actively resequestered into the sarcoplasmic reticulum, where it is stored by various proteins, including calsequestrin, until the next wave of depolarization occurs. Calcium is also extruded from the cytosol by various calcium pumps in the sarcolemma. The active removal of intracellular calcium by ATP ion pumps facilitates ventricular relaxation, which is necessary for proper ventricular filling during diastole.

Circulatory Physiology and the Cardiac Cycle

The term *cardiac cycle* describes the pressure changes within each cardiac chamber over time (Fig. 2-3). This cycle is divided into *systole*, the period of ventricular contraction, and *diastole*, the period of ventricular relaxation. Each cardiac valve opens and closes in response to pressure gradients generated during these periods. At the onset of systole, ventricular pressures exceeds atrial pressures, so the AV valves passively close. As myocytes contract, the intraventricular pressures rise initially, without a change in ventricular volume (isovolumic contraction), until they exceed the pressures in the aorta and pulmonary artery. At this point, the semilunar valves open, and ventricular ejection of blood occurs. When intracellular calcium levels fall, ventricular relaxation begins; arterial pressures exceed intraventricular pressures, so the semilunar valves close. Ventricular relaxation initially does not change ventricular volume (isovolumic relaxation). At the point at which intraventricular pressures fall below atrial pressures, the AV valves open. This begins the rapid and passive ventricular filling phase of diastole, during which blood in the atria empties into the ventricles. At the end of diastole, active atrial contraction augments ventricular filling. When the myocardium exhibits increased stiffness due to age, hypertension, diabetes, or systolic heart failure, the early passive phase of ventricular filling is decreased. The end result is reliance on atrial contraction to sufficiently fill the ventricle during diastole. In atrial fibrillation, the atrium does not contract; patients often have worse symptoms because this additional ventricular filling is lost.

Pressure tracings obtained from the periphery complement the hemodynamic changes exhibited in the heart. In the absence of valvular disease, there is no impediment to blood flow moving from the ventricles to the arterial beds, so the systolic arterial pressure rises sharply to a peak. During diastole, no further blood volume is ejected into the aorta, so the arterial pressure gradually falls as blood flows to the distal tissue beds and elastic recoil of the arteries occurs.

Atrial pressure can be directly measured in the right atrium, but the left atrial pressure is indirectly measured by occluding a small pulmonary artery branch and measuring the pressure distally (the pulmonary capillary *wedge* pressure). An atrial pressure tracing is shown in Figure 2-3. It is composed of several waves. The *a wave* represents atrial contraction. As the atria subsequently relax, the atrial pressure falls, and the *x descent* is seen on the pressure tracing. The x descent is interrupted by a small *c wave*, which is generated as the AV valve bulges toward the atrium during ventricular systole. As the atria fill from venous return, the *v wave* is seen, after which the *y descent* appears as the AV valves open and blood from the atria empties into the ventricles. The normal ranges of pressures in the various cardiac chambers are shown in Table 2-1.

Cardiac Performance

The amount of blood ejected by the heart each minute is referred to as the cardiac output (CO). It is the product of the stroke volume (SV), which is the amount of blood ejected with each ventricular contraction, and the HR:

$$CO = SV \times HR$$

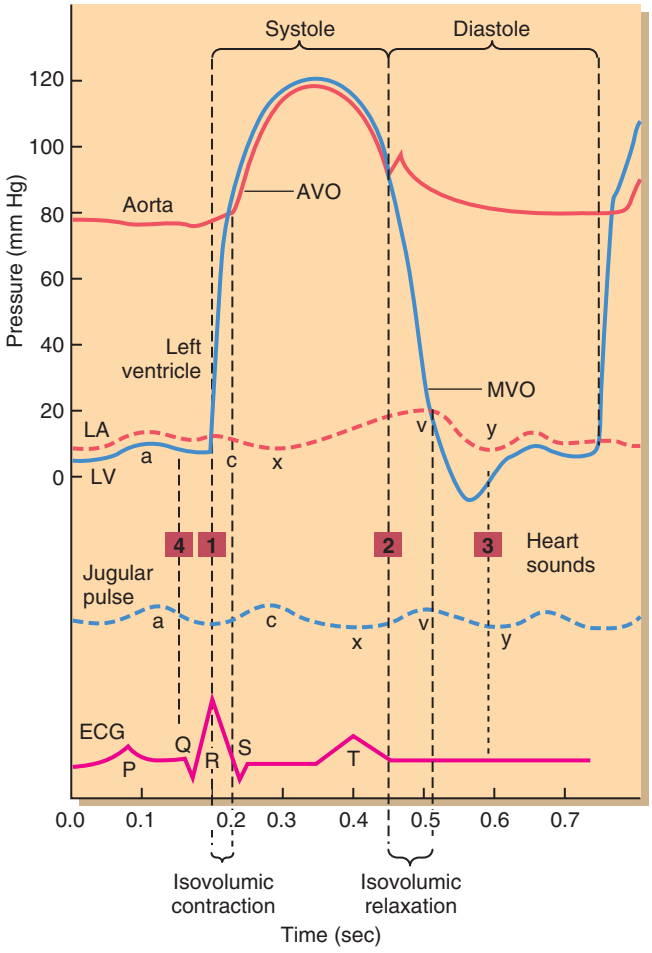

FIGURE 2-3 Simultaneous electrocardiogram (ECG) and pressure tracings obtained from the left atrium (LA), left ventricle (LV), and aorta and the jugular venous pressure during the cardiac cycle. (For simplification, pressures on the right side of the heart have been omitted. Normal right atrial (RA) pressure closely parallels that of the LA, and right ventricular and pulmonary artery pressures are timed closely with their corresponding left-sided counterparts; they are reduced only in magnitude. Normally, closure of the mitral and aortic valves precedes closure of the tricuspid and pulmonic valves; whereas valve opening reverses this order. The jugular venous pulse lags behind the RA pulse.) During the course of one cardiac cycle, the electrical (ECG) events initiate and therefore precede the mechanical (pressure) events, and the latter precede the auscultatory events (heart sounds) that they themselves produce *(red boxes)*. Shortly after the P wave, the atria contract to produce the a wave. The QRS complex initiates ventricular systole, followed shortly by LV contraction and the rapid buildup of LV pressure. Almost immediately, LV pressure exceeds LA pressure, closing the mitral valve and producing the first heart sound. After a brief period of isovolumic contraction, LV pressure exceeds aortic pressure and the aortic valve opens (AVO). When the ventricular pressure once again falls to less than the aortic pressure, the aortic valve closes to produce the second heart sound and terminate ventricular ejection. The LV pressure decreases during the period of isovolumic relaxation until it drops below LA pressure and the mitral valve opens (MVO). See text for further details.