Electrocardiogram in the Normal Rat and Its Alteration with Experimental Coronary Occlusion

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STUDY OF myocardial necrosis and infarction induced experimentally in rats would be aided by a reliable technique for recording the associated electrocardiographic changes. While electrocardiograms on rats have been made, the resolving power of the equipment has not been entirely satisfactory. Furthermore, the suitability of the leads for detecting myocardial necrosis, the stability of electrodes, and the constancy of the electrocardiographic pattern invited further study.

The electrophysiology of very rapid heart rates necessitates recording equipment with frequency response and paper speeds sufficient to resolve without distortion the P, QRS, and T components. Direct penwriting equipment with these characteristics has now been developed. When combined with subdermal electrodes—which allow easy placement, standardized contact surface, and the development of precordial leads—such a recording system affords reliable reproduction in serial tracings and resolution of QRS potentials as well as rapidity in handling the animals.

To our knowledge, electrocardiographic alterations with myocardial infarction in the rat have not previously been described. When applied to animals having myocardial necrosis associated with coronary ligation, this system of electrocardiography easily detected the electrical changes. The following describes the technique, its application, and its validation.

Methods

Electrocardiograms were recorded on normal male Sprague-Dawley rats under light ether anesthesia in the prone position. Electrodes consisted of 26-gauge needles placed subcutaneously for 1 cm. Standard limb leads were constructed from electrodes placed at the right and left forepaws and the tail, and in addition unipolar leads were located at the midstream anteriorly (V ant) and at the anterior axillary line lateral to the xiphoid process (V lea). The potentials were recorded with a Tektronix preamplifier and an Offner direct-writing ink recorder with frequency response of full amplitude to 200 c.p.s. and paper speed up to 250 mm. per second. Sensitivity was adjusted so that 1 millivolt was equal to a 30-mm. deflection. Tracings thus obtained have been compared with oscillographic recordings, and all components seen on the latter were resolved by the former.

Infarction was produced in 10 rats after the technique of Johns and Olson. A clean, but not aseptic, left thoracotomy incision was made with the animal under positive-pressure ether anesthesia administered by face mask. Atraumatic 00000 silk suture was used to ligate the left coronary artery distal to the branching of the circumflex artery and at the border of the left atrial appendage. Immediate blanching of the anterior left ventricle could be observed and the chest was closed with 0000 chromic suture and the skin with stainless steel clips. Of the animals operated upon, 10 survived the immediate postoperative period and are the subject of the study on myocardial infarction. For control purposes several animals were subjected to thoracotomy without coronary ligation.

Electrocardiograms were taken before and after operation at two hours, eight hours, one day, two days, four days, and seven days. The animals were sacrificed at seven days, and microsections of the heart, liver, and lungs were prepared and stained with hematoxylin and eosin, phosphotungstic acid hematoxylin, and Van Gieson's iron hematoxylin.

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Table 1
Amplitude and Duration of the Components of the Normal Rat Electrocardiogram Obtained on Forty-four Sprague-Dawley Rats

<table>
<thead>
<tr>
<th>Component</th>
<th>Average</th>
<th>Range</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (Gm.)</td>
<td>253.7</td>
<td>174-292</td>
<td>37.6</td>
</tr>
<tr>
<td>Rate (1 min.)</td>
<td>388.3</td>
<td>340-504</td>
<td>28.9</td>
</tr>
<tr>
<td>Electrical axis (degrees)</td>
<td>52.2</td>
<td>30-80</td>
<td>6.1</td>
</tr>
<tr>
<td>P-R (msec.)</td>
<td>50.97</td>
<td>48-60</td>
<td>5.4</td>
</tr>
<tr>
<td>Q-T (msec.)</td>
<td>53.6</td>
<td>50-70</td>
<td>5.4</td>
</tr>
<tr>
<td>P$_1$ (mv.)</td>
<td>0.028</td>
<td>0.00-0.05</td>
<td>0.012</td>
</tr>
<tr>
<td>P$_2$ (mv.)</td>
<td>0.030</td>
<td>0.00-0.05</td>
<td>0.012</td>
</tr>
<tr>
<td>P$_3$ (mv.)</td>
<td>0.005</td>
<td>0.00-0.05</td>
<td>0.010</td>
</tr>
<tr>
<td>P$_{st}$ (mv.)</td>
<td>0.041</td>
<td>0.00-0.05</td>
<td>0.015</td>
</tr>
<tr>
<td>P$_{st}$ (mv.)</td>
<td>0.054</td>
<td>0.00-0.05</td>
<td>0.023</td>
</tr>
</tbody>
</table>

*Amplitude is expressed in millivolts (mv.), duration in milliseconds (msec.).

