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Effects of Temperature on the Excised Frog Heart.*

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In a previous manuscript[1] it was reported that when the excised frog heart was placed in a controllable modulated high frequency field there resulted either reversible cardiac standstill or cardiac standstill followed by a type of cyclic activity. The cause or causes for such modified activity we were only able to conjecture.

The purpose of the present study was to see if similar results could not be obtained by the application of physical heat and to ascertain the influence of atropine and eserine upon the heat responses of the excised preparations since atropinized and eserinized preparations respond differently to the condenser field.[2]

The heart was arranged for perfusion as shown in Plate 1. The Ringer's solution from the perfusion bulb first passed through the heating bath d and then to the constricted portion of the heart cannula h where it could enter the ventricular chamber during diastole and in turn be forced back through the heart cannula during systole and eventually through the over-flow pipes spraying the outside of the heart. The temperatures recorded were those shown by the thermometer g, the bulb of which was immersed in the perfusion fluid in chamber e. This method allowed for constant perfusion pressure and for constant volume flow over the outside of the heart. Employing this method for perfusing the heart one of 3 variables was then introduced and kymographic records of heart activity recorded in each instance: The 1st variable introduced consisted of changing the temperature of the perfusion fluid going to the heart (controls); the 2nd consisted of changing the temperature of the perfusion fluid after atropine 1-50,000 had been added; the 3rd consisted of changing the temperature of the perfusion fluid after eserine 1-125,000 had been added.

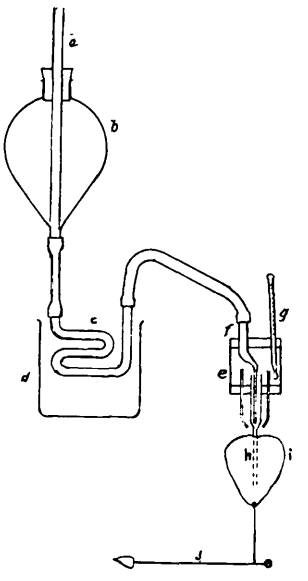

PLATE 1

Schematic illustration of perfusion apparatus. For description see text.

Results. Studies were made of records from 63 hearts, equally divided among the controls, atropinized and eserinized preparations. It was found that as the temperature of the perfusion fluid was slowly increased there developed a period of irregular activity which commenced at the average temperature of 29° C for the controls and for the atropinized hearts, and at 28° C for the eserinized preparations. The irregularity which developed at the above average temperatures and which persisted until a higher temperature had been attained in each instance, is difficult to describe because of the many dif-

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1 Fenning, Con, and Mott, Clarence R., *Am. J. Physiol.*, to be published.

2 Fenning, Con, and Mott, Clarence R., in preparation.

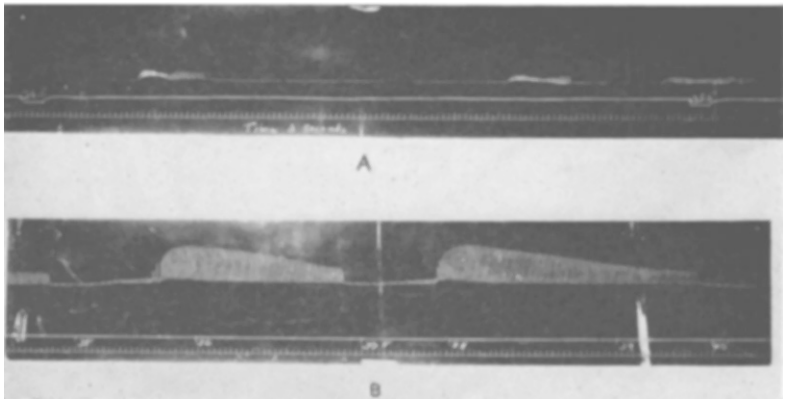

FIG. 1.
Shows types of kymographic records obtained from the excised frog heart when the temperature of the perfusion fluid was the only factor varied. (Controls.)

