cells after 8 weeks following exposure to the virus but was not observed at 3, 5 and 8 weeks in lung cells maintained under the same conditions.

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Received April 28, 1966. P.S.E.B.M., 1966, v122.

Effects of Ouabain on Potassium Contractures in Rabbit Atria.* (31348)

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Niedergerke(1) noted that frog heart ventricles took up extra amounts of calcium (Ca) ions when they were made to contract by treating the tissue with solutions containing either reduced sodium (Na) or increased potassium (K) concentrations. Hodgkin and Horowicz(2) observed that K-contractures in single skeletal muscle fibers were more transient in nature than that of the frog heart. They explained this feature by suggesting that there was only a limited quantity of a precursor, perhaps a Ca compound, which was rapidly depleted during activity of the twich fiber so that early relaxation occurred. Therefore, it would appear that in the contraction of the frog heart Ca is continuously available from transfer through the membrane, whereas in skeletal muscle the activator of contraction or its precursor resides in a cellular site, possibly the sarcoplasmic reticulum.

It has been noted in this laboratory that K-contractures in isolated rabbit left atria are transient in nature, and can be modified by ouabain. A summary of these studies is presented here.

Methods. Rabbits weighing between 1 and 2 kg were used. Animals were stunned by a blow to the head. Hearts were rapidly removed and left atria dissected free. The preparations were attached to platinum-iridium electrodes and suspended in 30 ml of a Ringer solution of the following composition (mM): NaCl, 154; KCl, 4.0; $CaCl_2$, 2.3; $NaHCO_3$, 2.4; and glucose 5.6. The solutions were vigorously aerated with O_2 and all experiments were carried out at 30°C. At this temperature contractile tension remains stable for long periods of time (up to 8 hours). Atria were then attached to Statham force displacement transducers and 2 g resting tension applied. Changes in isometric tension were recorded using a Grass polygraph. Atria were stimulated at a rate of 60 cycles/min with 20 volt square wave pulses of 1 msec duration only during the period they were in normal Ringer solution.

Preparations were first equilibrated for 1 hour in Ringer solution and then treated with K_2SO_4-Ringer solution of the following composition (mM) for 30 minutes: K_2SO_4, 116; $KHCO_3$, 2.4; $CaCl_2$, 2.4; and glucose 5.6. In the ouabain studies, atria were incubated an additional 15 minutes in Ringer solution containing the drug at a final concentration of 5×10^{-7} M before placing them in high-K solutions. At this time contractile tension had increased approximately 20%. This concentration of ouabain is in the therapeutic range for rabbit atria.

Some observations on Ca^{45} uptake and tissue Ca content were made during the first 6 minutes of the K-contracture and compared

* Supported in part by USPHS Grant HE08678.

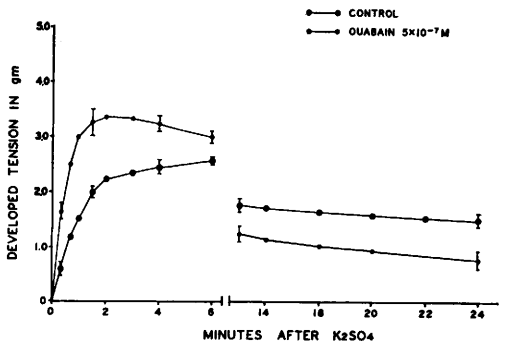

FIG. 1. Time course of developed tension in isolated left atria after application of K_2SO_4 Ringer solution. Each point is a mean of 10 experiments. Standard errors of the means were calculated for a number of points.

with similar determinations in normal Ringer solution. In the isotope studies atria were incubated for the prescribed time in normal Ringer solution or in K_2SO_4-Ringer solution and then washed 2 minutes with an inactive solution of the same composition. Tissue Ca determinations were made under identical conditions in nonradioactive medium. The analytical procedures employed are the same as those described in detail by Lüllmann and Holland(3).

Results. Fig. 1 is a summary of studies depicting the time course of tension development by left atria following the application of high-K medium in the presence and absence of ouabain (5×10^{-7} M). Only the first 24 minutes of developed tension are presented. In control atria tension developed slowly, reached a maximum at 6-8 minutes and gradually declined toward the base line.

Pretreatment with ouabain resulted in a more rapid rise of tension, a higher peak tension which was reached at an earlier time and a faster rate of decline. By 6 to 8 minutes, tension was below control values, and thereafter fell at a rate somewhat greater than in the non-treated preparations. The areas beneath the two curves were not significantly different. This was determined by plotting each curve separately in its entirety, cutting out and weighing the paper.

