SUMMARY. Flecainide acetate depresses the rate of depolarization of action potential ($V_{\text{max}}$), the so-called “membrane stabilizing action.” In the intact heart it has a unique profile of substantial effect on conduction with modest effect on refractoriness. After intravenous administration, clinical electrophysiologic studies show that conduction through atrial myocardium, atrioventricular (AV) node, His-Purkinje system, and ventricular myocardium is depressed, the most prominent effect being on the His-Purkinje system. Refractoriness of the normal atrial and AV nodal myocardium is not prolonged while that of the ventricular muscle is slightly increased. Atrial fibrillation (60% to 70%), atrial tachycardia (90% to 100%), and nodal and AV tachycardia (80% to 90%) are generally terminated, while flutter is usually slowed, but in a small proportion of patients (10% to 20%) might be terminated by the intravenous use of flecainide acetate. This drug has also been shown to be effective in terminating stable ventricular tachycardia (70%). However, it appears to be slightly less effective in suppressing inducibility of ventricular arrhythmias. Administered orally, flecainide is very effective in decreasing ventricular ectopic activity (80% to 95%) and nonsustained ventricular tachycardia. Thus, flecainide has a wide range of antiarrhythmic properties, making it a useful agent in the management of a variety of supraventricular and ventricular arrhythmias. In a small proportion of patients, however, its use can lead to apparent arrhythmogenic effects, the most dangerous being exacerbation of ventricular tachycardia.

KEY WORDS. Flecainide acetate, paroxysmal tachycardia, electrophysiology, monophasic action potential

Flecainide acetate is a relatively new antiarrhythmic agent which has received considerable attention in the last 5 years. Its wide range of electrophysiologic and clinical antiarrhythmic effects make it a “broad-spectrum” antiarrhythmic drug of considerable clinical potential. In this review we summarize the clinical electrophysiologic effects of the drug and question the validity of classification as a Vaughan Williams class 1c drug based on animal and human data.
fect on action potential duration, Harrison [6] proposed a subclassification of class 1 agents as follows: class la drugs, such as quinidine, procainamide, and disopyramide which significantly prolong action potential duration; class lb drugs such as lignocaine and tocainide which shorten the action potential duration; class lc drugs such as flecainide, encainide, and similar drugs which have little or no effect on myocardial action potential duration. Clinical experiments by Milne et al. [7] on the effect of various class 1 drugs on repolarization show analogous effects and therefore support the use of this classification. Although, flecainide has been classified as a class lc drug, several human [8-10] and animal studies [1, 2] have shown a significant increase in refractoriness (atrial and ventricular) and action potential duration (ventricular). However, in some respects it differs from class la drugs in that it markedly prolongs conduction (Q-R-S interval duration is increased) and does not significantly slow repolarization (J-T interval is not altered) [11]. Electrophysiologically, it is also distinct from class lb agents which, unlike flecainide, decrease the action potential duration of Purkinje fibers and ventricular muscle [12]. Furthermore, prolongation of conduction through the His-Purkinje system and myocardium as seen with flecainide is not seen with class lb agents [13, 14]. It shares most of its electrophysiologic effects with other agents of class lc, i.e., encainide and lorcanide [15, 16] with minor differences. Lorcanide, for example, slightly lengthens Purkinje cell action potential, while encainide has no effect on myocardial action potential duration.

Thus, better understanding of flecainide's electrophysiologic effects and its pharmacologic diversity has made it difficult to precisely classify flecainide, although at present it is best grouped under class lc.

Clinical Electrophysiology

The clinical electrophysiologic effects of flecainide have been studied mostly by the use of conventional intracardiac recording and stimulation techniques. Most of these data have been obtained after intravenous (rather than oral) drug administration. The usual intravenous dose in adults is 2 mg/kg given slowly over 10 to 15 minutes. The electrophysiologic actions detected using this technique [5, 17] may be categorized as follows:

1. Sinoatrial function.
2. Atrial refractoriness and conduction.
3. Atrioventricular (AV) nodal refractoriness and conduction.
5. His-Purkinje tissue refractoriness and conduction.
6. Ventricular myocardial refractoriness and conduction.
7. Stimulation thresholds.

The antiarrhythmic actions of flecainide have been investigated in relation to

1. Atrial tachycardias, including atrial flutter and fibrillation.
2. Paroxysmal junctional tachycardias.
3. Ventricular tachycardias.

Actions on the Sinus Node

The action of flecainide on sinus node function, as with many other class I agents, is most pronounced in patients with sinoatrial disorders [18]. Although flecainide has no major effects on the sinus rate [4, 5, 19], it may prolong derived variables such as sinoatrial conduction time (SACT) and sinus node recovery time (SNRT) [18]. The clinical importance of these effects is not clear but the implication is that patients with important sinoatrial disorders are more susceptible to the effects of the drug [18] and may develop long sinus pauses or sustained bradycardias. The mechanism of this action is not known. However, other drugs with class I (Vaughan Williams) properties are also known to aggravate abnormal sinus node function [20, 21].

Action on the Atrium

Intra-atrial conduction time as measured by the P-A interval appears to be prolonged by intravenous flecainide [5, 6]. Atrial refractoriness does not appear to be consistently affected. In one study no change was seen [5] but in two other studies a significant prolongation was noted [18, 22]. The reasons for such a major discrepancy of results is unclear. Oral flecainide has no consistent effect on the atrial refractory period although there is a tendency towards prolongation.

Actions on the Atrioventricular Node

The effective refractory period of the normal AV node is not significantly changed by flecainide in those