Contraction of Circular and Longitudinal Guinea Pig Ileal Sections by Cholecystokinin Concentrates and Histamine

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During the course of a study of the contractility of smooth muscle by cholecystokinin concentrates isolated from hog intestines, the effect of such extracts and histamine on longitudinal, as well as circular, ileal fibers was explored. Magnus (*1*) observed that circular preparations free of ganglia are obtained by stripping off the longitudinal musculature from the small intestine of the cat. Recently, Evans and Schild (*2*) have reviewed and extended the usage of this method.

In the present work, a simple procedure for mounting guinea pig intestinal strips was found which gave rise to contractions that are roughly traceable to the circular fibers, as illustrated in Fig. 1. A wire frame was employed to hold the longitudinal strip at right angles to the line-of-force to the lever that contacted a kymograph. Surgical wire had the advantage over thread in minimizing curling of the intestine.

Guinea pigs, ranging up to 1 kg in weight, were killed by a blow on the head, the abdomen was incised, and a portion of the terminal ileum was removed and placed in warm Locke-Ringer solution. The lumen was washed thoroughly with the medium, use being made of trocar and syringe. One section was mounted longitudinally with silk thread, and a shorter piece (approximately 10 to 15 mm in length) was arranged with surgical wire as described in the preceding paragraph. Denervation of the tissues was not attempted.

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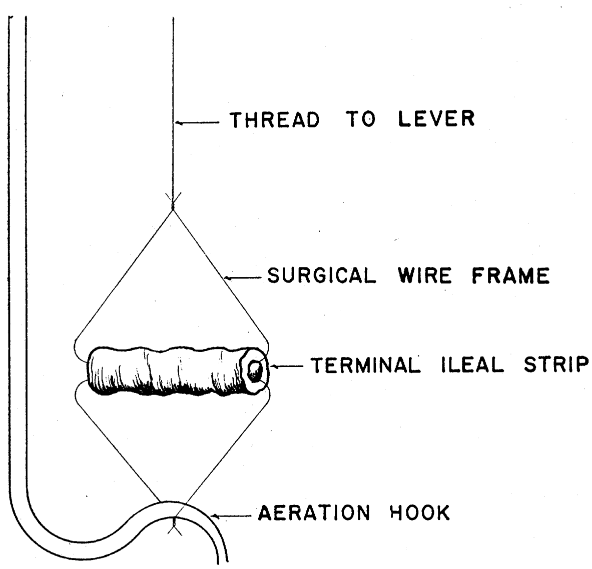

Fig. 1. Arrangement of the guinea pig ileal strip for the observation of circular fiber contractility.

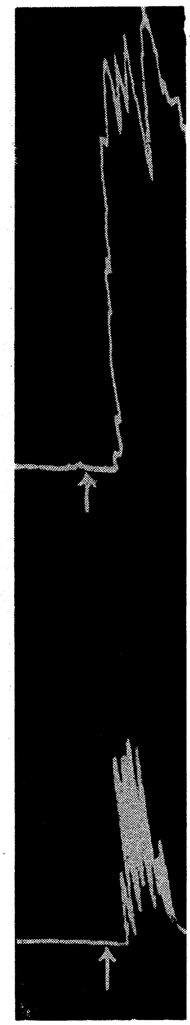

Fig. 2. Contraction of longitudinal (top) and circular (bottom) ileal sections by 13 units of cholecystokinin concentrate, CCK-X2. The duration of each contraction is less than 1 min. (×2.5)

In all operations, the strips were handled with instruments. The muscle bath, which was maintained at 37°C, contained a chamber of 45 ml capacity. The latter was equipped with two inlets, one for air (bubbled through aqueous sodium bicarbonate), which was bent in such a way as to allow for the attachment of the sections, and the other for the entrance of preheated Locke-Ringer solution; a siphoning arrangement provided for removal or flushing out of the bath fluid. Cholecystokinin concentrates and histamine (hydrochloride) were dissolved in warm Locke-Ringer medium and introduced into the chamber when constant conditions prevailed.

The simultaneous contraction of longitudinal and circular preparations by a cholecystokinin extract is exemplified by Fig. 2. Under the same conditions, 5 μg of histamine gave rise to an off-the-paper contraction of the longitudinal segment; with the circular section, an augmented tonicity occurred. The circular, and especially the longitudinal, ileal preparations generally contract in a stepwise manner that is associated with increased tone when cholecystokinin extracts are introduced. Thus, of a total of 96 trials with 45 longitudinal preparations employing concentrates assaying 0.5 to 24 units/mg (*3*), 81 comprised stepwise or ragged contractions; latent periods often preceded an effect as reported earlier (*4*). Except for relatively few cases with low dosages, histamine caused the usual sharp and rapid longitudinal contractions, but the circular sections were either contracted in a stepwise fashion or displayed increased tonic activity.

