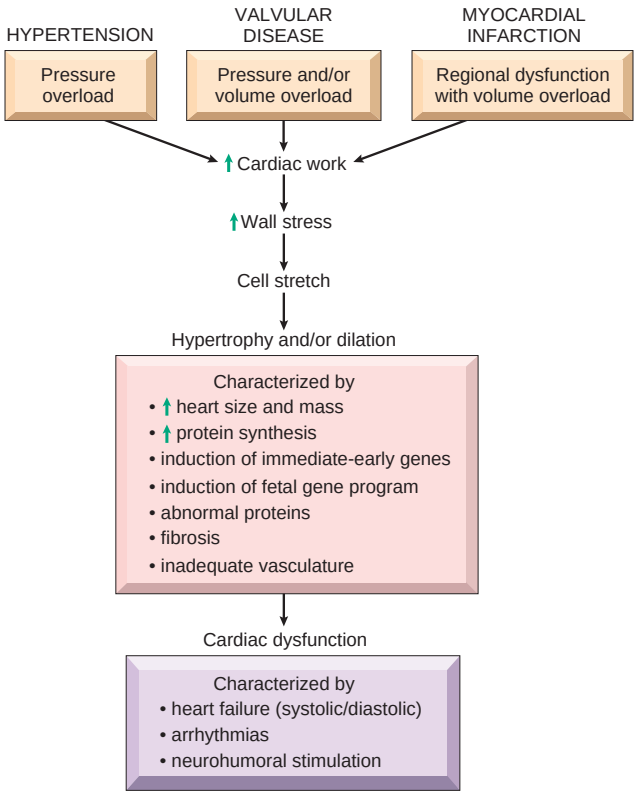

Figure 12-2 Schematic representation of the causes and consequences of cardiac hypertrophy.

Left-Sided Heart Failure

Left-sided heart failure is most often caused by:

- Ischemic heart disease
- Hypertension
- Aortic and mitral valvular diseases
- Primary myocardial diseases

The clinical and morphologic effects of left-sided CHF are a consequence of passive congestion (blood backing up in the pulmonary circulation), stasis of blood in the left-sided chambers, and inadequate perfusion of downstream tissues leading to organ dysfunction.

MORPHOLOGY

Heart. The heart findings depend on the disease process, ranging from myocardial infarcts, to stenotic or regurgitant valves, to intrinsic myocardial pathology. Except for failure caused by mitral valve stenosis or unusual restrictive cardiomyopathies (described later), the left ventricle is usually hypertrophied and often dilated, sometimes massively. The microscopic changes are nonspecific: primarily myocyte hypertrophy and variable degrees of interstitial fibrosis. Impaired left ventricular function usually causes secondary dilation of the left atrium, which increases the risk of atrial fibrillation. This in turn results in stasis of blood, particularly in the atrial appendage, which is a common site of thrombus formation.

Lungs. Pulmonary congestion and **edema** produce heavy, wet lungs, as described elsewhere (Chapters 4 and 15). Pulmonary changes—from mildest to most severe—include (1) perivascular and interstitial edema, particularly in the interlobular septa, responsible for the characteristic Kerley B and C lines noted on chest X-ray study in CHF, (2) progressive edematous widening of alveolar septa, and (3) accumulation of edema fluid in the alveolar spaces. Some red cells and plasma proteins extravasate into the edema fluid within the alveolar spaces, where they are phagocytosed and digested by macrophages, which store the iron recovered from hemoglobin in the form of hemosiderin. These *hemosiderin-laden macrophages* (also known as **heart failure cells**) are telltale signs of previous episodes of pulmonary edema. Pleural effusions arise from elevated pleural capillary pressure and the resultant transudation of fluid into the pleural cavities.

Early left-sided heart failure symptoms are related to pulmonary congestion and edema and may be subtle. Initially, cough and *dyspnea* (breathlessness) may occur only with exertion. As CHF progresses, worsening pulmonary edema may cause *orthopnea* (dyspnea when supine, relieved by sitting or standing) or *paroxysmal nocturnal dyspnea* (dyspnea usually occurring at night that is so severe that it induces a feeling of suffocation). Dyspnea at rest may follow. *Atrial fibrillation*, an uncoordinated, chaotic contraction of the atrium, exacerbates CHF owing to the loss of the atrial "kick" and its 10% to 15% contribution to ventricular filling.

A reduced ejection fraction leads to diminished renal perfusion, causing activation of the renin-angiotensin-aldosterone system as a compensatory mechanism to correct the "perceived" hypotension. This leads to salt and water retention, with expansion of the interstitial and intravascular fluid volumes (Chapters 4 and 11) that then exacerbate the ongoing pulmonary edema. If the hypoperfusion of the kidney becomes sufficiently severe, impaired excretion of nitrogenous products may cause azotemia (called *prerenal azotemia* because of its vascular origin; Chapter 20). In far-advanced CHF, cerebral hypoperfusion can give rise to *hypoxic encephalopathy* (Chapter 28), with irritability, loss of attention span, and restlessness that can progress to stupor and coma with ischemic cerebral injury.

Left-sided heart failure can be divided into systolic and diastolic failure:

- *Systolic failure* is defined by insufficient ejection fraction (pump failure), and can be caused by any of the many disorders that damage or derange the contractile function of the left ventricle.
- In *diastolic failure*, the left ventricle is abnormally stiff and cannot relax during diastole. Thus, although cardiac function is relatively preserved at rest, the heart is unable to increase its output in response to increases in the metabolic demands of peripheral tissues (e.g., during exercise). Moreover, because the left ventricle cannot expand normally, any increase in filling pressure is immediately transferred back into the pulmonary circulation, producing rapid onset pulmonary edema (*flash pulmonary edema*). Diastolic failure predominantly occurs in patients older than age 65 years and for unclear reasons is more common in women. Hypertension is the most common underlying etiology; diabetes mellitus, obesity, and bilateral renal artery stenosis may also