Electrocardiogram in Rabbit Fetuses

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With the technical assistance of G. Shine

Although indirect fetal electrocardiography in human pregnancies is becoming common,1,2 electrocardiograms of mammalian fetuses in utero by the direct approach are not. During a general electrophysiological study of rabbit fetuses, we found that electrocardiograms could be obtained easily with needle electrodes. We expanded our observations by making recordings of cardiac potentials via needle electrodes in two ways: 1. with the needle driven through the uterine wall and held against the fetus, and 2. with the fetus extracted and the electrode inserted into it.

Rabbits have a gestation period of 32 days. Transition from the embryonic to the fetal stage occurs at about 10 to 11 post-coital days. Until about the 11th or 12th day, the fetuses are tiny masses of gelatinous tissue about five mm long. Thereafter, they rapidly assume characteristic mammalian form and by the 16th day have a crown to rump length of 13 to 18 mm. Earlier studies in this laboratory3 have shown that the first visible movements occur at 17 days and the earliest electromyographic potentials occur at about the same day.

The earliest human fetal electrocardiograms were recorded through surface electrodes on the abdomen and back of the mother at 10 or 11 weeks. This age corresponds roughly to the rather advanced age of 21 days in the fetal rabbit. At 22 weeks, electrocardiograms are easy to obtain in human pregnancies. Although correlation of the stages of human and rabbit development is not completely reliable, we are confident that even at mid-term (16 days) the rabbit fetus is relatively much "younger" than the human fetus at 12 weeks.

Witschi's4 estimate suggests that the rabbit's 10-day-old embryo corresponds to the human 30-day-old and that the 12-day-old rabbit fetus corresponds to the 8-week-old human fetus. At eight weeks, Nyman has been credited by Bernstine5 with having obtained electrocardiograms from human fetuses by combined cervical and abdominal electrodes. Heard, Burkley, and Schaefer5 obtained direct recordings from aborted human fetuses as early as 10 weeks.

Methods

Our material consisted of 166 fetuses in 35 rabbits at the 10th to the 31st post-coital day (table 1). To avoid narcotizing the fetuses, our technique of chemomyelotomy was used in place of ordinary anesthesia.6 The general experimental and recording systems have been described earlier in a paper on electromyography,6 but special modifications were made for electrocardiograms. From a pair of precordial subcutaneous leads, the maternal electrocardiogram was recorded on film from one channel of the Tetronix dual-beam cathode-ray oscilloscope while the fetal electrocardiogram was recorded simultaneously from the other channel. Recordings for each fetus were made in two steps, the details of which follow:

1. Through a vertical laparotomy incision, individual nidation sites of the pregnant uterus were exposed, and a grounding wire-electrode was inserted into the uterine wall. The main electrode (which is a monel-metal needle insulated except for its tip) was plunged into the interior of the amniotic cavity that surrounds the fetus. Experience showed that skewering the mobile fetus is difficult if not impossible, but the needle tip could be placed easily in contact with the fetus, and gave good recordings. 2. Through a longitudinal incision on the antimesenteric border of the nidation site, the fetus was delivered into a special glass, constant-temperature chamber, and submerged in mineral oil. It could thus be kept in good condition for some minutes to hours, electrocardiograms persisting from about 30 to 90 minutes as a rule. Previously7 we had shown that severing the umbilical cord does not seem to affect the electrocardiogram; nonetheless, more than half of the fetuses were not separated from the pla-
TABLE 1

Incidence of Positive Electrocardiograms at Various Post-coital Ages (166 rabbit fetuses)

<table>
<thead>
<tr>
<th>Post-coital age</th>
<th>Number of fetuses</th>
<th>Intra-uterine ECG obtained</th>
<th>Extra-uterine ECG obtained</th>
<th>Number of mothers</th>
</tr>
</thead>
<tbody>
<tr>
<td>10½-11 days</td>
<td>30</td>
<td>0</td>
<td>1 (3.3%)</td>
<td>5</td>
</tr>
<tr>
<td>12 days</td>
<td>4</td>
<td>3 (75%)</td>
<td>4 (100%)</td>
<td>1</td>
</tr>
<tr>
<td>13-17 days</td>
<td>79</td>
<td>79 (100%)</td>
<td>79 (100%)</td>
<td>20</td>
</tr>
<tr>
<td>18-31 days</td>
<td>53</td>
<td>53 (100%)</td>
<td>53 (100%)</td>
<td>9</td>
</tr>
<tr>
<td>Totals</td>
<td>160</td>
<td>135</td>
<td>137</td>
<td>35</td>
</tr>
</tbody>
</table>

The main electrode was driven into various parts of the thorax and limb-buds, but generally, the best recordings were from the thorax. Extra-uterine electrocardiograms were recorded immediately after opening the uterus, and up to three minutes later, although monitoring usually continued for as long as one-half hour.

