a certain period of development. At no previous time are these procedures effective; not even when the magnitude of the forces is very much greater. This period of susceptibility coincides with the time of localization of the red pigment granules in a differentiated cortical layer of the cell. Hence it may be deduced that these forces do not act directly on the granules themselves, and it is concluded that the shearing forces act upon the "ground substance" (cortex) in which the granules are imbedded. In doing so they cause the bound calcium component of this cortex to disintegrate. The release of calcium ions is then reflected in the breakdown of the red pigment granules.

12004

Influence of Temperature on the Electrogram and Monophasic Action Potential of the Mammalian Heart.*

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Earlier studies in this laboratory demonstrated that warming or cooling portions of the external surface of the ventricles caused characteristic alterations in the T wave of the electrocardiogram.[1] The basis of these T wave changes was found to be alteration in the duration of one or the other of the two components of the electrocardiogram, *i. e.,* of the dextro- or the levocardiogram. Cold prolonged and heat shortened the duration of these components. The following experiments were undertaken to determine the cause of these alterations in the duration of the dextro- and levocardiograms.

Electrograms and monophasic action potentials were studied in 5 dogs by the method previously described,[2] one lead being taken from the anterior surface of the right ventricle and the other from the anterior surface of the left ventricle. Negativity at the lead on

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† Fellow in Physiology, Dazian Foundation.

[1] Hoff, H. E., and Nahum, L. H., *Am. J. Physiol.,* 1941, **131**, 700.

[2] Hoff, H. E., and Nahum, L. H., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 263.

the right ventricle gave an upward deflection of the beam. The influence of temperature was determined first on the electrogram, and then on the monophasic action potential. Variations in temperature were produced by applying a small tin chamber to the surface of the heart under one or the other electrode, and circulating through the chamber water at 5°C or 55°C.

The results of heating or cooling the surface of the heart under one or the other electrode are shown in Fig. 1. When the region under the right ventricle electrode was cooled, an upright end deflection was obtained, while when this region was warmed, the end-deflection was sharply inverted. The duration of the whole electrogram was prolonged when the heart was cooled, and was not materially altered by warming. Exactly opposite effects followed cooling and heating under the electrode on the left ventricle. Cooling produced a prolonged downward end-deflection, while heating produced an upward end-deflection of normal duration.

Monophasic action potentials were obtained from each of the two regions from which the electrogram was recorded by successively

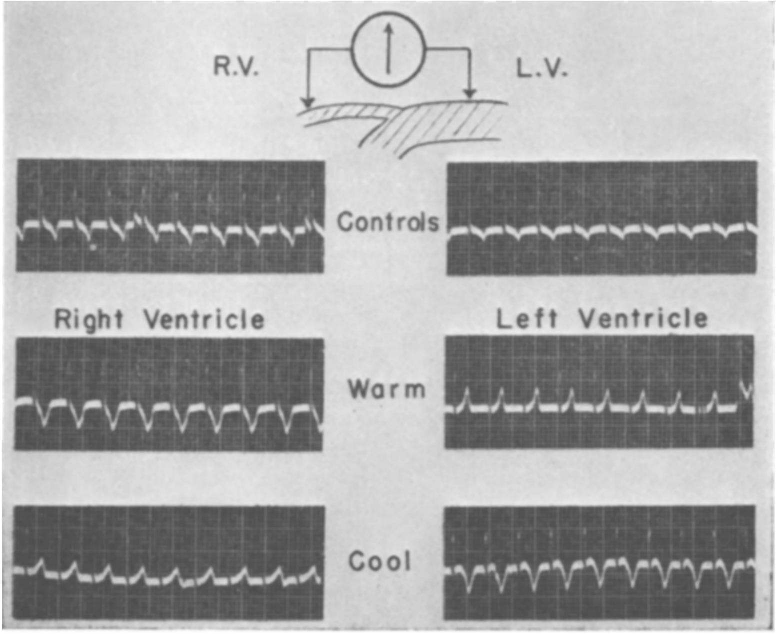

FIG. 1.

