The T Deflection of Isolated Mammalian Heart Muscle Electrogram

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Both bipolar and unipolar electrograms recorded from well-oxygenated isolated papillary muscle preparations consist of R and T deflections in the same direction. The T is inverted by anoxia, rapid rate, and injury. When cut linear strips of ventricular muscle are observed for many hours, during which time they presumably recover from the initial injury, the T deflection becomes upright in most cases, and then can be depressed and inverted by anoxia or rapid rates of stimulation. Since, in the absence of modifying factors, the T is in the same direction as the R deflection in a simple linear strip, it probably cannot be adequately explained on the basis of membrane repolarization. Since the nerve after-potentials are believed to represent processes involving oxidative metabolism, the T deflection may also be produced by metabolic processes, although this possibility cannot be excluded that it represents a combination of membrane repolarization and other processes.

ACCORDING to the commonly accepted theory of the genesis of the electrocardiogram, the R and T deflections are due to changes in polarization of the myocardial cell membrane. The R deflection is considered the result of depolarization, and the T is ascribed to repolarization. This concept is based to a large extent on experiments on heart muscle strips from various species.1

Preliminary studies on the papillary muscle preparation of Cattell and Gold2 yielded electrocardiographic patterns which did not seem entirely compatible with the classic theory of the T wave,3 but which were not convincing because relatively inadequate equipment was employed, and only a muscle-to-tendon lead was recorded. Therefore, the initial observations on the effects of anoxia and rapid rate were repeated and extended with both muscle-to-muscle, and muscle-to-tendon leads recorded simultaneously on improved apparatus to exclude possible artefacts. Furthermore, in order to evaluate more fully the changes produced by factors which may have complicated the earlier studies of other investigators, the present report includes the effects of injury and increased tension, unipolar lead recording, and the changes observed in the electrograms of cut strips of ventricular muscle.

A. EXPERIMENTS WITH BIPOLAR LEADS

Method

The papillary muscle was removed in the usual manner4 and mounted in a lucite holder with electrodes arranged as indicated in figure 1. The base was tied to an adjustable hook, and the chorda tendina attached by means of a fine silk thread to a strain gage. The muscles ranged from 7 to 14 mm. in length, and from 0.2 to 2 mm. in diameter, with parallel contractile fibers. In some muscles, the tapering toward the chorda tendina was fairly pronounced. However, in most preparations, no tapering was evident. Care was taken to avoid cutting, stretching, or touching the belly of the muscle with an instrument. Resting tension was adjusted to the minimal level producing a deflection in the record. The silver-silver chloride recording electrodes were arranged in pairs, with the members of each pair connected so that side-to-side movements would not cause variations in potential. Lead A was taken from the upper third of the muscle and the chorda tendina, while lead B was taken from the center of the muscle and the upper third (fig. 1). The connections were arranged so that negativity at the lower electrodes of each lead produced an upswing of the record from the baseline. (The connections were described incorrectly in the earlier study5.)

The two stimulating electrodes were placed so that the stimulus passed across the base of the
The stimulus artefact was usually visible as a small, rapid deflection just preceding the R. In each experiment, the stimulus artefact and R deflection were differentiated by varying stimulus voltage and polarity. Such variations produced corresponding changes in stimulus artefact, but not in the R deflection. Stimulus voltage was then adjusted to just over threshold (3 to 10 volts), and rate was usually 30 per minute.

The Locke's solution surrounding the muscle was gassed vigorously and continuously with a mixture of 95 per cent oxygen and 5 per cent carbon dioxide, and during recordings, was lowered below the base of the muscle to prevent short-circuiting of the recording electrodes.

Most experiments were repeated several times, using different stimulators, amplifiers, recorders, and species of mammal, to rule out the possibility that the electrocardiograms obtained were significantly altered by artefacts in the experimental situation. The most commonly used recorders were a Grass Model II, ink-writing oscillograph and a Dumont Model 279, two-channel cathode ray oscillograph.

Results

One hundred and two muscles were studied with a single lead recorded. In most, the electrogram taken after a 15 to 30 minute equilibration period consisted of an upright R deflection, followed by an upright T (fig. 1). In some preparations, usually short, thick muscles, an initially inverted T deflection, or a raised or lowered R-T segment became normal after a period of vigorous oxygenation.

The R-T interval varied considerably under control conditions. Thicker muscles usually had longer R-T intervals than thinner muscles.