**Results**

Table 1 shows the incidence at various ages of recordable electrocardiograms in the 166 fetuses. Incidence increases sharply after the 11th post-coital day. Except for a failure to obtain an electrocardiogram in one of the 12-day-old fetuses, all fetuses of 12 days or more gave good results both under intra-uterine and extra-uterine recording conditions. Only one fetus younger than this gave a positive electrocardiogram (this being recorded extra-uterine in a fetus at 10 days, 22 hours). Usually intra-uterine recordings were easier to get than extra-uterine recordings, with the former showing less electrical interferences. At 21 days or older, muscle potentials and movement artifacts make the interpretation of the electrocardiogram progressively more difficult.

**CARDIAC RATE**

The cardiac rate ranges from 150 to 200/min in the intra-uterine recordings, but falls to 80 to 140/min in the extra-uterine recordings. With the passage of even a few minutes, a progressive bradycardia appears in extra-uterine recordings, in one case down to 30/min. In other cases, the rate gets very irregular, especially in older fetuses.

**WAVE FORM**

The characteristic wave form consists of a pair of complexes, which in the intra-uterine recordings are 50 to 200 msec apart (fig. 1). The interval varies with the heart rate, being longest with the slow rates obtained in extra-uterine recordings. Though individual differences are apparent, various possible factors including age do not seem to be involved.

The first complex varies considerably in shape from fetus to fetus and changes in the same fetus from one type of recording to the other. In some recordings, it resembles the adult human QRS (fig. 2), in others it is a fairly simple double peak, and in still others it resembles a high, pointed P wave. This first complex generally becomes smaller or flatter with advancing age.

The second complex generally resembles the adult human QRS. In almost all recordings, distinct positive and negative components are evident.

**Discussion**

Autonomous heart-forming areas have been described in embryos as early as the gastrula stage. In man, a cardiogenic plate appears at the pre-somite stage. In chicks having one to four somites, two pairs of tubes are found; this stage corresponds to eight days in the rabbit and 24 days in man. The two tubes are the precursors of the dorsal aorta and primitive heart. As late as five days in chicks, 10½ days in rabbits and 37 in man, the heart is a single tube, and the interventricular septum is not completed until 13 days in rabbits and 50 to 55 days in man.

Cardiac muscle shows early contractile activity. In the 9-somite chick embryo, irregular fibrillations occur in the muscle cells of the ventricular area. This stage corresponds...
FETAL ELECTROCARDIOGRAM

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FIGURE 1
Intra-uterine (A, I) and extra-uterine (B, I) electrocardiograms of 13-day-old rabbit fetus. Arrows point to first and second complexes of fetal electrocardiogram. Regular small waves are artifacts and should be ignored. Channels A, II and B, II: simultaneous maternal electrocardiogram for reference. Sweep speed: 188 mm/sec.

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FIGURE 2
A, B and C: examples of various wave forms of one cardiac beat. 1, first complex; 2, second complex. Sweep speed: 260 mm/sec.

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The wave form of our early electrocardiograms is of considerable interest. Even the earliest recordings show a pair of complexes at each beat, the first probably corresponding to an atrial contraction but sometimes resembling closely the human adult QRS or ventricular complex. The second complex clearly resembles a QRS type of wave. The interval between the first and second complex increases with bradycardia in the same fashion as does the interval between the human P and QRS waves, providing further evidence that the first complex is atrial in origin.

The appearance of an obvious sinus rhythm in the rabbit fetus at 10 days and 22 hours...
indicates that the same should occur in human embryos at about the 5th week of gestation, considerably earlier than the 8th week and 10th week electrocardiograms previously noted.\(^2\,^5\) Although recordings by our technique from human embryos aborted in the fifth week would be interesting, we feel that the close general agreement of findings in chicks, rabbits and man is sufficient evidence for a firm conclusion. No doubt, direct intracardiac microelectrodes would reveal small potentials from cardiac muscle fibers before five weeks, but this human embryonic age can be taken as the one at which a regular electrocardiographic pattern is to be expected.

**Summary**

Electrocardiograms were recorded by needle electrodes in 137 of 166 rabbit fetuses at 10\(\frac{1}{2}\) to 31 days. Invariably, electrocardiograms were obtainable from the 12th day on, which in the rabbit is an early stage of development. The earliest electrocardiogram was obtained at 10 days, 22 hours, corresponding to about five weeks in human development. Sinus rhythm was evident from the start. The waveform consists of a pair of complexes 50 to 200 msec apart. The first complex is quite variable but appears to be atrial in origin; the second is surprisingly constant and appears to be ventricular.

**References**

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