Results

Normal Controls

The recording technique afforded good resolution of the QRS components in leads I, II, V$_{an}$, and V$_{int}$, but lead III tended to be isoelectric or indefinitely defined. Electrocardiograms were recorded on 10 normal animals serially on three successive days, and the tracings were found to be reproducible. Table 1 summarizes the comparative average, range, and standard deviation for the amplitude and duration of the different components of the normal electrocardiogram obtained from 44 Sprague-Dawley rats.

The values for the components of the normal electrocardiogram of the rat obtained by this technique serve to confirm those already on record and differ mainly in that the voltages recorded here are less; however, the range and standard deviations are also smaller. It should be emphasized that the T wave is partially superimposed upon the termination of the QRS complex so that there is no lead with a discernible S-T segment and accurate measurement of duration of the QRS is not possible. One animal in this series had an inverted T wave in lead I. Initial Q waves were not found.

Experimental Infarction

Following ligation of the left coronary artery in the rat, massive left ventricular necrosis is regularly produced and sometimes includes the interventricular septum and occasionally the right ventricle. In only two animals included in the series—those surviving the immediate postoperative period—was transmural infarction of the left ventricular wall not produced. In these instances small focal areas of necrosis were observed in the epicardium on the left ventricle near the site of the ligature and may have resulted from trauma rather than coronary occlusion (fig. 1 upper).

When examined seven days following injury, the infarcted areas were readily apparent; they were pale, soft, and flabby, and bulged a little. In one heart a ventricular aneurysm was noted. Ventricular rupture did not occur despite extensive infarction, and indeed all animals surviving the immediate postoperative period survived the next seven days.

Microscopically, the infarcts showed organization with vascularization and fibroblastic proliferation. Neither elastic fibers nor fibrin could be demonstrated, but small bundles of collagen were present between fibroblasts in the areas of organization. The area of infarct was sharply delineated, and the lesions which were transmural showed pronounced loss of striated muscle cells, so that the normally thick left ventricular wall was much thinner (fig. 2 upper). With extensive
infarction three zones were usually evident: an epicardial layer in which necrotic muscle was replaced by organization, a central layer of coagulative necrosis, and an endocardial layer of organizing necrotic muscle with a narrow band of subendocardial muscle fibers which retained striations. These presumably viable muscle fibers were not present in all areas, and for descriptive purposes the infarcts were considered to be transmural. There was no evidence of intraventricular mural thrombosis. Acute passive congestion of the liver was not observed and the lungs showed only patchy alveolar edema and atelectasis. In several animals focal subacute pneumonitis was present.

Serial electrocardiographic tracings were obtained on eight animals with transmural infarctions of the left ventricle and on two with epicardial lesions located near the site of the ligature. In the eight tracings obtained on animals with transmural infarction, a characteristic pattern emerged consisting of

![Image](https://via.placeholder.com/150)

Figure 1

(Upper) Focal epicardial lesions near left atrial appendage (right center). Hematoxylin and eosin, X 7. Electrocardiogram from this animal is shown in the lower section of this figure. (Lower) Electrocardiographic alterations with focal epicardial lesion near the left atrial appendage; 1 mv. equals 30 mm.; paper speed was 100 mm./sec.

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the presence of a Q wave with inversion of the T wave which, when present in more than one lead and evident on serial tracings, was considered to be diagnostic of myocardial infarction (fig. 2 lower). Changes in the S-T segment are not helpful in the diagnosis of myocardial infarction in the rat as the T wave follows immediately or is partially superimposed upon the QRS.

Although the presence of a Q wave was not observed in normal animals, it tended to appear early and persist through serial tracings of anterior or apical infarction and was particularly prominent in leads I, II, V_{anterior}, and V_{lateral}. No Q wave was observed in lead III. In two tracings of lead I made during the placement of the ligature, a Q wave associated with inversion of the T wave was immediately present upon ligation, but was transitory, lasting less than two minutes.