In each of eight muscles studied with two leads recorded simultaneously with the myogram, both the muscle-to-muscle and muscle-to-tendon leads showed upright R deflections followed by upright T deflections. Substitution of nitrogen for the oxygen in the gas mixture resulted in a gradual inversion of the T deflection in both leads, shortening of the R-T interval, slight widening of the R deflection (fig. 2A), and decrease in contractile force. Restoration of the oxygen resulted in a gradual return of the T deflection, R-T interval, R deflection, and contractile force to normal.

The T deflections recorded on the two-beam cathode ray oscillograph were enlarged and examined to see whether there was any measurable difference in the onset of the deflections in the two leads. No differences were detected. Similarly, examination of the T deflection peaks did not reveal any consistent differences. Usually, the peaks occurred at the same time.

In each of 10 muscles, an increase in stimulation rate from 30 to 180 per minute resulted
within one minute in inversion of the T deflec-
tion, shortening of the R-T interval and an
increased contractile force. Following the
restoration of the slower stimulation rate, the
T deflection, R-T interval and contractile force
returned to control levels.

Step-wise increases in stimulation rate
resulted in gradual inversion of the T deflec-
tion, shortening of the R-T interval and in-
crease in contractile force (fig. 2B).

Moderate injury, produced in five muscles
by two punctures with a sharp 26-gage needle,
resulted in inversion of the T deflection, usually
in the lead nearest the injured area. In two
muscles, however, a single puncture produced
inversion of the T deflection in both leads. In
four of the injured muscles, observed for
several hours after injury, the electrograms
returned to the control pattern in from one-
half to five hours (fig. 3A).

In five muscles, electrograms and myograms
taken within two minutes of severe injury
inflicted by a single longitudinal scalpel cut
showed little or no systolic force, and a single,
slow, upright deflection of varying voltage in

![Figure 2A](http://circres.ahajournals.org/)

**Fig. 2A.** The gradual changes in the electrogram following changes in oxygen tension.

**B.** The T deflection of the electrogram at different stimulation rates per minute. Records were taken one minute after increase in rate.

both leads, returning gradually to the iso-
electric line. After about 30 minutes, the elec-
trograms showed normal R deflections with
inverted T deflections, and a partial recovery
of systolic force. Following an additional inter-
val of from 1 to 3 hours, the electrograms and
myograms returned to normal (fig. 3B).

Gradually increased resting tension, tested
on five muscles, resulted in an increase in
systolic force (in accordance with Starling's law) and an elevation of the R-T segment. Restoration of the control resting tension resulted in a return of the R-T segment to the isoelectric line within three minutes (fig. 4A).

A sudden, severe stretching of four muscles produced a marked deformation of the electrogram and loss of systolic force (fig. 4B), resembling the effects of severe cutting injury.

B. Experiments with Unipolar Leads

Experiments were performed on cat papillary muscles immersed in a volume conductor to determine whether the unipolar electrogram is similar to the bipolar electrogram and whether it changes in the same manner.

Method

The muscles were removed and mounted in the usual manner in a chamber filled with Locke's solution, of about 5000 times the volume of the muscle. The preparation was stimulated at the base, and the connections arranged so that relative negativity of the exploring electrode produced an upswing of the writing pen. Because of the shunting effect of the volume conductor, the amplification of the recording instrument (Grass ink-writing oscillograph) had to be increased about 50 times. Only those preparations with very low thresholds of irritability could be used, since stimulus artefacts distorted the electrogram markedly in other preparations. The effects of rate changes were studied, and then a slow, spontaneous rhythm was induced by epinephrine, or a combination of epinephrine and sudden, slight stretching of the muscle.
Results

In the unipolar leads taken from the areas near the base of the muscle, both the R and the T were upright. In the leads taken from the tip of the muscle, both deflections were inverted.

With increased stimulation rate, the direction of the T changed until it was in the opposite direction to the R. Following a reduction in stimulation rate, the T returned to its original position.

Method

The strips, about 3 by 3 by 20 mm. were mounted in a holder and treated in the same manner as the papillary muscles. Higher stimulating voltages were usually needed. Single leads were recorded on the ink-writing oscillograph at intervals during a period of from 8 to 45 hours. When the T deflection became upright, the effects of rapid rates of stimulation and anoxia were tested in the manner previously described.