Electrograms recorded from the right ventricle (region of primary negativity) and the left ventricle, which was activated later. The effect of warming and cooling the region of one and the other electrode by means of a thermal chamber at 55°C and 5°C compares closely with the hypothetical diagram in Fig. 3.

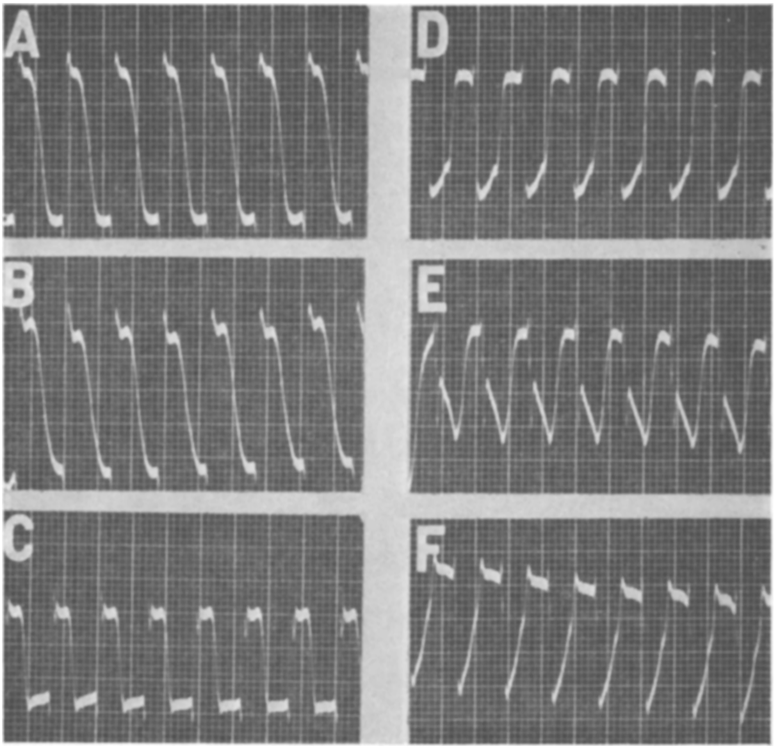

FIG. 2.

Monophasic action potentials recorded from the right ventricle (A, B, C), and the left ventricle (D, E, F), as in Fig. 1, but in another experiment. Cooling and warming the region from which the monophasic action potentials are derived lengthens (B, E) and shortens (C, F) the duration of the waves in comparison with the normal (A, D). This figure, and Fig. 1, demonstrate the correctness of the hypothesis presented in Fig. 3.

blocking one and then the other region with isotonic KCl, as described previously.[2] Fig. 2 shows the results of heating and cooling the regions from which the monophasic records were obtained. It can be seen that cooling (B, E) prolonged the action potential, while warming (C, F) curtailed it.

Fig. 3 illustrates the production of the electrogram by the interference (*i. e.,* algebraic summation) between the monophasic action potentials at the two electrodes, and shows how alterations in one of these two components must alter the end-deflection of the electrogram. In A both complexes (A1, A3) are of equal duration, and therefore the region under the electrode first activated has completely recovered while the tissue under the second electrode is still active, giving an inverted end-deflection (A2). In B recovery under the

