

29 (1989)

Influence of pancreatic perfusates upon the carbohydrate metabolism of depancreatized animals.

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Following the method of perfusion introduced by Clark¹, the effect of pancreatic perfusates upon the carbohydrate metabolism of entire animals was studied. The respiratory metabolism, the blood sugar, and the D:N ratio were studied in cats and dogs after depancreatization.

Perfusates were made by perfusing aseptically and at body temperature the pancreases of cats, dogs, pigs, and oxen with Locke's solution. The first perfusates were made with an alkaline medium, later perfusates were made with Locke's solution modified by the substitution of HCl varying in strength from 0.1 per cent. to 0.7 per cent. for sodium bicarbonate.

Respiratory quotients were obtained by a modified Jaquet method, the animal being confined in a respiration chamber through which a continuous stream of air was drawn for ventilation and from which a continuous sample of air was removed for analysis. In a later modification the stream of air from the respiration chamber was directed into a large gasometer for a twenty-minute period and the samples for analysis withdrawn from this total volume. Analyses were made by the Henderson and Bailey modification of Haldane's apparatus. The respiration chamber was frequently checked by analyses of outside air and by burning alcohol in it.

D:N ratios and respiratory quotients typical for diabetes were obtained in the depancreatized animals.

Following the administration of sugar in the form of dextrose or sucrose by stomach tube pancreatic perfusates were given subcutaneously, intravenously, and intraperitoneally. Significant increases were shown in the respiratory quotients and marked

¹ Clark, Admont H., *Jour. Exp. Med.*, 1916, **xxiv**, 621.

Ibid, 1917, **xxvi**, 721.

drops were observed in the blood sugar level (frequently to points below normal) and marked changes were demonstrated in the D:N ratio. These changes were demonstrated both for alkaline and for acid perfusates, but were greater and more constant with acid perfusates given neutral.

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The influence of pancreatic extracts upon the carbohydrate metabolism of depancreatized dogs.

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The experimental work reported dealt with the effects of extracts prepared in various ways from the pancreas of the dog, pig and ox upon the blood sugar, D:N ratio, respiratory quotient and clinical condition of depancreatized dogs.

A dog was given two days to recover from the operation and to become totally diabetic as shown by a D:N ratio of 2.8 or more. The dogs were fed ground beef in increasing amounts after the first day. The extracts were administered by stomach tube, intramuscularly, intravenously, subcutaneously and intraperitoneally.

Extract given by stomach tube caused no or very little fall in blood or urinary sugar. Injections of the extract into vein, tissue and peritoneum have been followed by abrupt lowering of the sugar in the blood and urine, the former at times even below normal and the latter has been made to completely disappear even when glucose had been previously administered. In the majority of cases the lowest level of blood sugar was reached in 4 hours from the time of injection whether the extract was given into vein, peritoneum, muscle or under the skin. Since harmful effects were experienced more frequently when the extracts were injected intravenously, intramuscularly and intraperitoneally than when given subcutaneously the last method was used most.

The first preparations used in this series of experiments were extracts of freshly removed, macerated dog's pancreas given