Results

Of the 11 strips studied, one maintained a rapid spontaneous rhythm and was therefore discarded. Two responded to stimulation when first placed in the chamber, and eight did not respond until periods of from one and one-half to five and one-half hours had elapsed. In one
strip, the first electrogram, taken 35 minutes after excision, showed an upright T deflection. The electrograms of the other nine strips had initially either monophasic potentials or inverted T deflections. In one strip, observations were discontinued at the end of eight hours, while the T was still inverted, and in another strip the T deflection remained inverted for 45 hours. In seven preparations, the T deflec-

tions gradually became upright after periods of from 3½ to 25 hours. When the T deflections had become upright, they remained so until the experimental conditions were changed. Anoxia, studied in four strips, resulted in depression and then inversion of the T deflection and shortening of the R-T interval, as was the case with the papillary muscles. Similarly, restoration of oxygen resulted in a return of the T deflection to an upright configuration (fig. 6).

An increased stimulation rate, studied in five strips, produced lowering and then inversion of the T deflection. Restoration of the original slow stimulation rate resulted in a rapid return of the T to its upright configuration (fig. 7).

In two respects, the electrogram of the cut strips differed slightly from the electrograms of the papillary muscles. The R-T intervals of the cut strips were much longer than the R-T intervals of the papillaries. Furthermore, several strips had fractionated R deflections, with two or three spikes very close together.

**DISCUSSION**

Some consideration should be given to the suitability of the preparations used in these studies. The upper part of the papillary muscle from which electrograms were recorded was substantially uninjured. Although the remaining fragment of ventricular wall below the stimulating electrodes was obviously subjected to severe injury, it is unlikely that injury potentials from it influenced the electrograms to any significant degree. The distance between the cut end and the nearest recording electrode was greater than the distance between stimulating and recording electrodes, and usually stimulus artefact was barely visible even though the stimulus voltage was many times greater than any injury potential. Although the oxygenation of this preparation does not reach in vivo levels, it is better than the oxygenation of thicker preparations, particularly since in many of the latter used in earlier studies, no special efforts were made to supply oxygen to the cells continuously.

The most striking observation on the papillary muscle preparation is the similarity of electrograms taken from it to the electrocardiograms of humans or animals under parallel conditions. Similar changes are produced in both by anoxia, rapid rate, injury, and various drugs (unpublished data). These similarities increase the validity of observations on the isolated cat papillary muscle in studying the electrical potentials produced by the heart. The experiments on cut ventricular strips confirm the results obtained on the papillary muscle, indicating that they apply to mammalian ventricular muscle generally.
The inversion of the T during rapid stimulation probably results from a relative anoxia, since with increased work, the oxygen requirement increases, while the supply of oxygen diffusing into the muscle remains about the same. The effects of injury and severe stretch are similar to the effects of excess potassium. It seems likely that following cutting or tearing of muscle fibers, potassium escapes from the injured fibers, increasing the concentration of the ion in the extracellular fluid surrounding the uninjured fibers, and diffusing out into the surrounding chamber at a relatively slow rate. Since the potassium concentration inside the cell is over 30 times that in the extracellular fluid, damage to a few fibers can cause the

![Graph](image-url)
liberation of enough of these ions to produce a profound effect on many surrounding fibers. When the excess potassium liberated by the damaged cells diffuses out into the surrounding Locke's solution, it would not produce a measurable change in its potassium concentration, since the volume of surrounding fluid is thousands of times greater than the volume of the muscle. Thus, recovery from the injury effects would occur. The mechanism whereby moderately increased tension produces elevation of the R-T segment of the electrogram is not clear, and may be unrelated to the elevation of the R-T segment in the electrocardiogram.

A discussion of the experimental preparations and technics used in the older experiments on which the present concepts of electrocardiography are based is also pertinent. Basically, the preparations fall into two groups: cut linear strips and whole chambers or hearts either isolated or in situ. The injury which is automatically produced by cutting or teasing out a linear strip is probably sufficient to alter the electrical patterns, unless a considerable period of time is allowed for recovery. Even the small amount of injury inflicted by a 26-gage needle puncture will cause inversion of the T deflection. Therefore, it seems that the inverted T deflections recorded in the earlier experiments on cut strips do not indicate the normal pattern, but may represent the effects of cutting, or stretching injury, from which the muscle did not have sufficient time to recover. In some cases, anoxia probably further complicated the effects. The occasional upright T found with the older preparations may have followed recovery from injury.

The observation that hearts and heart muscle strips obtained from frogs and turtles continue to beat for periods in air is not valid evidence that they are not injured or anoxic, since it has been shown that heart muscle preparations continue to contract despite anoxia and moderate injury.