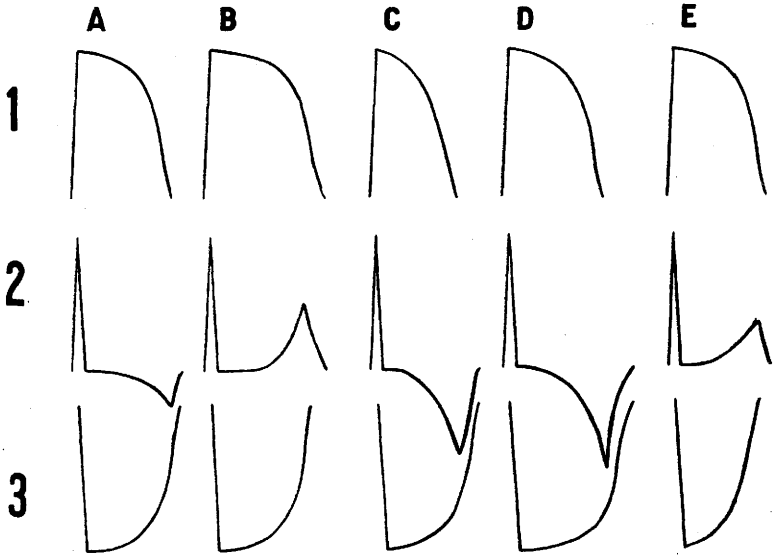

FIG. 3.

Graphic illustrations of the interference theory as applied to the genesis of the electrogram. Above (1) are shown monophasic action potentials as they might be recorded at the electrode first activated, and below (3) as they would be recorded at the second electrode. They would be opposite in polarity as shown, and the action potential at the second electrode would start somewhat later than at the first electrode. If the waves were of equal duration, then the end-deflection of the electrogram which results from the summation of the two would be negative (A). In B is shown the effect of cooling the heart at the first electrode. The monophasic electrogram at this region would be prolonged, and an upward end-deflection would result. In C the region of the first electrode is warmed, shortening the action potential, and accentuating the negativity of the end-deflection. In D and E are shown the results of cooling and heating the region of the second electrode, while the region of the first electrode remains unaltered.

first electrode (B1) is prolonged by cold, so activity persists here after termination of recovery at the second electrode (B3). This produces an upright end-deflection with prolongation of the whole complex (B2). In C, is illustrated the type of end-deflection produced by warming the region under the first electrode, while in D and E are portrayed the effects of cooling and warming the heart at the second electrode.

These experiments, and their interpretation, follow closely those of Burdon-Sanderson and Page,[3, 4, 5] who studied electrograms of the frog and tortoise heart, and who first suggested that differences in the rate of recovery at one or the other electrode will produce changes in the end-deflection.

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[3] Burdon-Sanderson, J., and Page, F. J. M., *J. Physiol.*, 1879-80, **2**, 384.

[4] Burdon-Sanderson, J., and Page, F. J. M., *Proc. Roy. Soc., Lond.*, 1878, **27**, 410.

[5] Burdon-Sanderson, J., and Page, F. J. M., *J. Physiol.*, 1883, **4**, 327.

These results provide an explanation for the changes in the dextro- and levocardiograms produced by temperature. It is demonstrated that alterations in the rate of recovery at an isolated region of the surface of the heart result from changes in temperature. When a large part of a single ventricle is similarly heated or cooled, the rate of recovery would be changed over the entire region, and this would be reflected in an alteration in the record of electrical activity from this ventricle, *i. e.*, by a change in duration of the dextro- or levocardiogram.

It should be pointed out that the monophasic records as derived in experiments of this type contain some conducted effects from portions of the ventricles at a distance from the electrodes. In the experiments reported here these conducted effects were unaffected by heating and cooling, since this treatment was restricted to the immediate area of the electrode. The changes recorded in the monophasic action potentials could, therefore, have been produced only by alterations of the action potential derived from the immediate vicinity of the active electrode.

12005

Effect of Pro-Oxidants upon Reproduction in Rats.

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Vitamin E is readily destroyed by oxidation in the presence of autoxidizing fats and this destruction can be prevented by suitable antioxidants or stabilizers. This oxidation is responsible for the production of muscle dystrophy in herbivora on certain diets containing cod liver oil. To insure the complete absence of vitamin E from diets designed to produce a deficiency in rats, the mixed rations are often allowed to stand at room temperature some days before use. Whether pro-oxidants can also accomplish the destruction of vitamin E in the tissues, or otherwise interfere with the normal progress of reproduction, is uncertain.

Waddell and Steenbock[1] believed that the "antivitamins" produced in a diet treated with ethereal ferric chloride damaged the reproductive capacity of female rats, because 4 to 6 weeks elapsed

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[1] Waddell, J., and Steenbock, H., *J. Nutrition*, 1931, **4**, 79.