Physiology of Atrioventricular Transmission

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This paper describes records of the transmembrane action potential of fibers from different parts of the specialized conducting system and electrograms recorded directly from these fibers in situ. On the basis of these records it is possible to describe certain physiologic mechanisms for conduction delay, block, and supernormal conduction. In general, impaired conduction is associated with a reduced level of membrane potential. This may be caused by incomplete repolarization or partial depolarization. In the normal conducting system, local differences in action-potential duration and local pacemaker activity most frequently are the cause of a low membrane potential. In disease states, on the other hand, many other factors may be operative. At the atrial margin of the atrioventricular (A-V) node, local anatomic and electrophysiologic properties of the fibers normally cause a very low conduction velocity. The safety factors for conduction here appear to be quite low, and delayed transmission or block often does not result from refractoriness or partial depolarization of nodal fibers. Supernormal conduction, at least in Purkinje fibers, seems to result from the high level of membrane potential reached at the end of repolarization. Whether other factors are responsible for supernormality within the A-V node remains to be seen.

During the normal cardiac cycle, electrical activity originates in some part of the sinoatrial node and spreads to the atrium and thence to the atrioventricular node. After some delay, activity then spreads through the bundle of His, the bundle branches, and the peripheral Purkinje fibers and finally reaches the musculature of the ventricles. In the normal heart, activity that is initiated in some part of the ventricles can spread in the reverse direction along this same path. However, under a wide variety of abnormal conditions either sequence of events may not take place. Atrial activity may be delayed excessively at the atrioventricular node or may fail to excite the bundle of His. Activity that does traverse the atrioventricular node may be delayed or blocked in its passage through the specialized conducting system, and this delay or block may be localized to one or another anatomic subdivision. Also, unidirectional conduction delay or block may be observed. Finally, most and perhaps all parts of the specialized conduction system may at times develop intrinsic rhythmicity and such ectopic pacemakers may compete with varying degrees of success with the normal sinus pacemaker.

A large number of comprehensive studies of normal and abnormal atrioventricular transmission has been carried out by careful analysis of the electrocardiogram. These studies have provided a fairly detailed picture of the physiology of the various parts of the atrioventricular (A-V) conducting system; however, the evidence in most instances has been somewhat indirect. This is so because electrical activity of the A-V node, the bundle of His, and the Purkinje fibers is not recorded directly in the conventional electrocardiogram. However, 2 methods can be used to demonstrate this electrical activity: through an intracellular microelectrode one can record the change in transmembrane potential associated with activity of a fiber from any part of the heart, and, by means of small electrodes placed directly over various parts of the specialized conducting system, one can record the local electrogram of the underlying structures.

We have employed these 2 technics to study certain aspects of the electrophysiology of fibers in the A-V node, the bundle of His, and the Purkinje system and to obtain some-
what more direct information on the physiologic mechanisms responsible for certain disturbances of A-V transmission. Experiments using microelectrodes were carried out on isolated preparations of rabbit or canine hearts. The methods have been described elsewhere in detail. Electrograms were recorded directly from various parts of the specialized conducting system of canine hearts in situ using small electrodes that had been attached to the endocardium during total cardiopulmonary bypass. The experiments were acute in some instances; in others, records were obtained from healthy animals in which electrodes had been implanted previously.

Activation of the Specialized Conducting System

The exact sequence of activation of the specialized conducting system in canine hearts has been determined by several investigators from bipolar electrograms recorded by means of electrodes closely placed over the bundle of His, the right and left bundle branches, and the peripheral Purkinje fibers and from unipolar electrograms recorded by way of electrodes in close proximity to the A-V node. In figures 1 and 2 are several such tracings recorded simultaneously with a standard limb-lead electrocardiogram. A fairly accurate estimate of the instant during the...
cardiac cycle when atrial activity reaches the A-V node can be obtained by noting the time at which atrial depolarization is recorded through leads located either over the bundle of His or below the ostium of the coronary sinus (fig. 1A). From such records it is apparent that the A-V node is excited early during the P wave of the electrocardiogram. The time required for activity to traverse the node can best be determined by recording the onset of propagated activity in the upper end of the bundle of His. This approach is necessary because the electrical activity of the A-V nodal fibers is not easily demonstrated in surface electrograms. Unipolar records from the node show a slow, predominantly positive deflection of low voltage (fig. 1B); however, it is likely that in many instances this deflection derives, in part, from currents associated with repolarization of nearby atrial muscle.

Electrodes located over the bundle of His, on the other hand, clearly signal the arrival of propagated depolarization in this structure. The electrogram deflection resulting from activity in the upper part of the common bundle.
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Figure 3

Transmembrane action potentials recorded from single fibers of atrium (A), upper node (B), mid and lower node (C, D, E), and upper of His bundle (F). Upper trace represents a line of zero potential and shows time calibration (dots) in intervals of 10 and 50 msec. Voltage calibration in A, from above down, shows in mv: −50 and −100. Overshoot in (A) is larger than that commonly recorded. (From Hoffman et al.*)

usually designated by the letter ‘‘H,’’ appears during the first half of the P-R interval. Identification of the complexes resulting from activity in different parts of the specialized conducting system often is facilitated if low frequency components of the tracing are filtered. This device allows the use of high amplification to increase the relative magnitude of the rapid complexes that result from activity in the bundle of His or the Purkinje fibers. It has been employed for the records shown in many of the illustrations; in each instance the filter settings of the preamplifier are noted in the legend. The time required for A-V nodal transmission in dogs, determined from records like those in figure 1, ranges from 40 to 50 msec. These findings have been the same both in acute experiments and in animals with chronically implanted electrodes. The electrogram recorded from the bundle of His varies somewhat in configuration and timing, depending on the location of the electrodes; however, during normal A-V transmission, it is apparent that excitation of the various fibers in the common bundle is quite synchronous.

Records obtained through electrodes located over the right or left bundle branches, the free-running Purkinje fibers in the false tendons of the left ventricle, and the peripheral Purkinje fibers at their junction with the papillary muscles of the left or right ventricle can
be employed to time the onset of activity in these structures (fig. 2). At each location the rapid deflection resulting from activity in the Purkinje fibers can be identified; since the recording electrodes are located progressively closer to the ventricular terminals of the specialized conducting system, the interval between this rapid deflection and the slower activity caused by depolarization of ventricular muscle decreases. The earliest activity recorded from the right or left bundle branches appears shortly after the midpoint of the P-R interval; that obtained from electrodes located at the Purkinje-fiber–papillary-muscle junction often is synchronous with the beginning of the initial deflection of the standard electrocardiogram. Electrodes located at appropriate sites on the endocardial surfaces of the ventricles record the local arrival of depolarization in the subendocardial Purkinje-fiber network as small rapid deflections that precede local ventricular activity by an interval of a few milliseconds.

**Conduction Velocity**

When the time in the cardiac cycle of electrograms recorded from each part of the specialized conducting system is considered in relation to the distance between recording sites, it is apparent that conduction velocity varies considerably during the spread of the impulse from the atria to the ventricles. Extremely slow propagation through the A-V node has been postulated for many years; recent studies of perfused dog hearts and isolated preparations of dog and rabbit heart have shown that, at the atrial margin of the node, the conduction velocity apparently falls to the extremely low value of 0.05 M./sec. or less. During normal A-V transmission the major delay in propagation is localized to the atrial margin of this structure. Within the node, conduction velocity increases progressively and in the bundle of His attains a value of 1.0 to 1.5 M./sec. It is likely that the rapidity of spread of the impulse increases progressively toward the periphery of the common bundle. Measurements of conduction velocity in the free-running Purkinje fibers in the right and left ventricles of canine hearts, obtained during cardiopulmonary bypass, give values for conduction velocity ranging from 3 to 4 M./sec. In the fine terminal ramifications of the Purkinje system, conduction velocity decreases and, in ventricular muscle, velocity is approximately 1 M./sec. During retrograde activation, which results from premature ventricular activity late in the cycle or from an idioventricular pacemaker firing at a low frequency, there is no demonstrable change from normal in the conduction velocity in the Purkinje fibers and in the bundle of His. Retrograde transmission from the A-V node to the atrium is slower than that recorded during normal activity, and again the delay appears to be localized to the atrial margin of the node. During such retrograde activation of the specialized con-

*Figure 4*

Drawings of transmembrane action potentials recorded from the following sites from above down: sinoatrial node, atrium, atrioventricular node (atrial margin), bundle of His, left bundle branch, Purkinje fiber in a false tendon, terminal Purkinje fiber, and ventricular muscle fiber. Note the sequence of activation at the various sites as well as the differences in the amplitude, configuration, and duration of the action potentials. (From Hoffman and Cranefield.)
Figure 5

Transmembrane action potentials recorded from single fibers of the atrial margin of the atrioventricular node (upper trace) and bundle of His (lower trace) in an isolated preparation of rabbit heart. A. Control; B-G, effects of acetylcholine added to perfusion fluid. Note progressive increase in slurring and notching of upstroke of nodal potential (B-D), normal nodal action potential caused by retrograde activation (E) and fragmentation of nodal response in F and G. (From Cranefield, Hoffman, and Paes de Carvalho.19)

The A-V Node

Transmembrane action potentials recorded from fibers located in different parts of the A-V node are compared to a record of an atrial transmembrane action potential in figure 3.* Several differences are apparent. The resting potential of the nodal fibers is lower than that of the atrium, the rate of rise of

*Figure 3 reproduced from Hoffman et al.: Circulation Research 7: 11, 1959. By permission of the American Heart Association, Inc.
the nodal action potential is much less, and the overshoot is reduced in amplitude. At the atrial margin of the node, records of transmembrane action potential often reveal one or more steps or notches on the upstroke.\textsuperscript{12, 14, 15} The recorded electrical activity differs in different parts of the node;\textsuperscript{12} the characteristics mentioned are most prominent at the atrial margin and become less pronounced in records obtained from fibers located closer to the bundle of His. The duration of the action potential is greater in the lower node than at the atrial margin of this structure and some slow diastolic depolarization is present in all records. Studies of conduction velocity within the node\textsuperscript{12, 16} have shown that extreme slowing is present only in the fibers at the atrial margin, i.e., in those fibers whose action potentials show the lowest rate of rise and lowest amplitude. Both of these properties of the nodal action potential—reduced amplitude and low rate of rise—would decrease conduction velocity. It is not known whether the extremely slow propagation of activity in this part of the node results mainly from the characteristics of the action potential or in part also from the anatomic and passive electrical properties of the fibers. A-V nodal fibers in canine hearts are 6 microns or less in diameter\textsuperscript{17} and, in some areas, have branches or extensions that are still smaller.\textsuperscript{18} In small fibers, other factors being the same, conduction velocity is reduced because the resistance to flow of current along the axis of the fiber is high. Accurate measurements of the membrane resistance and capacity and the threshold potential of fibers at the atrial margin of the node have not been made, and thus it is impossible to evaluate the extent to which the unusual action potential and conduction velocity depend upon these properties.
ever, even if one assumes that they are much the same as in other cardiac fibers, the safety factor for transmission in this part of the node undoubtedly is reduced.

The Bundle of His and the Purkinje Fibers

The action potential recorded from a single fiber in the bundle of His of the rabbit heart contrasts quite markedly with the nodal action potential (figs. 3 and 4*). The resting potential is higher, the upstroke of the action potential is rapid, and the amplitude is greater. The duration of the action potential is increased, and slow diastolic depolarization is minimal under ordinary conditions. The rapid depolarization and good amplitude of the action potential, in combination with the greater diameter of the fibers, undoubtedly are responsible for the increase in conduction velocity as activity spreads into this structure. Action potentials recorded from Purkinje fibers in the bundle branches and peripheral branches of the conducting system show other changes. There is a further increase in rate of rise and a small increase in the amplitude of the action potential in the bundle branches and false tendons, and then a progressive decrease in the terminal Purkinje fiber network. The duration of the action potential also increases with increasing distance from the common bundle and then decreases as the junction of the Purkinje fiber with ventricular muscle is approached (fig. 4). Diastolic depolarization is progressively less marked in records obtained from more peripheral fibers. Comparative data on fiber diameter and frequen-

*Figure 4 reproduced from Hoffman and Cranefield: Electrophysiology of the Heart. By permission of the McGraw-Hill Book Company.

Physiologic Basis for Disturbances in Conduction

An attempt to present a detailed description of the physiologic mechanisms responsible for any of the disturbances in A-V transmission observed in the clinic certainly is premature. On the other hand, it is possible to describe the changes in electrical activity that have been observed in association with experimental conduction disturbances and to indicate the extent to which these changes might cause certain electrocardiographic alterations.

Disturbances of A-V Nodal Transmission

Records from isolated preparations of A-V nodal tissue of rabbit and dog heart have shown that most changes in conduction through the
node and most instances of block are associated with altered electrical activity of fibers at the atrionodal junction. A typical example is the delay and block of nodal transmission caused by acetylcholine. Action potentials recorded from fibers in the lower node and bundle of His show only those changes that are produced by the acetylcholine-induced change in frequency. Transmembrane action potentials recorded from nodal fibers at the atrial margin, on the other hand, are profoundly altered. Under the influence of acetylcholine, the action-potential upstroke becomes slower and more notched, and the action potential decreases in amplitude (figs. 5 and 6). Often it is replaced by 1 or more small depolarizations that vary in size and to a greater or lesser degree undergo temporal summation. Delay and failure of transmission undoubtedly result from these changes; however, the exact cause of the changes noted is less certain.

During complete failure of A-V transmission owing to acetylcholine, activity originating in the bundle of His and propagating back to the same nodal fibers elicits an action potential of good amplitude (figs. 5 and 6). Moreover, the upstroke of this action potential often is free from slurring or notching even when these changes were prominent during normal A-V transmission. Although direct measurements of threshold are lacking, some estimate of the effect of acetylcholine on excitability of the nodal fibers can be obtained from an inspection of records similar to those in figure 6. The small depolarizations recorded during partial block show temporal summation; comparison of the level of depolarization caused by such summation, which is just sufficient to cause propagation through the node, with the level of membrane potential at which the action potential shows an abrupt transition from slow to rapid depolarization suggests that the threshold potential is not much changed by acetylcholine. It does not increase the resting potential of fibers in the A-V node as it does in the sinoatrial node; this observation at least does not give any positive support to the possibility that acetylcholine causes block by decreasing membrane resistance of nodal fibers. The block caused by acetylcholine thus appears to result from the failure of the fibers at the atrial margin of the node to develop an action potential, and this failure is associated in some way with asynchronous excitation of these fibers. Both the failure of excitation and the asynchronous excitation may be due to the action of acetylcholine on the atrial fibers at the atrionodal junction. Action potentials recorded from them are greatly decreased in amplitude during acetylcholine-induced block. This may be caused by the effect of acetylcholine on potassium permeability which is known to occur in atrial muscle: a greatly enhanced K+ efflux may partly cancel the depolarization caused by an inward Na+ current.

Disturbances of A-V transmission caused by premature atrial beats or a rapid atrial rate are associated with somewhat different changes in nodal action potentials. At the

*Figure 5 reproduced from Cranefield et al.: Circulation Research 7: 19, 1959. By permission of the American Heart Association, Inc.
Figure 10

A and B. Transmembrane action potentials recorded from an isolated Purkinje-fiber–papillary-muscle preparation of canine heart. Extrasystoles in the papillary muscle (lower trace) excite the Purkinje fiber at various levels of membrane potential during repolarization and elicit either premature action potentials or local responses (last action potentials in B). C. Transmembrane action potentials recorded from an isolated preparation of canine Purkinje fibers. Marked pacemaker activity has been induced by an excessive concentration of digitalis. Extrasystoles (arrows) caused by test pulses contrast markedly in terms of rate of rise and amplitude of the action potential with the action potentials of intrinsic origin.

atrial margin of the node, the amplitude of the transmembrane action potential is reduced and the rate of depolarization is slowed (fig. 7A). When these changes are extreme, records from fibers in the lower node may show a slow, steep-like depolarization of considerable duration preceding the local action potential (fig. 7B). During failure of transmission, only the graded steep-like depolarization is recorded. Block caused by agents such as digitalis or quinidine is associated with similar changes in nodal action potentials. During block of retrograde impulses that reach the node, the failure of conduction most often is localized to the atrioventricular junction. Also, action potentials recorded at different sites within the node are different during normal and retrograde transmission; the change is in the initial segment of the upstroke and probably is related to the anatomic arrangement of the various fibers.

Delay and Block Within the Bundle of His and Bundle Branches

Experimentally produced conduction disturbances within the bundle of His and bundle branches most often result from 2 factors: local differences in action-potential duration and/or the presence of slow diastolic depolarization associated with latent pacemaker activity. In both cases the failure of normal conduction results directly from the low membrane potential. If the transmembrane potential is reduced, because of either incomplete repolarization or local pacemaker activity, the rate of rise and amplitude of the action potential are decreased (fig. 8). The altered action potential may propagate at a reduced velocity or may constitute a purely local response. If the reduced conduction velocity permits the adjacent membrane to repolarize completely, the slowing of conduction may be localized to a small segment of the conducting system. If, on the other hand, slowing of conduction is caused by diastolic depolarization, adjacent areas of membrane will have reached still lower levels of membrane potential and decremental conduction and block may result.

Block at the Junction of Purkinje Fibers with Ventricular Muscle

During A-V transmission, block at the junction of Purkinje fibers with ventricular muscle fibers is unlikely for several reasons. The transition from the larger Purkinje fibers to the smaller muscle fibers is gradual, and thus there is not an abrupt increase in the area of excitable membrane. Also, the duration of the ventricular action potential is consider-
ably less than that of the Purkinje fibers in adult mammalian hearts (fig. 9). Hence the likelihood of a premature impulse reaching the ventricle before it is fully repolarized is reduced. However, premature depolarization of ventricular muscle may be delayed or blocked at the junction with the Purkinje system (fig. 10, A and B) and the impulse may propagate at reduced velocity for a considerable distance. Although a conclusive experimental demonstration is lacking, it is likely that excitation may enter some branches of the Purkinje system and fail to enter others. Whether this would cause local re-excitation of the ventricle has not yet been determined.

Supernormality

The term "supernormality" is used with 2 meanings in descriptions of cardiac excitability: it may refer to a reduced stimulus requirement or it may refer to conduction that is either faster than expected or takes place under conditions that might be expected to cause block. The cause of both forms of supernormality is clear from studies of transmembrane action potentials. Enhanced excitability is found during the terminal phase of repolarization; however, the action potential elicited at this time is reduced in amplitude and propagates slowly. A supernormal phase of conduction is observed in fibers which are partially depolarized or in which there is appreciable diastolic depolarization. In such fibers, membrane potential reaches its highest value just at the end of repolarization. An action potential elicited at this moment will show a higher rate of rise and greater amplitude than responses that occur later during the cardiac cycle (fig. 10B). Also, the larger action potentials will propagate more rapidly and will have a greater safety factor.

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