The present study indicates that the normal electrogram recorded from isolated heart muscle in which injury and anoxia effects have been minimized, consists of a negative (upright) R deflection followed by a T deflection in the same direction. Since the T deflection is normally in the same direction as the R, it is difficult to see how it can be ascribed to an opposite electrical process, that is, repolarization, unless the reason for its normally upright configuration can be presented. The following possibilities may be considered:

1. The T deflection may be produced by a wave of repolarization which begins at the part of the muscle stimulated last, that is, the tip, and may proceed in the direction opposite to that taken by the wave of stimulation. However, careful examination of cathode ray oscillograph records of T deflections taken from the two leads simultaneously does not support such an explanation. Furthermore, it is difficult to see how, in a thin strip with parallel fibers, the predictable gradual changes in the T deflection can be accounted for on the basis of change of direction of a wave of repolarization.

2. The normally upright T deflection of the isolated muscle may result from a ventricular gradient so constituted as to produce an upright T. Against such an interpretation, how-
ever, is the consideration that since the ventricular gradient is a vector expression of local or regional differences in the time-course of repolarization, its direction would be dependent to a large extent on the shape of the preparation studied. The many similarities between the papillary muscle electrogram, the electrogram of the cut strip allowed to recover from injury, and the electrocardiogram of the intact animal have been pointed out. The three preparations are all grossly different in shape and arrangement of muscle bundles, and it would therefore be a surprising coincidence if they all developed similar ventricular gradients under the same conditions.

The results of this study suggest that much of the evidence upon which the current theories of the T deflection are based may have been faulty in that factors of anoxia or injury may have been present in the preparations employed, and may have significantly altered the electrogram. On the other hand, there is considerable evidence which indicates that depolarization and repolarization occur, and are associated with the production of electrical potentials. Therefore, the results of the present study are not to be considered in opposition to the membrane theory as such, but as suggesting that the T deflection cannot be adequately explained by membrane repolarization, alone.

Neurophysiologists have shown that in addition to the potentials produced by membrane depolarization and repolarization, nerves produce a number of after-potentials. In several ways, the nerve after-potentials which should be considered as a whole closely resemble the T deflection of heart muscle. The nerve after-potentials are also depressed by anoxia and recover when oxygen is reintroduced. The supernormal period in nerve is coexistent in time with the after-potential, while the supernormal period in heart muscle corresponds in time to the latter half of the T deflection, or to the U deflection when present. Finally, veratrine produces a marked prolongation in the after-potentials of nerve, accompanied by a less marked increase in their magnitude, without any change in the spike potential. The actions of veratrine on the T deflection of the heart muscle electrogram are the same as the effects on the nerve after-potential (unpublished data). These similarities suggest a similar nature for the T deflection of heart muscle and the after-potentials of nerve. Since neurophysiologists believe that the nerve after-potentials, taken as a whole, represent an oxidative recovery process, it may be that the T deflection similarly reflects one or more oxidative recovery processes.

Another possibility is that the T deflection may represent a combination of membrane repolarization and oxidative recovery processes. Thus, the inverted T may be produced largely by repolarization, while the upright T may result from an algebraic summation of a positive (inverted) repolarization potential, and negative (upright) potentials, produced by oxidative metabolism.

**Summary**

The bipolar electrogram recorded from the relatively uninjured, well oxygenated isolated papillary muscle preparation consists of an upright (negative) R deflection followed by a T deflection in the same direction. Similarly, the unipolar electrogram under control conditions exhibits a T deflection in the same direction as the action potential. The T is inverted by anoxia, rapid rate (relative anoxia) and injury. Cut linear strips of ventricular muscle initially produce electrograms in which the T deflection is inverted. However, when the cut strip is observed for many hours, while it presumably recovers from the initial injury, the T deflection becomes upright in most cases. This upright T deflection is then depressed and inverted by anoxia or rapid rates of stimulation in the same manner as the T deflection of the papillary muscle electrogram.

Since the earlier experiments on heart muscle were complicated by anoxia, uncontrolled rates, or injury, the results obtained in such studies do not represent the electrical potentials characteristic of heart muscle under relatively physiologic conditions. Since, in the absence of modifying factors, the T is in the same direction as the R deflection in a simple
linear strip with parallel fibers, it is unlikely that it is produced by an opposite process. Therefore, repolarization does not adequately account for the production of the T deflection.

The T deflection of heart muscle and nerve after-potentials are similar in the following respects: they are depressed by anoxia, they coincide with a phase of supernormal excitability, and they are increased and prolonged by veratrine.

Since neurophysiologists believe that the after-potentials of nerve represent oxidative metabolic processes, it seems likely that the genesis of the T deflection is similar. The experiments described do not exclude the possibility that the T deflection may represent a combination of membrane repolarization and other processes.

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