Table I summarizes Ca^{45} uptake and tissue Ca studies during a 6 minute period in normal Ringer solution prior to the application of K_2SO_4-Ringer solution and during the first 6 minutes of tension development in high-K medium. On going from a normal Ringer solution to a high-K medium tension development was accompanied by increased Ca^{45} uptake with no detectable change in tissue Ca content in the control preparation. Ouabain had a small but nonsignificant effect on uptake of isotope or tissue Ca when added to normal Ringer solution, but caused an increased entry of Ca^{45} during tension development resulting from application of high-K solutions when compared with the appropriate control. Again no significant change was noted in tissue Ca content during this interval.

Discussion. The main findings of the present work are: (1) High-K solutions induce a transient contracture of isolated left atria. (2) The development of tension is accompanied by increased uptake of Ca^{45} with no detectable change in tissue Ca content. (3) Pretreatment of atria with ouabain resulted in an increase in rate of rise of tension, a higher peak tension and faster rate of decline of tension. (4) The enhanced rate of rise and the higher peak tension induced by the drug

TABLE I. Effect of High-K Medium and Ouabain on Ca^{45} Entry and Tissue Ca Content. P value calculated as the effect of ouabain on Ca^{45} entry in K_2SO_4-Ringer solution using the control mean in K_2SO_4 solution.

Experiment	Solution	No.	Ca^{45} uptake, cpm/g/6′ $\times 10^{-4}$ ± S.E.M.	Tissue Ca content, mM/kg wet wt ± S.E.M.
Control	Ringer	10	.61 ± .02	3.29 ± .6
	K_2SO_4-Ringer	20	.81 ± .05 P <.02	3.37 ± .5
Ouabain 5×10^{-7} M	Ringer	10	.69 ± .03 P <.50	3.38 ± .3
	K_2SO_4-Ringer	20	1.04 ± .07 P <.01	3.33 ± .5

were accompanied by a further increment in Ca^{45} entry with no significant change in tissue Ca. Thus, in many respects, the K-contracture in mammalian heart muscle resembled qualitatively that in the single skeletal muscle fiber.

A tentative explanation of the above data is that proposed by Hodgkin and Horowicz (2). They suggested that high-K, by depolarizing the cell membrance, released an activator (probably Ca or a compound of Ca) from a limited quantity of a precursor; the activator was then rapidly inactivated. Contraction would last until the precursor of the activator was nearly exhausted. They also suggested that the precursor might be stored in the sarcoplasmic reticulum. Such a hypothesis would account for the time course of the K-contracture in atria, and also for the finding that during tension development tissue Ca content did not change, but became more exchangeable.

In light of this hypothesis ouabain might produce its effects by promoting the rate of liberation of the activator from its precursor and possibly by reducing the rate at which the precursor is resynthesized. The observed action of ouabain on the time course of tension development in K-contracture as well as its effect on Ca^{45} uptake is in agreement with this hypothesis.

Summary. The K-contracture in isolated rabbit atria is transient in nature, resembling qualitatively that seen in single skeletal muscle fibers, but differing from that found in frog ventricle. Tension development is accompanied by an increase Ca^{45} entry with no detectable change in tissue Ca content. The rate of rise of tension, the level of peak tension and the rate of decline of tension is increased by ouabain. It was concluded that K releases an activator (probably Ca) from a precursor stored at a cellular site, and then is rapidly inactivated; the contraction lasting until the precursor is exhausted. Ouabain is believed to act by promoting the release of activator and possibly by reducing the rate at which the precursor is reformed at its storage site.

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Received April 28, 1966. P.S.E.B.M., 1966, v122.

Alteration in Lipid Content of the Liver in the Rat After Partial Hepatectomy.* (31349)

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Significant metabolic alterations occur in the liver within 24 hours after partial hepatectomy(1-4). Among these changes a remarkable rise in total lipid concentration, due mostly to accumulation of triglycerides, is apparent as early as 6 hours after partial hepatectomy(5).

As indicated by Johnson and Albert(6,7), the higher levels of lipids found in the liver after surgery appear to reflect the utilization of fatty acid originating from the peripheral adipose tissue and not by increased synthesis *in situ*. According to these authors, based on studies with ^{14}C-acetate, fatty acid synthesis is low during the 24-hour period after partial hepatectomy(7), during which time the accumulation of lipids in the liver is most pronounced.

The increased liberation of fatty acids (F.A.) from peripheral fat depots in euglycemic animals involves the participation of several hormones, such as ACTH and the

* Supported in part by Research Grant CY 6473 from Nat. Inst. Health, USPHS.