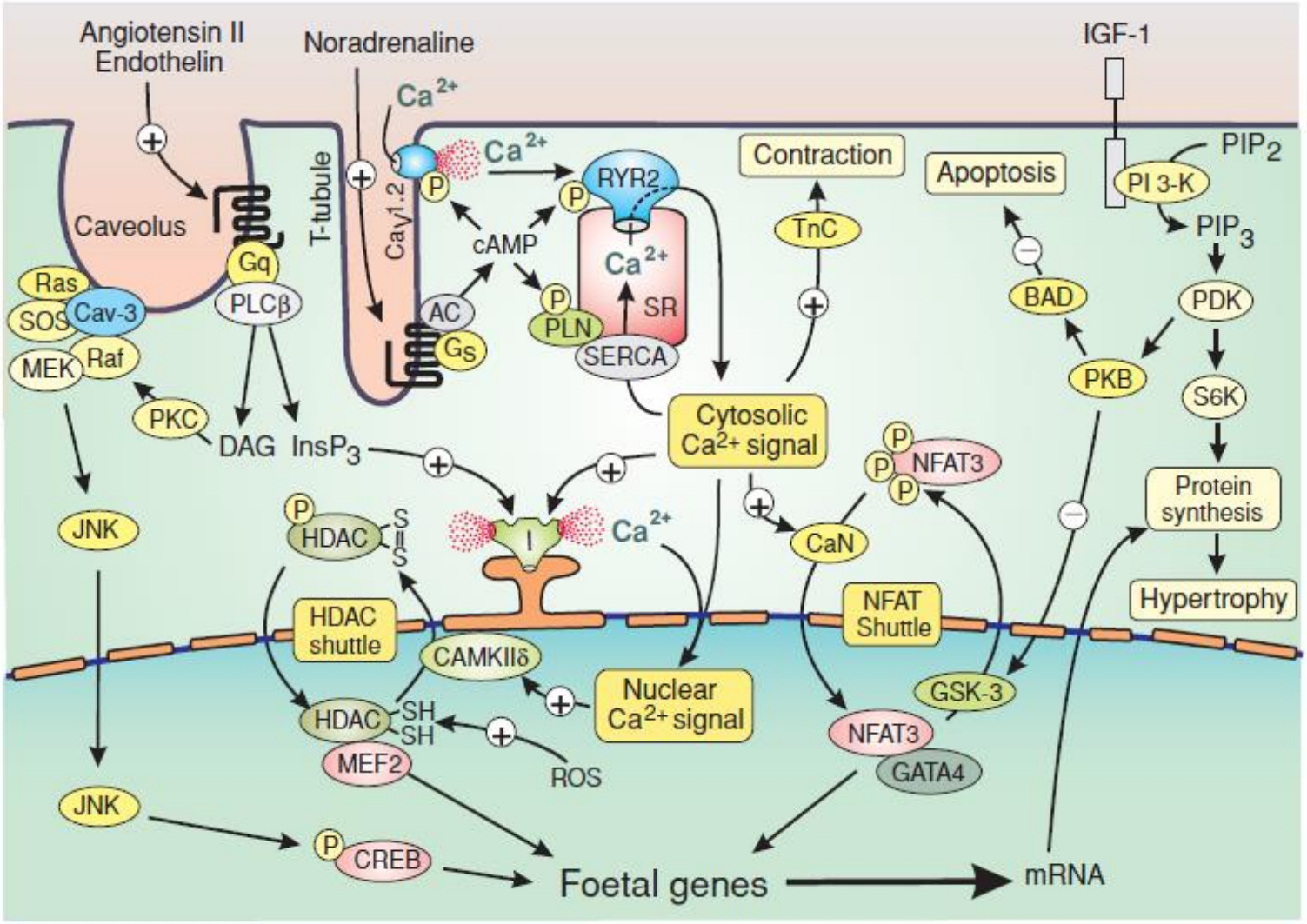
The normal transients drive both contraction and the transcription of adult genes to maintain phenotypic stability. Under conditions that induce hypertrophy, the modified Ca^{2+} transients (increase in amplitude or width) are such that they can induce both contraction and the activation of foetal genes that bring about the phenotypic remodelling that leads to cardiac hypertrophy.