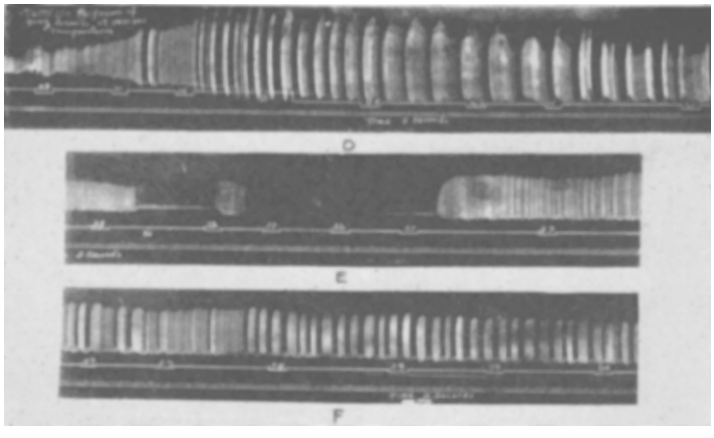

FIG. 2.
Shows types of kymographic records obtained from the excised frog heart when the temperature of the perfusion fluid was the only factor varied. (Controls.)

ferent patterns in which it presented itself. We have observed brief ventricular stoppage with the atria continuing their activity (Fig. 2 E); an abrupt 100% increase in rate; changes in amplitude and rate (Fig. 2 D); complete but momentary cardiac standstill and many other patterns. However in all instances there developed subsequently (average temperature of 32.6° C for the controls, 38.5° C for the atropinized and 37° C for the eserinized preparations) a type of cyclic activity which varied widely from preparation to preparation and, furthermore, may have varied from moment to moment in the same preparation as shown in Fig. 1 and 2 for the controls, Fig. 3 for the atropinized hearts and Fig. 4 for the eserinized preparations. M and N of Fig. 4 are continuations of L. A 7-minute period of the record in which no activity occurred was removed between L and M and again between M and N. In all the eserinized preparations marked tonus, or tonus-like, changes occurred between the periods of activity as noted on the records of Fig. 4. These characteristic tonus changes were not observed in the atropinized or control hearts.

The cycles which came on at the above stated temperatures would persist for some time providing the temperature was maintained at the proper critical level. We have observed continuance of cyclic activity under

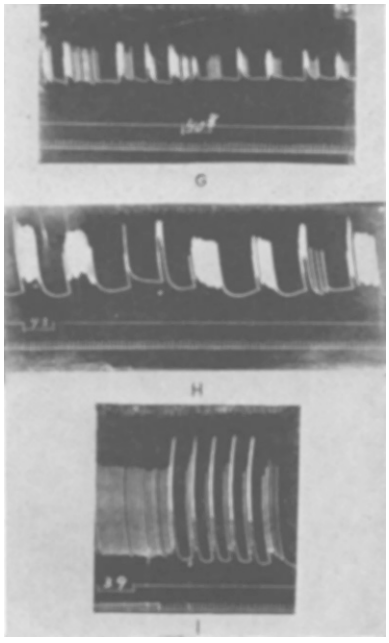

FIG. 3.

Shows types of kymographic records obtained from the excised atropinized frog heart when the temperature of the perfusion fluid was varied.

the above conditions for a period of two hours and there is no reason to believe it would not have continued longer. In all cases rhythmic activity was restored when the temperature was lowered. Occasionally it was observed that once cycles had been well established the temperature could be lowered 2-4 degrees below the temperature at which they commenced and still maintain continuance of cyclic activity. In other preparations apparently adaptation occurred and in order to maintain cycles it was necessary to raise the temperature a few degrees above that at which they first commenced. It should be pointed out that in the control hearts especially there was a tendency for the ventricle to become cyclic (Fig. 1B; 2E,F) while the atria remained active. When the temperature was raised somewhat higher, however, the atria too would become cyclic. This phenomenon was observed occasionally in the atropinized hearts but not in the eserinized preparations.

When the perfusion fluid temperature was increased to about 45° C activity would cease except for a slowly developing heat response which was also reversible providing the temperature was subsequently lowered. In no instance with the above approach did we obtain cycles which resembled in all respects those induced by the modulated high frequency condenser field, although cycles occurred in 100% of the hearts studied. Just why cycles occurred in these preparations and why the onset temperature differed with atropine and with eserine we are at present unable to state.

