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Effect of Calcium on the Action of Pilocarpine and Atropine.

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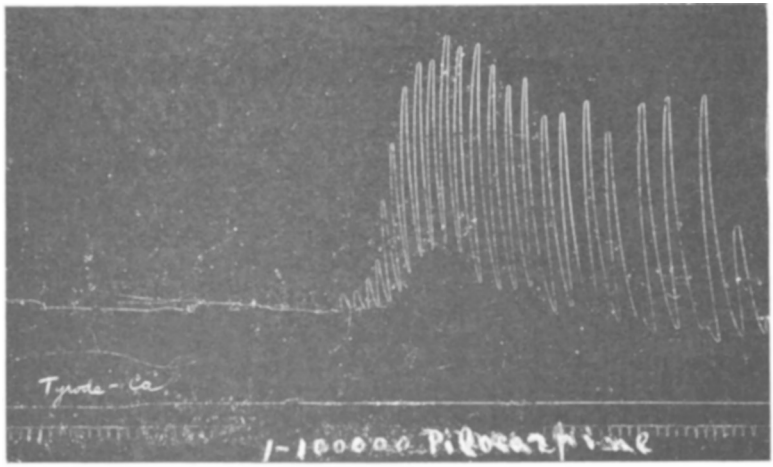
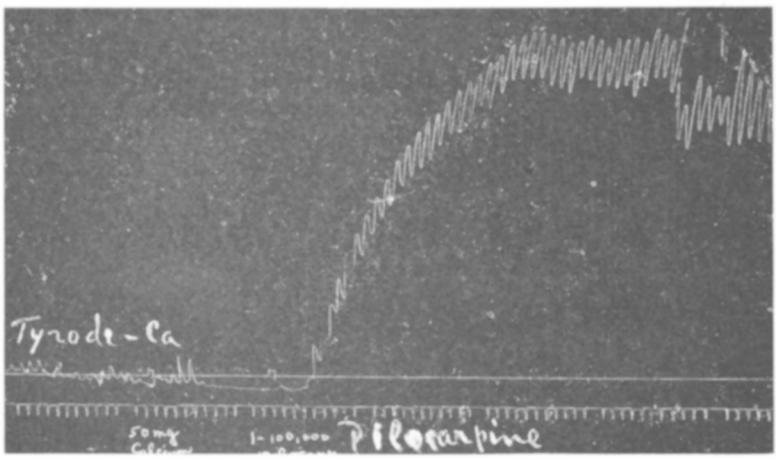
When segments of the small intestine of the cat or rabbit are suspended in calcium free Tyrode solution, rhythmic contractions as well as tonus are abolished. The intestinal movements may be stimulated, however, by pilocarpine. A concentration of 1-500,000 was sufficient to provoke rhythmic contractions of moderate force which became much stronger with increasing amounts of pilocarpine. In no case, however, did the amplitude attain the size produced by the same concentrations in normal Tyrode solution. The rate was also slower, the latent period was considerably longer, usually about one minute, while tonus, with all concentrations, was very low. The movements were markedly stimulated, the tonus being enormously increased when a small quantity of calcium chloride was added to the calcium free solution containing pilocarpine in a concentration of 1-500,000. But the same amount of calcium produced only a very slight increase of tonus and provoked slight rhythmic contractions in the intestine suspended in calcium free Tyrode without pilocarpine. The combined action of calcium and pilocarpine is, therefore, not one of summation but is apparently due to potentiation. Excessive amounts of calcium likewise decrease intestinal motility. The addition of calcium making a concentration of 1-2,000 abolished the contractions produced by pilocarpine in Tyrode minus calcium.

Experiments were also made on the effect of calcium on the action of pilocarpine on the isolated frog heart. Calcium deficiency produced the usual effect. In some cases, however, heart action, though feeble, continued for a few minutes. The presence of pilocarpine in Ringer solution containing no calcium or minimal amounts only was without effect. But in several of these experiments in which atropine in concentration of 1-500,000 was perfused heart action was distinctly slowed. This reversal of effect occurred when pilocarpine was perfused before atropine as well as when no pilocarpine was used. In experiments in which the amount of calcium in Ringer solution was increased 3 times the following results were obtained. A concentration of 1-100,000 pilocarpine in normal Ringer reduced the force of the heart beat 50-60% in 7-12 minutes

and decreased its frequency nearly 14%. The same amount of pilocarpine in Ringer containing an excess of calcium produced only a moderate decrease of the amplitude in some experiments and scarcely any change in others, while the rate was decreased 21.5%.



A



B

FIG. 1.

A. Expt. 18. Intestinal movements disappeared when segments of the cat's intestine were suspended in Locke's solution minus calcium. The addition of pilocarpine to the solution stimulated the rhythmic contractions but not the tonus.

B. Expt. 26. The same concentration of pilocarpine as in A stimulated the tonus after calcium was added to the solution.

Reduced one third.

