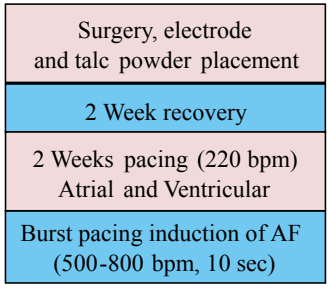

FIGURE 7.14 The pacing model of atrial fibrillation (AF) is similar to the sterile pericarditis model, but an additional 2 weeks of rapid pacing is added to the protocol. This induces extensive physical and electrical remodeling of the heart that promotes atrial fibrillation.

fully recovered from surgery, the pacemaker is adjusted to approximately 220 beats per minute (tachycardia), and this heart rate is sustained for 2–3 weeks. Tachycardia-induced physical and electrical remodeling of the chambers of the heart occurs during this time. This includes alteration of ionic currents and gene expression of ion channels that propagate electrical signals in the heart which promotes the occurrence of AF. At the end of this 2- to 3-week remodeling period, severity of AF can be assessed in a similar manner as that described for the sterile pericarditis model of AF. Once again, compounds with antiarrhythmic properties will demonstrate a decrease in the average duration of AF and the AF inducibility as compared to vehicle treatment.

Models of Heart Failure

An estimated 23 million patients worldwide[37] suffer from heart failure (HF), also referred to as congestive heart failure (CHF), a condition that is the final stage of many diseases of the cardiovascular system. In simple terms, cardiac output (volume of blood pumped by the heart in 1 min) is insufficient to meet the needs of the body. Conditions that decrease myocardial efficiency, such as ischemic events, can lead to the development of HF. In fact, ischemic heart disease is thought to be the most important risk factor for HF,[38] but other conditions such as hypertension and amyloidosis (deposition of protein in the heart muscle) can also contribute to the development of this condition. Over time, decreased cardiovascular efficiency leads to detrimental changes in the heart itself as it attempts to compensate for the increased workload. The heart undergoes hypertrophy (increase in size) as the muscles of the heart increase in size in an effort to improve contractility and increase cardiac output. At the same time, heart rate increases in an attempt to compensate for decreased efficiency, blood vessels narrow to maintain blood pressure, and the production of important effectors of the cardiovascular system such as renin, vasopressin, angiotensin, and aldosterone are altered as part of the body's compensatory mechanism