

HOSPITAL PHYSICIAN®

CARDIOLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Cardiology Board Review Manual* is a peer-reviewed study guide for fellows and practicing physicians preparing for board examinations in cardiology. Each bi-monthly manual reviews a topic essential to the current practice of cardiology.

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Rational Choices in Antiarrhythmic Pharmacotherapy

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Rational Choices in Antiarrhythmic Pharmacotherapy

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INTRODUCTION

Cardiac arrhythmias were responsible for approximately 20% of all deaths in the United States in 1999.¹ Although device therapy with implanted cardiac defibrillators has supplanted drugs as the primary therapy for malignant ventricular arrhythmias, antiarrhythmic drugs frequently are used concurrently in patients with implanted defibrillators to suppress arrhythmias and their attendant device discharges and as primary therapy for supraventricular rhythms. Often, decisions regarding antiarrhythmic pharmacotherapy are made based on a combination of lore and familiarity. However, the efficacy of individual antiarrhythmic drugs varies across the different types of arrhythmia. In order to make informed decisions when initiating pharmacotherapy for cardiac arrhythmia, clinicians must understand the mechanism of cardiac arrhythmias and the action of antiarrhythmic drugs.

MECHANISMS OF ARRHYTHMIA

Classically, there are 3 mechanisms of arrhythmia: automaticity, triggered activity, and reentry. Two forms of enhanced automaticity are recognized: normal automaticity, which involves tissue for which impulse initiation is a normal property, and abnormal automaticity, which involves tissue that typically is not spontaneously active. An example of each form is sinus tachycardia and reperfusion arrhythmias, respectively. In triggered activity, abnormalities in the repolarization phase of one action potential cause subsequent membrane potential oscillations that reach threshold, prematurely triggering another action potential. Triggered arrhythmias are divided into 2 types based on when the oscillations start in relation to repolarization. With the early afterdepolarization (EAD) type, prolongation of the action potential (QT interval on the surface electrocardiogram [ECG]) causes oscillations before full repolarization has occurred. This mechanism is thought to initiate the

polymorphic ventricular tachycardia known as torsades de pointes. The second type is delayed afterdepolarizations (DADs), in which oscillations occur after the action potential has repolarized. DADs seem to be related to cellular Ca^{2+} overload, as seen in digoxin toxicity. The third type of arrhythmia is reentry, which is a continuous short circuit of electrical activity rotating in the cardiac syncytium. A minimum requirement for this type of arrhythmia is a transient unidirectional conduction block. The rhythm is favored by slow conduction and tissue heterogeneity. Sodium channels and gap junctions are the main dynamic determinants of conduction velocity. The slowing of conduction velocity with the blocking of sodium channels leads to widening of the QRS interval, a property that is used to follow dosing of some antiarrhythmic drugs.

THE IONIC BASIS OF THE CARDIAC ACTION POTENTIAL

The surface ECG is a manifestation of the underlying cardiac electrical activity that is the result of cell depolarization initiating a cardiac action potential. The shape of this action potential is determined by a choreographed sequential activation and closure of various ion channels (Figure 1). Ion channels are transmembrane proteins that control the movement of ions across the cell membrane by opening and closing a central aqueous pore, a function called gating. The movement of ions through their respective channels changes the membrane potential. The extracellular current flow associated with the changes in membrane potential manifests as the ECG. A few channels are always open, while others open in response to stimuli such as ligand binding (ligand-gated), changes in voltage (voltage-gated), or mechanical forces (stretch-activated). The cardiac sodium and calcium channels as well as most potassium channels are voltage-gated ion channels. These channels are the targets of most available antiarrhythmic drugs.

Because arrhythmias are an electrical disorder, the ion channels are obvious targets for prevention and