SUMMARY OF CURRENT THERAPY

New Concepts in the Approach to Digitalis Therapy for Atrial Fibrillation*

Leonard S. Dreifus, M.D., Thomas F. McGarry, M.D. and Demetrios Kimbiris, M.D.
Philadelphia, Pennsylvania

Classically, digitalis or its glycosides have been exhibited to control the ventricular response in the presence of atrial fibrillation. It is customary to administer increasing dosages of digitalis until the ventricular rate approaches 85/min. and there is no appreciable increase in the rate with ambulation.1 Failure to slow the ventricular rate following adequate digitalis administration has usually been ascribed to advanced heart disease or associated pathologic or metabolic derangements, as the hyperthyroid state, sepsis or recurrent pulmonary emboli.

Recent experimental observations concerning the mechanisms of abnormal impulse formation and conduction in the atioventricular junction following excess digitalis and hypokalemia,2 as well as earlier clinical observations by Pick, Langendorf and Katz,3 suggested that the ventricular response in the presence of atrial fibrillation may be governed by four major factors: (1) the absolute refractory period of the atioventricular junction; (2) entrance block into the atioventricular node, (3) exit block from the atioventricular node and (4) incomplete propagation of impulses into the atioventricular junction (concealed conduction) with consequent effects on the effective refractory period of the junctional tissues.

Because of certain anatomic and electrophysiologic considerations, atrial impulses bombarding the head of the A-V node arise from only a small rim of atrial tissue surrounding the A-V node.4 Theoretically, any combination of the multitude of fibrillatory stimuli could discharge the A-V node with subsequent ventricular excitation at the termination of the absolute nodal refractory period. Under these circumstances, the ventricular rate would be quite regular and specifically regulated by the absolute refractory period of the A-V junctional tissues. However, frequent incomplete propagation (concealed conduction) of the atrial impulses into the A-V junction, discharging portions of the junctional tissues without propagation to the ventricles, engenders a grossly irregular ventricular response. In the undigitalized patient, the absolute refractory period of the A-V junction is approximately 0.32 seconds, and very rarely does the ventricular response exceed 190/min. The parasympathetic effects of digitalis on the atioventricular junction are utilized to reduce the number of impulses passing through the A-V junction and thereby control the ventricular response. A classic response to digitalis is shown in Fig. 1. Digitalis in its therapeutic range may produce entrance block into the A-V junctional tissues with subsequent escape of a subsidiary nodal pacemaker for one or several beats as in seen in Fig. 2A. The nodal escape beats (E) are terminated by a rather long and constant R-R interval. At times, an even longer R-R interval is noted (Ê) indicating that atrial impulses have penetrated the A-V junction, discharging the subsidiary nodal pacemaker and delaying subsequent discharge of the escape beat.

*From the Cardiovascular Section, Department of Medicine, Hahnemann Medical College. This study was in part aided by the United States Public Health Service, Grant HE 07136.
FIGURE 1: A. Atrial fibrillation is present with a rapid ventricular response. A common R-R interval of 0.32 seconds is representative of the effective refractory period of the A-V junctional tissues. The longer and irregular R-R intervals result from incomplete propagation of the atrial impulses into the A-V junction. B. Following 0.5 mg. of acetyl strophanthidin the ventricular rate slows (minimal R-R interval of .44 second) with more frequent and longer R-R intervals. This action of digitalis suggests, (1) an increased effective refractory period of A-V junctional tissues and (2) more frequent incomplete propagation of atrial impulses into the A-V junction. Hence, fewer atrial impulses reach the ventricles.

On the other hand, excessive administration of digitalis may then produce high grade entrance block with independent activation of atria and ventricles (Fig. 2B). The regular rhythm may be misinterpreted at the bedside as a sinus mechanism while the patient is actually a victim of digitalis excess. Failure to withhold digitalis at this time may produce an additional exit block below the nodal pacemaker and consequently shift the subsidiary pacemaker to the ventricle (idioventricular pacemaker).

Final, multiple ventricular premature systoles or ventricular tachycardia may ensue.

