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THE RELATION BETWEEN TEMPERATURE AND CHANGES IN ION CONCENTRATION ON VENTRICULAR FIBRILLATION INDUCED ELECTRICALLY

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Further observations have been made on ventricular fibrillation induced by electrical stimulation in the isolated rabbit heart, in extension of the finding that fibrillation was arrested by cooling from 37° to 32°. The observations now made suggest that at 37° the isolated rabbit heart perfused with Locke solution is on the edge of anoxia, but that at 32° the oxygen supply is adequate. At the lower temperature the proportion of hearts fibrillating at any given potassium concentration was reduced, so, although the proportion of hearts fibrillating rose as the potassium concentration fell, even when the latter was one-quarter of the normal the proportion was not higher than 67%. The relation of the concentration of calcium ions to the proportion of hearts fibrillating changed from biphasic at 37° to almost rectilinear at 32°, the proportion increasing as the concentration of calcium ions rose. It was confirmed that a reduction in sodium concentration also raises the proportion of hearts fibrillating.

Ventricular fibrillation can be produced in the Langendorff preparation of the isolated rabbit heart by electrical stimulation of the ventricles. When the stimulation is stopped the heart either reverts to normal rhythm or fibrillation continues. Armitage, Burn, and Gunning (1957) investigated various factors which determined whether it continued, among them the amount of potassium and of calcium ions in the perfusing solution. They found, for example, that the proportion of hearts which continued to fibrillate rose as the amount of potassium was reduced. Kärki (1958) made a more complete study of changes in ion concentration, and Goodford (1958) investigated the action of metabolic inhibitors. He found that metabolic inhibitors caused fibrillation to persist and also that a lack of dextrose would precipitate fibrillation. In the course of his work he observed that, when a heart was in continuous fibrillation at 37°, the fibrillation was arrested on cooling to 32°. At that temperature, electrical stimulation did not induce fibrillation, though when the temperature was raised to 37° it did so once more. Goodford suggested that this effect might depend on the relation between the amount of oxygen available and the amount required by the heart. The oxygen available was the amount in solution, which was much less than the amount in blood. Since the oxygen requirement was greater at 37° than at 32° it might be that the occurrence of fibrillation at the higher temperature was due to an insufficient supply of oxygen at that temperature. Kärki, for example, found that at 37° no less than 15 out of 28 hearts fibrillated continuously after electrical stimulation although the fluid perfusing them was of the usual ionic concentration.

These observations suggested that a clearer picture of the effect of changes in ionic concentration would be obtained if experiments were made at 32°. Such experiments are now described.

METHOD

The method used was similar to that described by Armitage *et al.* (1957). The hearts, which were freshly excised from rabbits, were perfused through the coronary vessels by the method of Langendorff. The temperature of the fluid perfusing the heart was maintained constant despite variations of coronary flow by using the device of Saxby (1956).

The usual perfusion fluid described by McEwen (1956) contained NaCl 132 mM, KCl 5.6 mM, $CaCl_2$ 2.2 mM, NaH_2PO_4 0.92 mM, $NaHCO_3$ 2.5 mM, dextrose 11.1 mM, sucrose 13.1 mM. The solution was saturated with O_2 95% + CO_2 5%. The pressure head at which the hearts were perfused was 54 cm. water.

The ventricles were stimulated by platinum electrodes, one piercing the wall of the left ventricle at the apex, and the other near the base midway between the origins of the right and left coronary arteries. When stimulation was not being applied, the electrodes were used as leads to an electrocardiograph (Cossor model 1314). A mechanical record was obtained on a smoked drum by a thread attached to the electrode in the apex of the left ventricle. The stimuli were rectangular current pulses of 0.75 msec. duration and approximately 1 to 2 mA. Stimulation was begun at a rate of about 580/min., and the rate was increased until fibrillation was observed, the maximum rate being 1,200/min. The hearts were stimulated for 5 min.

When stimulation stopped each heart was observed to see if it reverted to a normal rhythm. Hearts reverting within 15 min. were recorded as "not fibrillating"; hearts not reverting within this time were recorded as "fibrillating."

The hearts were first perfused for 30 min. with the normal solution; this was then changed to the solution under test, and at the end of a further 30 min. stimulation was applied.

Results

Variations in Potassium Concentration

Observations were made at the usual potassium concentration, 5.6 mM, and at concentrations one-half and one-quarter of this. The results are given in Table I together with the results obtained at 37° by Kärki. The general trend was the same at 32° as at 37°, the proportion of hearts which fibrillated increasing as the potassium concentration fell. At each concentration, however, the proportion fibrillating was much less at 32° than at 37°. The difference was particularly noticeable when the potassium concentration was 1.4 mM because at 37° many hearts fibrillated spontaneously without stimulation, while at 32° only 6 out of 9 fibrillated when stimulated.

TABLE I

PROPORTION OF HEARTS FIBRILLATING AT DIFFERENT POTASSIUM CONCENTRATIONS, WHEN PERFUSED AT 32° OR 37°

Ion Conc. mM	37°		32°	
	Proportion	%	Proportion	%
11·2	0/8	0		
5·6	15/28	54	2/8	25
2·8	12/13	92	3/9	33
1·4	10/10	100	6/9	67

Six hearts were examined at 27°; at this temperature, even when the potassium concentration was only 1.4 mM, none fibrillated. The relation between potassium concentration and the proportion of hearts fibrillating is shown in Fig. 1 (curve **A**).

