

which vasomotor reactions seem to be most marked. Studies are in progress to determine the maximum circulation which can be attained in the various skin areas, as well as to examine the effects of peripheral vascular disease on the blood supply of these areas.

9936 P

Studies on the Effects of the Administration of Insulin by Iontophoresis.

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We have been able to show that by iontophoresis a large molecule such as acetyl beta methylcholine could be introduced through the intact skin and be absorbed into the blood stream.¹ Acetyl beta methylcholine bears a positive charge and was electrolysed at the anode. Insulin bears a negative charge, for experimental purposes the effects of electrolysis at each pole was attempted.

Dogs were used as the experimental animal. They were in an 18-hour postprandial state when the experiments were performed. The hair from the abdomen and one thigh was carefully shaved. The animal was restrained in a supine position and a folded piece of asbestos paper, saturated with insulin U-80 was placed on the bare abdominal skin. It was covered by a piece of block tin of sufficient size to fit within the limits of the paper. The other pole was placed on the thigh and held in place by means of a cotton bandage.

The instrument used was a simple but effective one consisting of a 45-volt B battery with rheostat control and an attached ammeter capable of measuring milliamperes. The circuit was closed and the amperage was slowly raised to 30 milliamperes and kept there 30 to 60 minutes as indicated in Table I. Capillary blood sugar estimations were made by the Folin micro method.² The control level was determined just before the circuit was closed. Subsequent estimations were made after the circuit had been broken for 30, and for 60 minutes, and then at hourly intervals for 6 hours.

Two control tests were made with distilled water. In one instance it was placed beneath the cathode and in the other anode.

¹ Martin, L., *New England J. of Med.*, 1937, **207**, 202.

² Folin, Otto, and Malmros, Haqvin, *J. Biol. Chem.*, 1929, **83**, 115.

TABLE I.

Date	Polarity	Material used	Control	Treat- ment hr	Blood sugar end of treat- ment	1/2 hr	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr	Remarks
						after treat- ment	after treat- ment	after treat- ment	after treat- ment	after treat- ment	after treat- ment	after treat- ment	
4-13	+	Insulin	70	1/2	74	71	83.5	71.5	73	65.8	75.8		
4-20	—	"	96.6	1/2	95.2	89	86	84.4	77	78.5	80		
4-28	—	"	88.6	1	89	82	86	86	83	77.2	76		
5-5	—	"	78	1	73	52.6	54	62.7	63.5	62.5	71.8	68.6	
5-12	—	"	59	1	43	33.3	36.6	46.5	43.8	54	51.8	58.3	Considerable Shivering
5-19	—	"	81.6	1	74.1	77	75.1	70.1	72.7	68	70.8	66.6	Bad Burn
5-26	—	"	107	1	96.7	91.3	89	89	80.6	80	74.4	78.6	" "
6-2	+	Distilled water	77	1	77	70.5	78.3	84.9	77	78.5	80	84.9	" "
6-16	—	"	89	1	91.5	92	91.5	102	91	92.6	87		

No significant change in blood sugar level was noted. In the one instance when the insulin was placed beneath the positive pole there was no important change in blood sugar level.

On 6 occasions insulin was placed beneath the negative pole and in each experiment there was a drop in blood sugar. The smallest fall was 12 mg per 100 cc; the largest 32 mg per 100 cc. In one dog the level of blood sugar dropped from 59 mg per 100 cc to 33 mg per 100 cc and at this period the animal showed signs of an hypoglycemic reaction.

It was not possible to predict when the sugar would fall. At times it occurred within an hour or two after the termination of iontophoresis. In other experiments it occurred later.

The thought naturally occurs as to the propriety or advisability of using such a form of administration in the treatment of diabetes in man. The data we have obtained do not permit us to draw any conclusions. However, it might be pointed out, as we have noted not only in these experiments but in those in which acetyl beta methylcholine was used in man, that there is apparently considerable variation in skin resistance in different individuals. It is conceivable that a technic might be developed which could control the variable skin resistance and deliver a known amount of insulin to the body. Such a method would offer the particularly desirable condition of providing a slowly absorbable supply of insulin.

Summary. A fall in blood sugar in dogs has been demonstrated following cathode iontophoresis with insulin.

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Physiological Effects of Some Thio-Esters of Choline.

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The effects on blood pressure and respiration produced in cats and dogs under morphine-urethane, nembutal and chloralose anesthetics, by intravenous injections of thio-acetyl choline chloride, thio-acetyl-gamma-homo-choline chloride and thio-acetyl-beta-methyl choline chloride have been observed and recorded.* Eighteen

*The chemistry of these compounds will be reported separately.