- Right heart failure is most often due to left heart failure, and less commonly to primary pulmonary disorders; symptoms are chiefly related to peripheral edema and visceral congestion.

Congenital Heart Disease

Congenital heart disease (CHD) is a general term designating abnormalities of the heart or great vessels that are present at birth. Most congenital heart disease arises from faulty embryogenesis during gestational weeks 3 through 8, when major cardiovascular structures form and begin to function. The most severe anomalies are incompatible with intrauterine survival and significant heart malformations are common among premature infant and stillborns. On the other hand, defects that affect individual chambers or discrete regions of the heart are often compatible with embryologic maturation and eventual live birth. In this category are septation defects, unilateral obstructions, and outflow tract anomalies. Septal defects, or "holes in the heart", include atrial septal defects (ASDs) or ventricular septal defects (VSDs). Stenotic lesion can be at the level of the cardiac valve or entire cardiac chamber, as in hypoplastic left heart syndrome. Outflow tract anomalies include inappropriate routing of the great vessels from the ventricular mass. These forms of congenital heart disease usually produce clinically important manifestations only after birth—unveiled by the transition from fetal to perinatal circulation.

Incidence. With an incidence of up to 5%, congenital cardiovascular malformations are among the most prevalent birth defects and are the most common type of pediatric heart disease. Approximately 1% of individuals have significant forms of congenital heart disease that are diagnosed in the first year of life. However, milder forms of congenital heart disease such as bicuspid semilunar valves, with an incidence itself of 1-2%, may not become evident until adulthood. Twelve disorders account for about 85% of cases; their frequencies are listed in Table 12-2.

The number of individuals who survive into adulthood with congenital heart disease is increasing rapidly and is estimated at nearly 1 million individuals in the United States. Many have benefited from advances in early postnatal (and even intrauterine) surgical repair of their structural defects. In some cases, however, surgical repairs fail to restore complete normalcy; patients may have already sustained pulmonary or myocardial changes that are no longer reversible, or may suffer from arrhythmias due to surgical scarring. Other factors that impact the long-term outcome include risks associated with the use of prosthetic materials and devices (e.g., substitute valves or myocardial patches), and the cardiovascular stressors associated with childbearing that may tip a repaired heart into failure.

Cardiac Development. The diverse malformations seen in congenital heart disease are caused by errors that occur during cardiac morphogenesis (Fig. 12-3). The earliest cardiac precursors originate in lateral mesoderm and move to the midline in two migratory waves to create a crescent of cells consisting of the first and second heart fields by about day 15 of development. Both fields contain multipotent progenitor cells that can produce all of the major cell types of the heart: endocardium, myocardium, and smooth muscle cells. However, each heart field is differentially marked by the expression of distinct gene sets. Thus, the first heart field expresses the transcription factor Hand1, whereas the second heart field expresses the transcription factor Hand2 and the secreted protein fibroblast growth factor-10.

Even at this very early stage of development, each heart field is destined to give rise to particular portions of the heart. Thus, the left ventricle largely derives from cells originating in the first heart field, whereas cells from the second heart field become the outflow tract, right ventricle, and most of the atria. By day 20, the initial cell crescent develops into a beating tube, which loops to the right and begins to form the basic heart chambers roughly 8 days later. At the same time, two other critical events occur: (1) neural crest–derived cells migrate into the outflow tract, where they participate in the septation of the outflow tract and the formation of the aortic arches, and (2) interstitial connective tissue that will become the future atrioventricular canal and outflow tract enlarges to produce swellings known as endocardial cushions. By day 50, further septation of the ventricles, atria, and atrioventricular valves produces a four-chambered heart.

Proper orchestration of these remarkable transformations depends on a network of transcription factors that are regulated by a number of signaling pathways, particularly the Wnt, hedgehog, vascular endothelial growth factor (VEGF), bone morphogenetic factor, TGFβ, fibroblast growth factor, and Notch pathways (Chapter 1). In addition, specific micro-RNAs play critical roles in cardiac development by coordinating patterns and levels of transcription factor expression. The heart is a mechanical organ that generates pulsatile blood from its earliest stages of development. It is therefore likely that hemodynamic forces play an important role in cardiac development, just as they influence adaptations in the adult heart such as hypertrophy and dilation.

Table 12-2 Frequencies of Congenital Cardiac Malformations*

Malformation	Incidence per Million Live Births	%
Ventricular septal defect	4482	42
Atrial septal defect	1043	10
Pulmonary stenosis	836	8
Patent ductus arteriosus	781	7
Tetralogy of Fallot	577	5
Coarctation of the aorta	492	5
Atrioventricular septal defect	396	4
Aortic stenosis	388	4
Transposition of the great arteries	388	4
Truncus arteriosus	136	1
Total anomalous pulmonary venous connection	120	1
Tricuspid atresia	118	1
Total	9757	

*Presented as upper quartile of 44 published studies. Percentages do not add up to 100% because of rounding.
Source: Hoffman JIE, Kaplan S: The incidence of congenital heart disease. J Am Coll Cardiol 39:1890, 2002.