Many circular segments proved to be refractory or of a very low order of sensitivity, often requiring massive dosages of potent cholecystokinin concentrates for an effect. Such intestinal strips are greatly affected by initial handling. It should be noted that the longitudinal preparation is able to contract over a greater distance than the circular ileal sections. In the latter, the diameter of the lumen is a limiting factor.

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The Effect of Insulin on the Oxygen Consumption of Mammalian Muscle*

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The first indication that insulin can stimulate the oxidation of carbohydrate was the work of Krebs and Eggleston (*1*) in which insulin was shown to increase the O_2 consumption of pigeon breast muscle brei in the presence of phosphate, citrate, and boiled muscle juice. Shorr and Barker (*2*) repeated and extended these experiments. On the whole, the stimulation was found to be far less—approximately 25 percent; and no effect at all was observed in minced skeletal muscle of the dog, cat, and rabbit, or in diabetic or fasted muscle of the dog. Stare and Baumann (*3*) likewise reported that insulin caused a 20-percent increase in the O_2 consumption of minced pigeon breast muscle, and a 60-percent increase in the O_2 consumption of muscle from depancreatized birds. Stadie, Zapp, and Lukens (*4*) corroborated the findings of Shorr and Barker but, contrary to Stare and Baumann, did not find any stimulation when they used minced muscle from diabetic pigeons and cats. Ricketts and Stare (*5*), however, reported that insulin in some cases stimulated the O_2 consumption of minced human diabetic muscle. Recently Stadie (*6*) has reviewed all aspects of this controversy.

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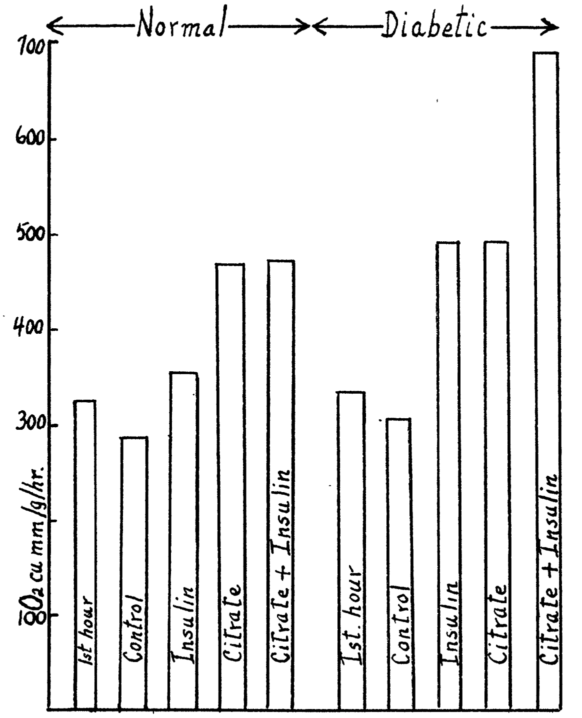

Fig. 1. Oxygen consumption in cubic millimeters per gram, per hour, in normal and diabetic muscle strips.

It is noteworthy that almost all of this work has been done with tissue minces, very little with relatively intact muscle. Moreover, Shorr and Barker (*2*) showed that the respiration of minced tissue differs greatly both quantitatively and qualitatively from that of tissue slices. Fisher, Hall, and Stern (*7*) reported that the O_2 consumption of intact isolated frog muscle was increased under certain conditions by insulin alone, under others when combined with citrate. More recently Villee and Hastings (*8*) have shown that pyruvate utilization and O_2 consumption are sharply reduced in diabetic rat diaphragm and that insulin when added *in vitro* remedies this condition.

Table 1. Data for normal and diabetic animals. All O_2 consumptions are in cubic millimeters per gram wet-weight, per hour.

	1st hour	Average 2nd and 3rd hours after dumping			
	All vessels	Control	Insulin	Citrate	Insulin and citrate
Normal	322 ± 6(24)	284 ± 7(27)	350 ± 5.3(21)	467 ± 7(27)	471 ± 6(23)
Diabetic	340 ± 7.3(29)	302 ± 8.5(34)	491 ± 7(28)	487 + 6.5(26)	685 ± 8.3(33)