Figure 2
(Upper) Transmural infarction of the left ventricular wall following ligation of the left coronary artery. Hematoxylin and eosin, ×7. Electrocardiogram from this animal is shown in the lower section of this figure. (Lower) Electrocardiographic alterations with transmural infarction of the left ventricle; 1 mv. equals 30 mm.; paper speed was 100 mm./sec.
with return to the preocclusive pattern. By
two hours after operation the Q wave was
gain prominent and persistent, suggesting
an initial injury-potential followed by rapid
evolution of the infarction pattern.

Increased amplitude of the R wave was
noted to occur with infarction, but the change
was not persistent, often appearing in leads I, V₃₉₄, and V₅₉, by two hours, but return-
ting to the value of the preoperative trac-
ing or below by seven days. S waves were
prominent in lead III and were occasionally
noted in leads I and II.

Inversion of the T wave was consistently
observed in the presence of a Q wave occur-
ing in leads I, II, V₃₉₄, and V₅₉, but not
in lead III. It should be recalled that a nega-
tive T wave in lead I may be normal.

Disturbances of rate were not noted in any
of the animals despite extensive infarction.
Heart rate, amplitude of P wave, and the
P-R interval remained constant. On the other
hand, a consistent prolongation of the Q-T
interval was noted, from an average of 53.6
to 82.0 msec. at 24 hours.

In the two cases of small epicardial lesions
near the border of the atrial appendage,
tracings diagnostic of infarction were not
obtained. The tracings were considered ab-
normal, however, for, although Q waves and
inverted T waves were not observed, the Q-T
interval was prolonged, amplitude of the R
wave was increased, and the S wave was
prominent (fig. 1 lower). Animals with tho-
racotomy alone showed no significant electro-
cardiographic changes from preoperative
tracings.

Discussion
For ease of manipulation of animals and
to standardize the contact surface, needle
electrodes have been employed in this study
in preference to saline conduction media.
With reduction of contact surface, however,
the amplitudes recorded by needle electrodes
are of lesser magnitude than those previously
reported for saline, paste, or wire. The ad-

tantages of this electrode system coupled
with direct-writing recording equipment are
in the accurate and distinct resolution of the
electrical forces, the ability to reproduce
serial tracings, and the ease and rapidity
with which animals may be recorded. The
electrocardiograms obtained from normal rats
in this way are similar to those previously
reported with respect to configuration and
time constants. Component voltages are less
than previously reported, but also show less
variability in serial tracings and less deviation
from animal to animal.

Anterior and apical transmural infarctions
reliably produced alterations in the electro-
cardiogram consisting of Q-wave deformity,
increased amplitude of the R wave, lengthen-
ing of the Q-T interval, and inversion of the
T wave. The presence of a QR or Q-S con-
figuration was considered the most reliable
indication of infarction and usually appeared
from two to eight hours following coronary
ligation. The early appearance of a Q wave
with the QR configuration becoming a Q-S
pattern suggests progressive myocardial ne-
crosis, which is consistent with the histology
of the infarcts at seven days.

Small epicardial lesions failed to produce
a Q-wave deformity in any lead, although
augmentation of the R wave and Q-T pro-
longation was observed. Such lesions histo-

gically did not involve the inner 80 per cent
of the myocardium thought to be productive
of Q-wave deformity.

Although extensive transmural infarction
of the left ventricular wall and interventricu-
lar septum was produced, arrhythmias were
not obtained, and there was no instance of
mural intraventricular thrombosis. Arrhyth-
mias are frequently encountered following
coronary ligation in dogs. Mural thrombi
have been observed in the atri of aged rats
and following infarction in rats on high-fat
diets. In the presence of extensive necrosis
of the left ventricular wall, it is not clear
why mural thrombi did not occur.

Summary
A reliable and reproducible method of re-
cording rat electrocardiograms is described,
including the use of precordial electrodes.
This system was utilized in studying 44 normal animals and in recording the electrical abnormalities associated with the ligation of the left coronary artery in 10 rats. The characteristics of the normal electrocardiogram of the rat are described. Following apical and anterior infarction, Q waves in association with transitory R-wave augmentation appeared, with prolongation of the Q-T interval, electrical axis deviation, and inversion of the T wave. No abnormal conduction patterns were noted. The pathological lesions are described, and attention is called to the absence of mural intraventricular thrombosis despite transmural infarction.

References
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