Physiologic and patologic myocardial hypertrophy

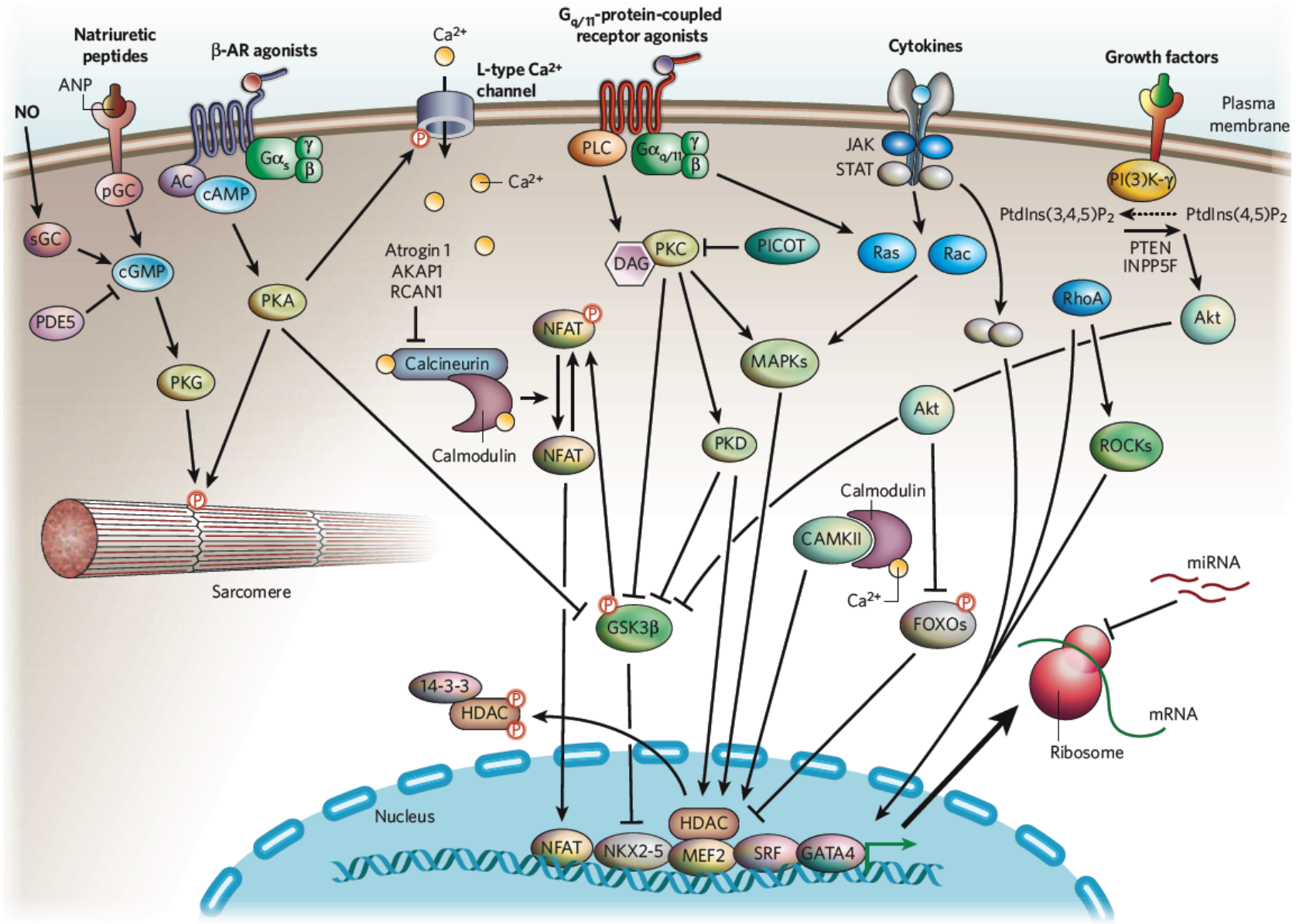


In physiological hypertrophy, action potentials generate a Ca^{2+} signal that controls contraction and may also stabilize the normal cardiac signalsome by maintaining the adult genes. The insulin-like growth factor 1 (IGF-1) that is produced during exercise uses this adult template when it activates protein synthesis, acting through the PtdIns 3-kinase (PI 3-K) signalling pathway. During pathological hypertrophy, pressure overload activates signalling pathways that alter the nature of the Ca^{2+} signal (∗), which activates a foetal set of genes that results in a remodelled cardiac signalsome that results in heart disease.

