calcium loaded (e.g., in ischemia or congestive heart failure) to develop arrhythmias, particularly on exposure to action potential–prolonging drugs.

EAD-triggered arrhythmias exhibit rate dependence. In general, the amplitude of an EAD is augmented at slow rates when action potentials are longer. Indeed, a fundamental condition that underlies the development of EADs is action potential and QT prolongation. Hypokalemia, hypomagnesemia, bradycardia, and, most commonly, drugs can predispose to the generation of EADs, invariably in the context of prolonging the action potential. Antiarrhythmics with class IA and III action (see below) produce action potential and QT prolongation intended to be therapeutic but frequently causing arrhythmias. Noncardiac drugs such as phenothiazines, nonsedating antihistamines, and some antibiotics can also prolong the action potential duration and predispose to EAD-mediated triggered arrhythmias. Decreased $[K^+]_o$ paradoxically may decrease membrane potassium currents (particularly the delayed rectifier current, I_{Kr}) in the ventricular myocyte, explaining why hypokalemia causes action potential prolongation and EADs. In fact, potassium infusions in patients with the congenital long QT syndrome (LQTS) and in those with drug-induced acquired QT prolongation shorten the QT interval.

EAD-mediated triggered activity probably underlies initiation of the characteristic polymorphic ventricular tachycardia, torsades des pointes, seen in patients with congenital and acquired forms of LQTS. Structural heart disease, such as cardiac hypertrophy and heart failure, may also delay ventricular repolarization (so-called electrical remodeling) and predispose to arrhythmias related to abnormalities of repolarization. The abnormalities of repolarization in hypertrophy and heart failure are often magnified by concomitant drug therapy or electrolyte disturbances.

Abnormal Impulse Conduction: Reentry The most common arrhythmia mechanism is reentry resulting from abnormal electrical impulse conduction and is defined as the circulation of an activation wave around an inexcitable obstacle. The requirements for reentry are two electrophysiologically dissimilar pathways for impulse propagation around an inexcitable region (Fig. 273e-4). Reentry can occur around a fixed anatomic structure (e.g., myocardial scar), with a stable pattern of cardiac depolarization moving in series over the anterograde and retrograde limbs of the circuit. This form of reentry, referred to as *anatomic reentry* or *excitable gap reentry* (see below), is initiated when a depolarizing wavefront encounters an area of unidirectional conduction block in the retrograde limb of the circuit. Conduction across the anterograde limb occurs with a delay that, if of sufficient duration, allows for recovery of conduction in the retrograde limb with reentry of the depolarization wave into the retrograde limb of the circuit. Sustained reentry requires that the functional dimension of depolarized tissue or the tachycardia wavelength (λ = conduction velocity × refractory period) fits within the total anatomic length of the circuit, referred to as the path length. When the path length of the circuit exceeds the λ of the tachycardia, the region between the head of the activation wave and the refractory tail is referred to as the excitable gap. Anatomically determined, excitable gap reentry can explain several clinically important tachycardias, such as AV reentry, atrial flutter, bundle branch reentry ventricular tachycardia, and ventricular tachycardia in scarred myocardium.

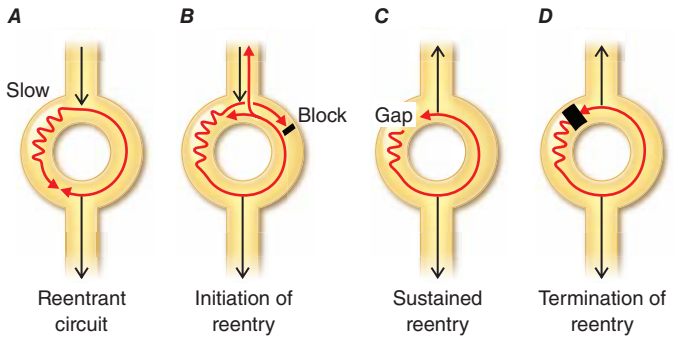

FIGURE 272-4 **Schematic diagram of reentry.** ***A.*** The circuit contains two limbs, one with slow conduction. ***B.*** A premature impulse blocks in the fast pathway and conducts over the slow pathway, allowing the fast pathway to recover so that the activation wave can reenter the fast pathway from the retrograde direction. ***C.*** During sustained reentry utilizing such a circuit, a gap (excitable gap) exists between the activating head of the wave and the recovering tail. ***D.*** One mechanism of termination of reentry occurs when the conduction and recovery characteristics of the circuit change and the activating head of the wave collides with the tail, extinguishing the tachycardia.

Reentrant arrhythmias may exist in the heart in the absence of an excitable gap and with a tachycardia wavelength nearly the same size as the path length. In this case, the wavefront propagates through partially refractory tissue without a fixed anatomic obstacle and no fully excitable gap; this is referred to as *leading circle reentry*, a form of functional reentry (reentry that depends on functional properties of the tissue). Unlike excitable gap reentry, there is no fixed anatomic circuit in leading circle reentry, and it may, therefore, not be possible to disrupt the tachycardia with pacing or destruction of a part of the circuit. Furthermore, the circuit in leading circle reentry tends to be less stable than that in excitable gap reentrant arrhythmias, with large variations in cycle length and a predilection to termination. There is strong evidence to suggest that less organized arrhythmias, such as atrial and ventricular fibrillation, are associated with more complex activation of the heart and are due to functional reentry.

Catheter-based and pharmacologic therapies for reentrant arrhythmias are designed to disrupt the anatomic circuit or alter the relationship between the wavelength and path length of the arrhythmia circuit, eliminating pathologic conduction. For example, antiarrhythmic drugs that prolong the action potential (Class III) are effective if they sufficiently prolong the λ such that it can no longer fit within the anatomic circuit. Catheter ablation is often undertaken with the goal of identifying and destroying a critical limb of the reentrant circuit (i.e., ablation of the cavotricuspid isthmus in the treatment of typical, right atrial flutter). Due to the less defined pathways of myocardial activation seen in functional reentry, ablation of these rhythms tends to target initiating triggers (e.g., pulmonary vein potentials in catheter ablation of atrial fibrillation) rather than the anatomic circuit.

Structural heart disease is associated with changes in conduction and refractoriness that increase the risk of reentrant arrhythmias. Chronically ischemic myocardium exhibits a downregulation of the gap junction channel protein (connexin 43) that carries intercellular ionic current. The border zones of infarcted and failing ventricular myocardium exhibit not only functional alterations of ionic currents but also remodeling of tissue and altered distribution of gap junctions. The changes in gap junction channel expression and distribution, in combination with macroscopic tissue alterations, support a role for slowed conduction in reentrant arrhythmias that complicate chronic coronary artery disease (CAD). Aged human atrial myocardium exhibits altered conduction, manifest as highly fractionated atrial electrograms, producing an ideal substrate for the reentry that may underlie the very common development of atrial fibrillation in the elderly.

APPROACH TO THE PATIENT: Cardiac Arrhythmias

The evaluation of patients with suspected cardiac arrhythmias is highly individualized; however, two key features—the history and ECG—are pivotal in directing the diagnostic workup and therapy. Patients with cardiac arrhythmias exhibit a wide spectrum of clinical presentations that range from asymptomatic ECG abnormalities to survival from cardiac arrest. In general, the more severe the presenting symptoms are, the more aggressive the evaluation and treatment are. Loss of consciousness that is believed to be of cardiac origin typically mandates an exhaustive search for the etiology and often requires invasive, device-based therapy. The presence of structural heart disease and prior myocardial infarction dictates a change in the approach to the management of syncope or ventricular