hypoplasia of the left ventricle and ascending aorta, sometimes accompanied by dense, porcelain-like left ventricular endocardial fibroelastosis. The ductus must be open to allow blood flow to the aorta and coronary arteries, and the constellation of findings is called the *hypoplastic left heart syndrome*. Unless a palliative procedure is done to preserve PDA patency, duct closure in the first week of life is generally lethal. However, less severe congenital aortic stenosis can be compatible with long survival.

Subaortic stenosis is caused by a thickened ring or collar of dense endocardial fibrous tissue below the level of the cusps. *Supravalvular aortic stenosis* is a congenital aortic dysplasia with thickening of ascending aortic wall and consequent luminal constriction. In some cases it is a component of a multiorgan developmental disorder resulting from deletions on chromosome 7 that include the gene for elastin. Other features of the syndrome include hypercalcemia, cognitive abnormalities, and characteristic facial anomalies (*Williams-Beuren syndrome*). Elastin gene mutations may cause supravalvular stenosis by disrupting elastin–smooth muscle cell interactions during aortic morphogenesis.

Subaortic stenosis is usually associated with a prominent systolic murmur and sometimes a thrill. Pressure hypertrophy of the left ventricle develops as a consequence of the obstruction to blood flow, but congenital stenoses are well tolerated unless very severe. Although mild stenoses can often be managed conservatively with antibiotic prophylaxis (to prevent endocarditis) and avoidance of strenuous activity, the resulting left ventricular hypertrophy still carries a risk of sudden death with exertion.

KEY CONCEPTS

Congenital Heart Disease

- Congenital heart disease represents defects of cardiac chambers or the great vessels; these either result in shunting of blood between the right and left circulation or cause outflow obstructions. Lesions range from relatively asymptomatic to rapidly fatal. Environmental (toxic or infectious) and genetic causes both contribute, and the manifestations depend on the timing of the environmental insult or which step in cardiac development is affected.
- Left-to-right shunts are most common and are typically associated with ASDs, VSDs, or a PDA. These lesions result in chronic right-sided pressure and volume overloads that eventually cause pulmonary hypertension with reversal of flow and right-to-left shunts with cyanosis (*Eisenmenger syndrome*).
- Right-to-left shunts are most commonly caused by TOF or TGA. These are cyanotic lesions from the outset and are associated with polycythemia, hypertrophic osteoarthropathy, and paradoxical emboli.
- Obstructive lesions include aortic coarctation; the clinical severity of the lesion depends on the degree of stenosis and the patency of the ductus arteriosus.

Ischemic Heart Disease

Ischemic heart disease (IHD) represents a group of pathophysiologically related syndromes resulting from *myocardial ischemia*—an imbalance between myocardial supply (perfusion) and cardiac demand for oxygenated blood. Ischemia not only limits tissue oxygenation (and thus ATP generation), but also reduces the availability of nutrients and the removal of metabolic wastes (Chapter 2). Thus, cardiac ischemia is generally less well tolerated than hypoxia *per se,* such as may occur with severe anemia, cyanotic heart disease, or advanced lung disease.

In more than 90% of cases, myocardial ischemia results from reduced blood flow due to obstructive atherosclerotic lesions in the epicardial coronary arteries; consequently, IHD is frequently referred to as coronary artery disease (CAD). In most cases there is a long period (up to decades) of silent, slow progression of coronary lesions before the sudden onset of symptoms. Thus, IHD is often the late manifestation of coronary atherosclerosis that began during childhood or adolescence (Chapter 11).

IHD can present as one or more of the following clinical syndromes:

- *Myocardial infarction (MI)*, where ischemia causes frank cardiac necrosis
- *Angina pectoris* (literally "chest pain"), where ischemia is not severe enough to cause infarction, but the symptoms nevertheless portend infarction risk
- *Chronic IHD with heart failure*
- *Sudden cardiac death (SCD).*

In addition to coronary atherosclerosis, myocardial ischemia can be caused by coronary emboli, myocardial vessel inflammation, or vascular spasm. Moreover, otherwise modest vascular occlusions may become consequential in the setting of increased cardiac energy demand (e.g., myocardial hypertrophy or increased heart rate), hypoxemia, or systemic hypotension (e.g., shock). Some conditions can have multiple deleterious effects. Thus, tachycardia increases oxygen demand (because of more contractions per unit time) while decreasing functional supply (by decreasing the relative time spent in diastole, when cardiac perfusion occurs).

Epidemiology. IHD is the leading cause of death in the United States (one of every six deaths in 2008; more than 400,000 individuals) and other developed nations (approximately 7 million total per year). As high as these numbers are, they represent a substantial improvement relative to just one to two generations ago. Since peaking in 1963, the overall death rate from IHD has fallen in the United States by approximately 50%. This remarkable improvement can be attributed to:

- *Prevention*, achieved by modifying important risk factors, such as smoking, blood cholesterol, and hypertension. Additional risk reduction and prevention may potentially be achieved by maintenance of normal blood glucose levels in diabetic patients, control of obesity, and exercise.
- *Diagnostic and therapeutic advances*, allowing earlier and more effective treatments. The latter include new medications, including the use of cholesterol lowering drugs such as statins, coronary care units, thrombolysis for MI, percutaneous transluminal coronary angioplasty, endovascular stents, coronary artery bypass graft (CABG) surgery, and improved control of heart