A second and even more serious manifestation of digitalis excess is acceleration of the nodal pacemaker (non-paroxysmal nodal tachycardia 70-130/min.) (Fig. 3). This variety of digitalis intoxication may be misleading from several aspects; (1) the ventricular rate could be precisely regular and rapid due to a concomitant entrance block into the A-V junctional tissues. Beats 6 and 7, nodal escape beats (E), terminate a long but constant R-R interval as was seen in many other portions of this tracing. Beat 2 (E) is terminated by a somewhat longer R-R interval due to incomplete propagation of atrial impulses into the A-V junction, discharging the nodal pacemaker and delaying its escape. B. A slow but constant R-R interval is present due to complete A-V dissociation engendered by a high grade (3rd degree) entrance block of the atrial impulses into the A-V junction. The slow nodal rate may be due to (1) a slow rate of discharge of the subsidiary nodal pacemaker or (2) a persistent second degree exit block below an accelerated subsidiary nodal pacemaker (see Fig. 3). The regularity of the rhythm may be misinterpreted as a sinus mechanism at the bedside. Digitalis should be withheld under these circumstances and a bipolar catheter pacemaker inserted into the out-flow tract of the right ventricle if the rate is too slow to maintain an adequate cardiac output.
tissues engendering independent activation of atria and ventricles (Fig. 3A), or (2) a slower but irregular response with group beating could result from a second degree exit block below the accelerated nodal pacemaker (Fig. 3B). Even though carotid pressure may temporarily slow the ventricular rate, continuation of digitalis may produce a more sinister cardiac mechanism by further accelerating the nodal pacemaker. Hence, the drug must be withdrawn under these circumstances.

Finally, it must be realized that excessive digitalis administration often produces varying combinations of entrance and exit block in the presence of an accelerated nodal pacemaker. In addition, incomplete propagation of atrial impulses into the A-V junction may interfere with the rhythmicity of the accelerated nodal pacemaker, resulting in a grossly irregular ventricular response. Unless long electrocardiographic strips are taken for precise analysis, digitalis may be inappropriately continued. Many of these patients with complex nodal arrhythmias are in intractable congestive heart failure and are considered to have advanced myocardial disease refractory to digitalis. Further digitalis administration fails to slow the ventricular rate. 1

Nodal rates between 130-170/min. in the presence of intermittent A-V dissociation present the most difficult diagnostic and therapeutic problems. Even though an accelerated nodal pacemaker can be detected from the electrocardiogram, further digitalis may produce exit block and slow the ventricular response. Intravenous acetyl strophanthidin (0.5 mg.) may be of critical diagnostic value under these circumstances (Fig. 1).

Several electrocardiographic clues may alert the clinician to the presence of digitalis excess: (1) further acceleration of the ventricular rate following digitalis administration; (2) obvious independent activation of atria and ventricles (inordinately slow, rapid or precisely regular ventricular...
patients (Fig. 2B, 3); (3) obvious group beating, (bigeminy, trigeminy, quadrageminy). This is particularly diagnostic when advanced entrance or second degree exit block of the Wenkebach type is present (Fig. 3B); (4) determination of the rate of the accelerated nodal pacemaker to be between 70-130/min. This is done by dividing the time between two nodal beats each following upon the longest R-R intervals by the number of beats within this interval plus 1 (Fig. 3B).

It is possible that rates less than 50/min. may represent a high grade exit block from an accelerated nodal pacemaker. On the other hand, intermittent independent activation of the atria and ventricles (A-V dissociation) with rates between 50-70/min. should not preclude further digitalis administration. However, further acceleration or slowing of the ventricular rate is an absolute indication to withhold digitalis.

Antiarrhythmic agents (potassium salts, procaine amide, or antazoline) may be required if cardiac output is severely compromised due to the rapid rate. On the other hand, it may be necessary to insert a bipolar electrode into the outflow tract of the right ventricle for electronic pacing of the heart when the ventricular rate is too slow to maintain an adequate cardiac output.

SUMMARY AND CONCLUSIONS

It has been the purpose of this presentation to bring into sharp focus the precise electrophysiologic mechanisms that may be associated with atrial fibrillation. An approach to the interpretation of these serious cardiac mechanisms has been outlined. Irregularity of the ventricular rate in the presence of atrial fibrillation may be due to a combination of the following electrophysiologic events in the atrioventricular junction: (1) physiologic effective refractory period of the A-V node junctional tissues; (2) interference of subsidiary escape or accelerated A-V nodal pacemakers; (3) concealed A-V conduction into the A-V junction; (4) entrance block into the A-V nodal tissues, and (5) exit block in the lower regions of the A-V nodal tissues.

Finally, digitalis should be withheld in the presence of independent activation of atria and ventricles due to advanced entrance or exit block, or accelerated nodal rhythm (70-130/min.) A trial of intravenous acetyl strophanthidin (0.5 mg.) may be required when the accelerated nodal rate is greater than 130/min., with intermittent periods of A-V dissociation.

REFERENCES


2 DREIFUS, L. S. AND Watanabe, Y.: "Electrophysiologic Observations Concerning the Genesis of A-V Nodal Rhythm Due to Digitalis," In Preparation.


For reprints, please write Dr. DREIFUS at 230 North Broad Street, Philadelphia, Pennsylvania.