Table 12-1 Changes in the Aging Heart

Chambers
Increased left atrial cavity size
Decreased left ventricular cavity size
Sigmoid-shaped ventricular septum
Valves
Aortic valve calcific deposits
Mitral valve annular calcific deposits
Fibrous thickening of leaflets
Buckling of mitral leaflets toward the left atrium
Lambl excrescences
Epicardial Coronary Arteries
Tortuosity
Diminished compliance
Calcific deposits
Atherosclerotic plaque
Myocardium
Decreased mass
Increased subepicardial fat
Brown atrophy
Lipofuscin deposition
Basophilic degeneration
Amyloid deposits
Aorta
Dilated ascending aorta with rightward shift
Elongated (tortuous) thoracic aorta
Sinotubular junction calcific deposits
Elastic fragmentation and collagen accumulation
Atherosclerotic plaque

pressure spikes with each cardiac contraction that are transmitted to distal organs.

Compared with younger myocardium, "elderly" myocardium has fewer myocytes, increased collagenized connective tissue and, often the deposition of extracellular amyloid (most commonly due to poorly catabolized transthyretin; see Chapter 6).

Most importantly, the progressive atherosclerosis (Chapter 11)—over a period of 50 to 60 years—finally ends up causing significant stenosis, or weakens the wall sufficiently to give rise to catastrophic dissection of the aortic wall (see later).

Overview of Cardiac Pathophysiology

Cardiovascular dysfunction can be attributed to one (or more) of six principal mechanisms:

- *Pump failure.* In some conditions, the myocardium contracts weakly during systole and there is inadequate cardiac output. Conversely, myocardium may relax insufficiently during diastole to permit adequate ventricular filling.
- *Flow obstruction.* Lesions can obstruct blood flow through a vessel (e.g., atherosclerotic plaque) or prevent valve opening or otherwise cause increased ventricular chamber pressure (e.g., aortic valvular stenosis, systemic hypertension, or aortic coarctation). In the case of a valvular blockage, the increased pressure overloads the chamber that pumps against the obstruction.
- *Regurgitant flow.* A portion of the output from each contraction flows backward through an incompetent valve, adding a volume overload to the affected atria or ventricles (e.g., left ventricle in aortic regurgitation; left atrium and left ventricle in mitral regurgitation).
- *Shunted flow.* Blood can be diverted from one part of the heart to another (e.g., from the left ventricle to the right ventricle), through defects that can be congenital or acquired (e.g., following myocardial infarction). Shunted flow can also occur between blood vessels, as in patent ductus arteriosus (PDA).
- *Disorders of cardiac conduction.* Conduction defects or arrhythmias due to uncoordinated generation or transmission of impulses (e.g., atrial or ventricular fibrillation) lead to nonuniform and inefficient myocardial contractions, and may in fact be lethal.
- *Rupture of the heart or a major vessel.* In such circumstances (e.g., gunshot to the left ventricle, or aortic dissection and rupture), there is cataclysmic exsanguination, either into body cavities or externally.

Most cardiovascular disease results from a complex interplay of genetics and environmental factors; these may disrupt signaling pathways that control morphogenesis, impact myocyte survival after injury, or affect contractility or electrical conduction in the face of biomechanical stressors. Indeed, the pathogenesis of many congenital heart defects involves an underlying genetic abnormality whose expression is modified by environmental or maternal factors (see later). Moreover, genes that control the development of the heart may also regulate the response to various forms of injury including aging. Subtle polymorphisms can significantly impact the risk of many forms of heart disease, and, as discussed later, a number of adult-onset heart disorders have a fundamentally genetic basis. Thus, cardiovascular genetics provides an important window on the pathogenesis of heart disease and increasingly molecular diagnoses are becoming a critical part of its classification.

Heart Failure

Heart failure, often called *congestive heart failure (CHF)*, is a common, usually progressive condition with a poor prognosis. Each year in the United States, CHF affects more than 5 million individuals (approximately 2% of the population), necessitating more than a million hospitalizations, and contributing to the death of nearly 300,000 people.

CHF occurs when the heart is unable to pump blood at a rate sufficient to meet the metabolic demands of the tissues or can do so only at an elevated filling pressure. It is the common end stage of many forms of chronic heart disease, often developing insidiously from the cumulative effects of chronic work overload (e.g., in valve disease or hypertension) or ischemic heart disease (e.g., following myocardial infarction with heart damage). However, acute hemodynamic stresses, such as fluid overload, abrupt valvular dysfunction, or myocardial infarction, can all precipitate sudden CHF.

When cardiac workload increases or cardiac function is compromised, several physiologic mechanisms maintain arterial pressure and organ perfusion: