Monophase Action Potentials in Man

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SUMMARY
Monophasic action potentials with an amplitude of up to 70 mv were recorded with suction electrodes from the endocardial surface of the right atrium and both ventricles during diagnostic cardiac catheterization. The method was simple and safe. The monophasic action potential of human beings had the same shape and the same relation to the electrocardiogram as the transmembrane action potential of animals has. Also changes in heart rate and administration of calcium and digitalis had the same effect on the monophasic action potential of man as on the transmembrane action potential of animals.

When injections of contrast material into the coronary arteries produced T-wave changes, the monophasic action potential from the ventricle perfused by the contrast medium lengthened, but the monophasic action potential from the other ventricle did not change.

Our study suggests that the monophasic action potential may be helpful in estimating the refractory period at the site of recording and in explaining the pathogenesis of abnormal repolarization in the electrocardiogram.

Additional Indexing Words:
T-wave abnormalities  Refractory period  Calcium  Coronary arteriography  Repolarization

Electrical activity from the surface of the injured myocardium has been recorded since the earliest days of electrophysiological investigation. In a classical monograph Schütz described methods of recording monophasic action potentials with suction electrodes and discussed the relationships of such records to the duration of refractoriness and the surface electrocardiogram. Hecht discussed in detail the relation of injury potentials to true transmembrane potentials and calculated the amplitude of the injury potentials to be smaller because of short circuits caused by cellular injury. Hecht emphasized that conclusions based on injury effects have to be accepted with caution although he demonstrated that injury potentials reflect many of the characteristics of intracellular recordings.

Studies in isolated perfused rabbit hearts have shown that monophasic action potentials recorded with suction electrodes have the same shape and duration as transmembrane action potentials recorded with intracellular microelectrodes. This suggests that the monophasic action potential from the human heart might faithfully represent the shape and duration of the transmembrane action potential. To our knowledge there is only one report in the literature of monophasic action potentials recorded with suction electrodes in vivo from man; that of Kosgren and his associates who recorded monophasic action potentials from the right atrium in three patients. We independently devised a simpler method of recording monophasic action potentials from the endocardial surface of the human heart by means of suction electrodes incorporated into ordinary cardiac catheters.
The purpose of this paper is to describe the method, report preliminary results, and discuss the application of this technique.

Methods

The apparatus consisted of a stainless steel wire of 0.1 inch in diameter inserted into a thin-walled no. 7 or 8 cardiac catheter that had terminal openings but no side holes. One end of the wire was positioned 1 mm proximal to the tip, and the other end was attached to the hub. The indifferent electrode was attached to the right arm. The catheter was connected by Tygon tubing to wall suction which provided a negative pressure of 75 mm Hg.

Clinical studies were preceded by dog experiments designed to test the safety of the suction method. Monophasic action potentials from the left and right ventricles were recorded with electrode catheters identical to those subsequently used in patients. Suction with a negative pressure of 75 mm Hg was applied for 60 to 90 minutes. The dogs were sacrificed, and the hearts were removed with the catheters in position to locate the recording sites. The tissue at and around the catheter tip was excised for gross and microscopic study.

The clinical studies were performed during diagnostic cardiac catheterization. The catheter was advanced into the right atrium or into the right or left ventricle, and the tip was placed against the endocardium while the intracavitary electrocardiogram was monitored. Gentle pressure against the wall transformed the intracavitary electrocardiogram into a monophasic action potential. Suction was applied when the monophasic action potential was distinct and the catheter did not provoke an arrhythmia. When the catheter tip was properly positioned against the cardiac wall, blood was not aspirated into the tubing. Suction increased the voltage of the monophasic action potential, stabilized the diastolic base line, and minimized the superimposed electrocardiographic artifacts. Monophasic action potentials were recorded continuously for periods ranging from a few seconds to 2 minutes. Suction was discontinued between recordings. Monophasic action potentials from one or two cardiac chambers were recorded simultaneously with the electrocardiogram on a multichannel recorder* and photographed on paper moving at speeds ranging from 50 to 200 mm/sec. Precautions were taken to prevent a current leak into the heart.

We recorded monophasic action potentials during the intravenous administration of: (1) 7 to 10 ml of 10% calcium chloride solution at a rate of 100 mg/min (three patients); (2) 300 ml of 1% Na2EDTA solution in saline at a rate of 200 mg/min (one patient); (3) 1.5 mg of acetyl-

*Electronics for Medicine, Inc., DR 8, White Plains, New York.

Results

Dog Studies

The monophasic action potentials had the same shape as transmembrane action potentials recorded in other studies.7 The monophasic action potentials were distorted by superimposed electrocardiographic artifacts which were as a rule least pronounced in the records with the greatest amplitude. Technically satisfactory monophasic action potentials with an amplitude greater than 20 mv were recorded in all dogs during the first 5 to 14 minutes after the application of suction. Thereafter the amplitude decreased progressively. No arrhythmias were encountered after the initial placement of the catheters. Gross and microscopic examination of the recording sites and adjacent tissues revealed no endocardial or myocardial lesions.

Clinical Studies

The onset of the upstroke could be readily identified. It occurred in the right ventricle usually during the inscription of the first 0.02 sec of the QRS complex and in the left ventricle during the inscription of the first 0.04 sec of the QRS complex. The upstroke and
Figure 1

Record of a monophasic action potential (continuous trace) illustrating the methods of measurement of the duration of phases 2 and 3 and the total AP duration. The dashed vertical line, the spike, and the initial portion of phase 2 are drawn to illustrate the portions of the monophasic action potential which would be expected to appear in a record free from artifacts. The tangents to the slopes of phases 2 and 3 intercept at X. The horizontal projection of X to the downslope, B₁, is taken as the end of phase 2. The duration of phase 2 is taken as AB (=A,B₁). The slope of phase 3 is extended to the base line at C. The duration of phase 3 is taken as BC and that of the total action potential as AC. Paper speed 200 mm/sec.

early repolarization of the ventricular monophasic action potential were invariably distorted by the QRS artifact (figs. 1 and 2). The upstroke and early repolarization of the right atrial monophasic action potential were distorted by the P wave (fig. 3). The repolarization limb of the monophasic action potential could be divided into an initial slow phase 2 and a terminal rapid phase 3 (figs. 1, 2, and 3). Figure 1 shows that the early portion of phase 2 was not recorded. The end of phase 2 was taken as the intercept of the tangents to the flat portion of phase 2 and the steepest portion of phase 3. The duration of phase 2 was measured as the interval from the onset of the monophasic action potential to the end of phase 2 (fig. 1).

In some records, the T artifact distorted the terminal portion of phase 3 of the ventricular monophasic action potential. When this was present, the end of the monophasic action potential was not visible but could be estimated by extending the slope of phase 3 from the beginning of the artifact to the base line (fig. 1). The QRS artifact distorted phase 3 of the right atrial monophasic action potential (fig. 3). The duration of the monophasic action potential was measured from the onset of the monophasic action potential to the end of phase 3. We made no attempt to measure upstroke velocity or to analyze portions of the monophasic action potential distorted by electrocardiographic artifacts.

In records without large terminal artifacts the monophasic action potential amplitude varied from 15 to 70 mv. An example of a record with an amplitude of 70 mv is shown in figure 2.

The slopes of phase 2 were identical in both ventricles; likewise the slopes of phase 3 were also identical in both ventricles. This relationship held over a wide range of R-R intervals (fig. 4). The interval between the end of the right ventricular monophasic

Figure 2

Normal monophasic action potentials and normal electrocardiogram in a patient with mitral stenosis.
Figure 3

Effect of rate on the right atrial monophasic action potential. The duration of the right atrial monophasic action potential cannot be accurately measured because the QRS artifact distorts phase 3. However, phase 2 is not distorted. Phase 2 is longer in the sinus beats (first and third potentials) than in the atrial premature beat (second potential) with aberrant ventricular conduction. The P wave of the extrasystole is not clearly visible in lead II. Esophageal and intracavitary right atrial leads simultaneously recorded with the standard leads (not shown in this figure) suggested that the extrasystole originated in the left atrium.

Figure 4
MONOPHASIC ACTION POTENTIALS

Effect of rate on the right ventricular monophasic action potential in two patients. (A) The ventricular monophasic action potential of an atrial extrasystole (second beat) is narrower than the monophasic action potential of the preceding and the succeeding beats. (B) Five monophasic action potentials during ventricular tachycardia are narrower than the monophasic action potential of the sinus beat which occurs after a longer R-R interval.

The duration of atrial and ventricular monophasic action potentials increased with increasing duration of the preceding R-R interval (figs. 3, 4, and 5). These rate dependent

Left and right ventricular monophasic action potentials are superimposed during injection of contrast medium into the right coronary artery. (A) Electrocardiogram (lead II) shows transient atrioventricular block immediately after injection. The monophasic action potential in the first and second beats is slightly longer than that in the third and the fourth beats, but the repolarization slopes of the two action potentials do not diverge. (B) Sinus bradycardia immediately after injection into another patient. The repolarization slopes of the two monophasic action potentials do not diverge.

Figure 5

Figure 6

Effect of administration of CaCl₂ in hypoparathyroidism. (Top left) Plasma calcium 2.5 mEq/L. Phase 2 of the right ventricular monophasic action potential and the S-T segment in lead II are prolonged. Retouched tracings of left ventricular pressure and its first derivative are superimposed on the first complex. (Top right) After intravenous administration of 0.7 g of CaCl₂. Plasma calcium concentration = 5.0 mEq/L. Note shortening of phase 2 of the right ventricular monophasic action potential and of the S-T segment and increased left ventricular pressure and first derivative.

potential ended in all beats at or before the end of the T wave. The interval between the end of the monophasic action potential and the end of T ranged from 0 to 60 msec.
Figure 7
Effect of intravenous administration of 1.5 mg of acetylstrophanthidin on the right ventricular monophasic action potential and lead II. Heart rate before and after acetylstrophanthidin is nearly the same; S-T segment is slightly depressed; and the Q-T is shortened. Note the steeper phase 2 and shorter monophasic action potential after acetylstrophanthidin.

Figure 8
changes were caused by changes in the slope of phase 2 while the slope of phase 3 was unchanged.

Simultaneous shortening of the S-T segment and phase 2 of the ventricular monophasic action potential occurred when plasma calcium concentration was raised to 7.5 to 8.0 mEq/L. Simultaneous lengthening of the S-T segment and phase 2 of the ventricular monophasic action potential occurred when plasma calcium concentration was lowered to 2.7 mEq/L by Na₂EDTA administration. Figure 6 shows shortening of phase 2 and of the S-T segment during calcium infusion in a patient with hypocalcemia secondary to accidental parathyroidectomy.

Acetylstrophanthidin depressed the S-T segment slightly, shortened the Q-T interval, and increased the slope of phase 2 of ventricular monophasic action potentials (fig. 7). The slope of phase 2 was increased even when acetylstrophanthidin slowed the heart rate.

**Ventricular Extrasystoles**

The interval between the end of the mono-

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**Effect of ventricular extrasystoles on right ventricular (upper tracing) and left ventricular (lower tracings) monophasic action potentials. Discussion in text.**

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phasic action potential and the end of the T wave in ventricular extrasystoles was usually longer than in nonpremature beats. It ranged from 30 to 130 msec. The shortest monophasic action potentials and the longest intervals between the end of the monophasic action potential and the end of the T wave were recorded in the extrasystoles with the shortest coupling intervals.

Figure 8 shows monophasic action potentials in both ventricles of two extrasystoles that arise in the right ventricle. The slope of phase 2 is steeper in the extrasystoles than in the nonpremature beats. The extrasystole in the upper strip has a shorter coupling interval than the extrasystole in the lower strip, but in both the slope of phase 2 is steeper in the right ventricular monophasic action potential than in the left ventricular monophasic action potential, although this difference is greater in the extrasystole with the shorter coupling interval. The steeper slope of phase 2 in the right ventricular monophasic action potential suggests that it may be shorter than the left ventricular monophasic action potential. However, this

![Diagram](image_url)
cannot be proved because a large T artifact distorts phase 3 of the right ventricular monophasic action potential. The interval between the onset of right and left ventricular monophasic action potentials is longer in the extrasystole with the shorter coupling interval which suggests a longer interventricular conduction time. The right ventricular monophasic action potential begins before and the left ventricular monophasic action potential begins after repolarization of the preceding impulse is completed. With longer coupling intervals, the conduction time between the ventricles shortens, and both monophasic action potentials begin after repolarization of the previous impulse is completed.

Shortening of the monophasic action potential in an early extrasystole originating during incomplete repolarization is demonstrated in figure 9. When the ventricles are paced at a rate of 48 beats/min (R-R interval, 1280 msec) the duration of the monophasic action potentials is 320 msec (fig. 9A). When the ventricles are paced at a rate of 160 beats/min (R-R interval, 370 msec) the duration of the monophasic action potentials is 265 msec (fig. 9B). The coupling interval of a spontaneous extrasystole (fig. 9C) measures 370 msec which is identical to the R-R interval in figure 9B, but the monophasic...
action potential duration of this ventricular extrasystole is 240 msec. Figure 9C and D illustrates monophasic action potentials of early ventricular extrasystoles in which the R wave interrupts the T wave.

**Effect of Coronary Arteriography**

Injection of contrast medium into the coronary arteries frequently produced a transient increase of T amplitude and prolongation of Q-Tc. Figure 10 illustrates right ventricular monophasic action potentials recorded when these electrocardiographic changes followed injection into the right coronary artery. Electrocardiographic changes appear in the seventh beat, are most prominent in the ninth and tenth beats, and disappear in the twentieth beat. The heart rate does not change appreciably during this period. The figure shows that progressive widening of the T wave is accompanied by progressive lengthening of the right ventricular monophasic action potential. This appears to be caused by slowing of both phase 2 and phase 3.