A second and perhaps more drastic approach was then instigated as follows: The heart was arranged for perfusion as above shown. The perfusion fluid passing to the heart was either stopped or maintained at room temperature, and then from 5-10 cc of Ringer's solution brought to temperatures varying between 40-95° C was poured over the outside of the heart. Cyclic activity of short duration was induced by this approach in most instances and could be made to appear at any temperature between 40-95° C. Fig. 5-O shows the usual response: Immediate cessation of activity, followed by an abrupt rise in tone (heat response) which slowly declined and usually one or more periods of cyclic activity supervened before the return to apparently normal rhythmic activity. What appeared to be sinus tachycardia frequently occurred at the very peak of the heat response. Again there may have been cardiac arrest followed by the heat response but with no cyclic activity occurring between the time the hot Ringer's was applied and the return to apparently normal activity. In one instance following the application of 95° C Ringer's to the heart the usual heat response occurred and there then supervened a period of 90 minutes before activity commenced.

Attention is called to the record shown in Fig. 5 P which was obtained after a continuous recording of 96 minutes during which time the heart was subjected to Ringer's heated to 80° C 3 different times, to Ringer's brought to 55° C once, and to Ringer's at 40° C once, following which there occurred the type of activity shown. There were 7

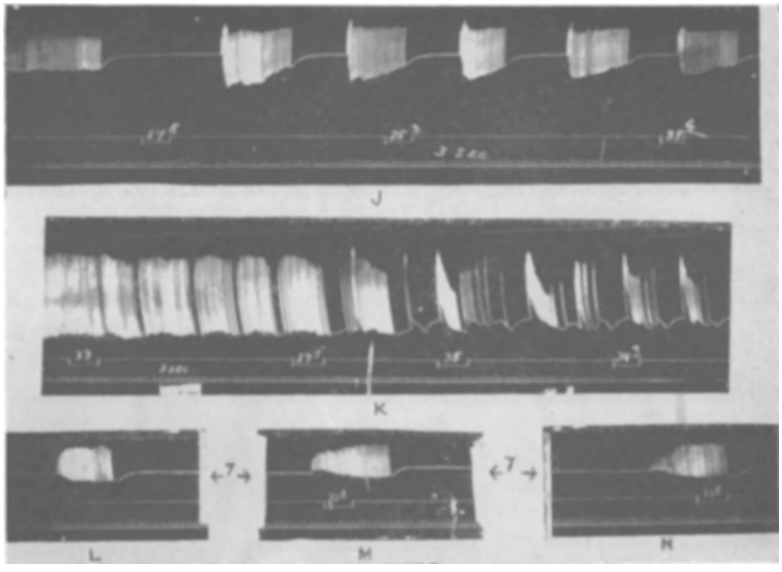

FIG. 4.
Shows types of kymographic records obtained from the excised eserinized frog heart when the temperature of the perfusion fluid was varied.

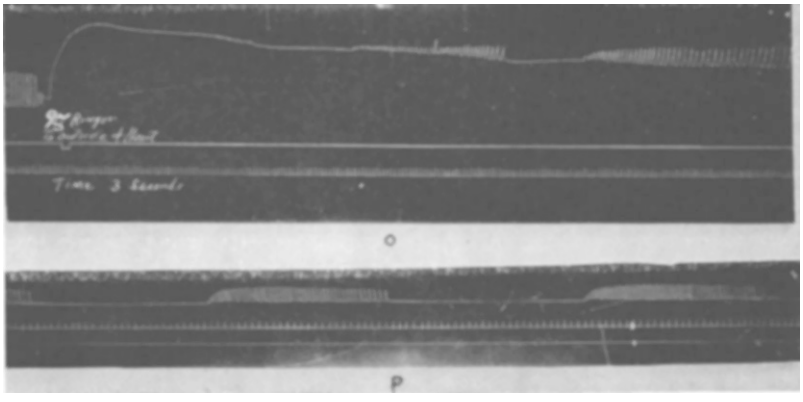

FIG. 5.
O shows the type of response obtained when hot Ringer's is applied directly to the outside of the heart. P shows a type of cycle which resembled those obtained when the frog heart was placed in modulated high frequency field.

such periods of intermittency before the return of continuous activity. The cycles were regular in manner of onset, manner of stoppage, duration of activity, duration of standstill and in all respects resembled one type of cycle brought about by the modulated high frequency condenser field mentioned above except they did not persist as long.

Conclusions. Atropine and eserine apparently raise the critical temperature threshold for the thermal responses of the excised frog heart preparation. Differentially, atropine has a greater effect than eserine. The response of the excised frog heart to a slowly rising temperature does not warrant the assumption that the modulated high frequency condenser field operates entirely in the same manner.