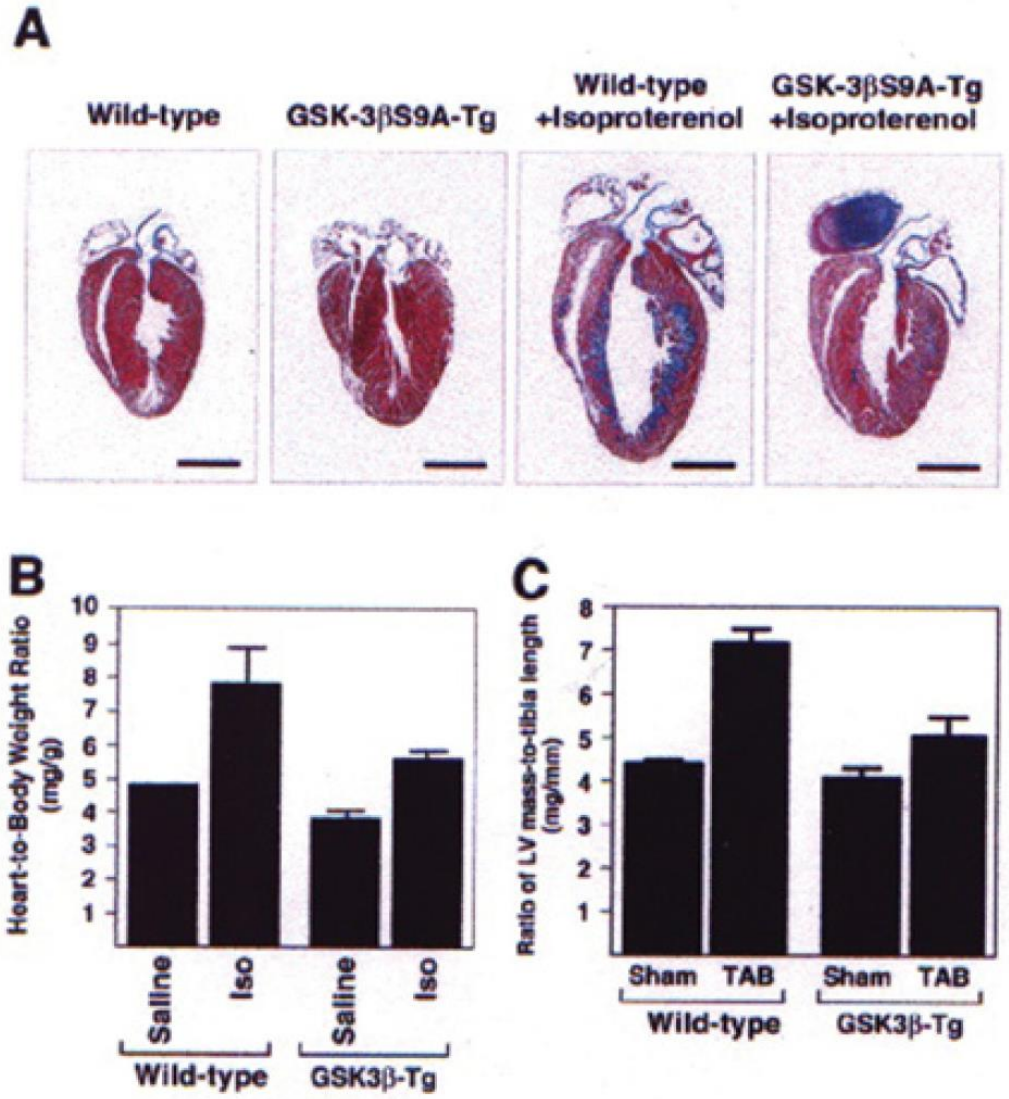
Signaling processes involved in cardiac remodelling



Parallel pathways and nodes in HF signaling



GSK-3β and cardiac hypertrophy



Molecular changes during chronic heart failure