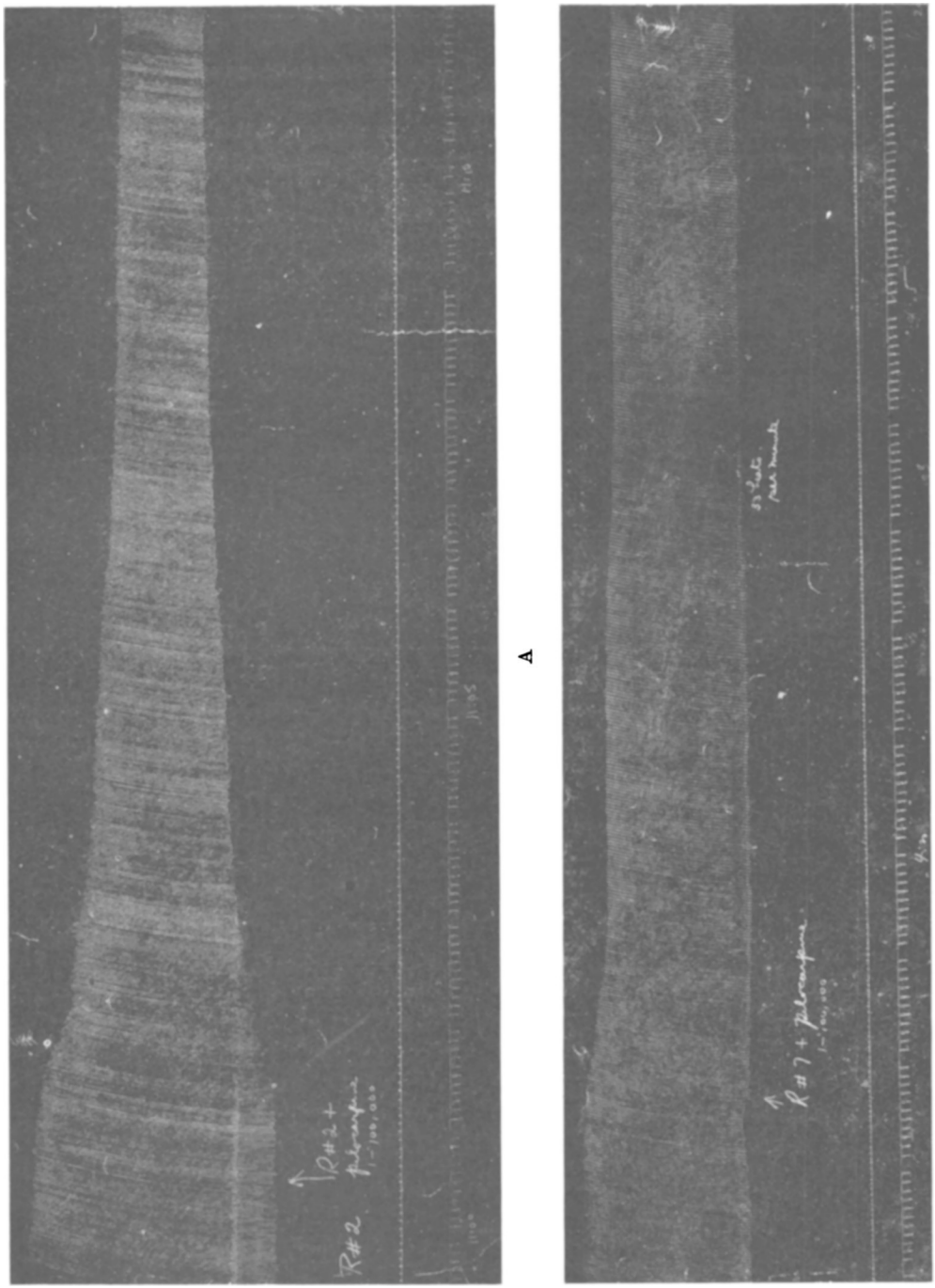


FIG. 2.

A. Expt. 9. Frog's heart perfused with normal Ringer's solution containing 1-100,000 pilocarpine. B. Expt. 15. Shows that the same concentration of pilocarpine in Ringer's solution containing three times the amount of calcium as in A produced only a slight decrease in the strength of the contractions, but the slowing was greater than in A.

Reduced one third.

Summary: 1. Pilocarpine stimulates intestinal movements in the absence of calcium in the surrounding medium, but tonus is only slightly increased. 2. Excess calcium depresses the effect of pilocarpine on the intestine. 3. Pilocarpine sensitizes the intestine to calcium. 4. Pilocarpine in Ringer minus calcium is without effect on the isolated frog heart. 5. Excess calcium antagonizes the depression produced by pilocarpine. 6. The action of atropine is reversed by calcium deficiency, thus causing a slowing of the heart.

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The Iodine Values of "Physiological" or "Synthetic" Rat Fat.

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Male albino rats taken at weaning when 21 days of age were fasted for 2 days in order that a partial depletion of the stored fat might ensue, thereby lessening its influence on the later resulting "synthetic" fat. The rats were then fed a diet consisting of 18% casein (extracted with alcohol and ether), 77% sucrose, and 5% salt mixture (Osborne and Mendel), supplemented daily by the following: a hot water extract of pig's liver (≏ 0.4 gm. dried liver), 100 mgm. of yeast concentrate (Harris), 20 mgm. of a non-saponifiable fraction of cod liver oil (a pasty material, Oscodal†—Iodine Number 110), and 0.016 mgm. of irradiated ergosterol (dissolved in alcohol). Four other groups of rats (5 or more in a group) were fed this "fat free" diet modified so that the first group received an addition of 20 mgm. of peanut oil (Iodine Number 84); the second had the non-saponifiable fraction of cod liver oil substituted by 20 mgm. of cod liver oil (Iodine Number 160); the third received the same diet as the second group with the addition of 20 mgm. of peanut oil; and the last had the extracted casein replaced by commercial casein, the yeast concentrate substituted by yeast and the irradiated ergosterol omitted.‡ From the analyses of the die-

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† Kindly supplied by Dr. H. E. Dubin of the H. A. Metz Laboratories.

‡ A paper is now in press in the *J. Biol. Chem.* on the "Growth of Rats on 'Fat Free' Diets."