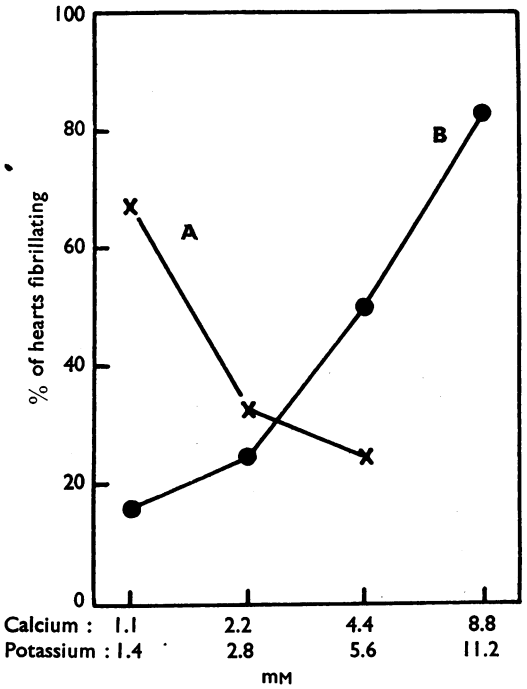

FIG. 1.—Percentage of hearts fibrillating at 32°. **A.** Calcium 2·2 mM and different potassium concentrations. **B.** Potassium 5·6 mM and different calcium concentrations.

Variations in Concentration of Calcium Ions

When the potassium concentration was kept at 5.6 mM and the concentration of calcium ions was varied, the proportion of hearts fibrillating varied with the calcium ion concentration, rising to 83% when this was increased fourfold and falling to 16% at half the usual concentration (see Fig. 1, curve **B**, and Table II).

TABLE II

PROPORTION OF HEARTS FIBRILLATING AT DIFFERENT CALCIUM ION CONCENTRATIONS, WHEN PERFUSED AT 32° OR 37°

Ion Conc. mM	37°		32°	
	Proportion	%	Proportion	%
8·8	—	—	5/6	83
4·4	12/12	100	3/6	50
2·2	15/28	54	2/8	25
1·1	7/15	47	1/6	16
0·55	3/8	38	—	—
0·275	6/21	29	—	—

Variations in Sodium Concentration

When the concentrations of potassium and calcium ions were kept normal, and the sodium concentration was reduced to one-half, the percentage of hearts fibrillating at 37° rose from

54 to 100. In experiments at 32°, when a similar reduction in sodium concentration was made, the tonicity being maintained by adding sucrose, 4 out of 6 hearts fibrillated, the percentage rising from 25 to 67.

Effect of Changes in Ionic Concentration on Normal Cardiac Rhythm

Observations were also made on the amplitude and rate of beat of the heart. At 32° the amplitude was larger and an increase in rate was often observed when either the potassium or the sodium concentration was reduced, and also when the calcium ion concentration was increased.

At 37°, when hearts were perfused with 1.4 mM potassium, it was usually observed that the amplitude increased steadily and the rate slightly until eventually there was spontaneous fibrillation. At 32°, in 5.6 mM potassium, the beats were small and irregular, but on changing to 1.4 mM potassium they became large and regular.

It was also noticed that it was more difficult to cause a heart to fibrillate by electrical stimulation at 32° than at 37°. This was especially noticeable in 1.1 mM calcium. Currents as large as 10 mA. could be used with some hearts without causing fibrillation.

Discussion

The results obtained give general support to the conclusions already reached by Kärki (1958) that a reduction of potassium and of sodium favours fibrillation while a decrease of calcium ion makes fibrillation less likely. The curve relating the proportion of hearts fibrillating to the calcium concentration which Kärki (1958) obtained, though free from the two peaks described by Armitage *et al.*, was of curious shape, and indicated the influence of more than one factor. The present observations at 32° have not this complexity, and they show that the effect of varying the concentration of calcium ions affects the proportion of hearts fibrillating in a roughly rectilinear manner. This is a more probable result.

The observation that hearts could not be made to fibrillate at 27°, even when the potassium concentration was reduced to 1.4 mM, is in agreement with the results recently published by Covino and Beavers (1958), who found that rabbit hearts would not fibrillate at temperatures below 27°. They considered that this depended on the species, since fibrillation occurred at low temperatures in the dog.

The observations made by Kärki (1958) on the effect of changes in potassium, calcium, and sodium concentration seem to have been complicated by the fact that at 37° the isolated rabbit heart perfused with Locke solution very often suffers from an insufficient oxygen supply. The conditions which favour fibrillation (low potassium and sodium and high calcium concentrations) are generally accompanied by an increase in amplitude of the heart beat. Thus it appears likely that this increased work done by the heart, which would require extra oxygen, contributes to the spontaneous fibrillation which often occurs at 37° when the potassium concentration is low. That the isolated rabbit heart perfused at 37° may be on the border of anoxia is not generally known, and, while it has long been the practice to study isolated atria at 29°, it has been customary to perfuse the whole heart at 37°. The evidence now described suggests that the temperature should not be higher than 32°.

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