Figure 11 illustrates simultaneous left and right ventricular action potentials recorded during injection of contrast medium into the right coronary artery in another patient. After the injection, the T wave becomes wider and more deeply inverted, and the duration of the right ventricular monophasic action potential increases. However, the left ventricular monophasic action potential remains unchanged. The time between the onset of the right and left ventricular monophasic action potentials remains the same throughout the procedure. However, both before the injection and after recovery from the effects of the contrast material, the right ventricular monophasic action potential ends before the left. During the period of maximal T and Q-T alteration, the right ventricular monophasic action potential ends after the left.

The monophasic action potential remained unchanged when injection of contrast into the coronary arteries did not produce T-wave changes. Figure 4A shows the electrocardiogram and monophasic action potential of a patient after injection of contrast medium into the right coronary artery. The injection produced transient A-V block but no T abnormalities and no difference between the repolarization slopes of the right and left ventricular action potentials.

**Discussion**

These experiments suggest that the monophasic action potential recorded from the human heart faithfully reflected the shape and duration of the transmembrane action potential at the recording site; the shape of the monophasic action potential was similar to the shape of the transmembrane action potential in animals, and the relationship between the electrocardiogram and the monophasic action potential was the same as the relationship between the electrocardiogram and the transmembrane action potential in animals. Calcium, heart rate, and acetylstrophanthidin had identical effects on the human monophasic action potential as on the transmembrane action potential of animals. As in the rabbit heart, the duration of the S-T segment paralleled the duration of phase 2, while T-wave changes reflected the slope of phase 3.

The theory of the monophasic action potential and the differences between the monophasic action potential and the transmembrane action potential have been discussed elsewhere. The monophasic action potential has a lower amplitude and contains no information about the resting membrane potential or the upstroke velocity of the action potential. However, the monophasic action potential does reflect the duration of the transmembrane action potential and represents the repolarization slope with fidelity. In our records the early portion of repolarization was obscured by electrocardiographic artifacts, but it may prove possible to remove such artifacts by electronic subtraction.

The duration of the monophasic action potential approximates the duration of the refractory period at the recording site. In most of our records with normal QRS duration and upright T waves in the standard leads, monophasic action potentials from the
ventricular cavities ended at or slightly before the end of the T wave. Assuming that the end of the T wave coincides with the end of ventricular repolarization, the refractory period in the subendocardial regions appears to have approximately the same duration as the refractory period of the entire ventricular myocardium. The long interval between the end of the monophasic action potential and the end of the T wave in ventricular extrasystoles demonstrates the large difference between the refractory period of the subendocardial region and that of the entire ventricular myocardium. This difference is attributed to increased duration of depolarization and subsequent repolarization of the extrasystoles. Shortening of the ventricular monophasic action potential in extrasystoles with short coupling intervals may be caused by two factors: the short coupling interval itself and the onset of depolarization during incomplete repolarization. In figure 8 the right ventricular monophasic action potential in the extrasystole with the shorter coupling interval began before repolarization was complete and appeared shorter than the left ventricular monophasic action potential which began after the completion of repolarization. Because of the T artifact, the end of the right ventricular monophasic action potential was not registered but was estimated; therefore we could not be certain of the duration of the monophasic action potential. However, the monophasic action potential of a ventricular extrasystole that began during incomplete repolarization and had a coupling interval of 370 msec was 25 msec shorter than the monophasic action potentials which began after repolarization during pacing with an R-R interval of 370 msec (fig. 9). Our studies suggest that monophasic action potentials may be useful in estimating differences between refractory periods in different areas of the heart, especially when the sequence and duration of activation are abnormal.

Monophasic action potential recording may help to clarify mechanisms responsible for abnormal T waves. The monophasic action potential may be abnormal when the T-wave change is primary but not when it is secondary to a QRS change. There are two types of primary T-wave abnormalities. The first is caused by a change in repolarization in all ventricular fibers. This occurred presumably after the administration of calcium or digitalis. In the second type of primary T-wave change, the repolarization abnormality is confined to a portion of the ventricular myocardium. Our study suggests that this type of primary T-wave change sometimes follows coronary arteriography.

Electrocardiographic changes after injection of contrast medium into the coronary arteries have been described previously and have been attributed to the effects of sodium in the contrast agent. In our studies, injection of 3% sodium chloride into the coronary arteries induced monophasic action potential changes that were identical to those seen after the injection of contrast medium. Coronary arteriography may also alter the duration and vector of the QRS complex resulting in secondary T abnormalities. The T-wave changes in some of our cases were attributed to a combination of primary and secondary abnormalities.

References
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