The Effect of Crystalline Glucagon on the Blood Sugar of the Fowl[1]

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Kimball & Murlin (4) discovered a hyperglycemic factor in extracts of the pancreas more than 30 years ago, but only in the last decade has this substance, glucagon, been definitely established as a second pancreatic hormone. Evidence from several lines of approach support the earlier assumption that glucagon has its origin in the alpha cells of the Islets of Langerhans (2, 9).

Glucagon has been extracted from the pancreas of mammals, teleosts and birds (1, 5, 10). The existence of glucagon in a wide variety of vertebrates has therefore been established. The relative importance of the hormone's role in regulating carbohydrate metabolism in various groups of vertebrates is still unknown. Glucagon's primary physiological action in the regulation of carbohydrate metabolism appears to be an enhancement of liver glycogenolysis, thereby elevating the blood sugar level (8).

The effect of injected crystalline glucagon on blood sugar level has been described for some mammalian species (6, 7). Of the mammals thus far investigated, the cat seems to be the most sensitive to small doses of the hormone. The purpose of the investigation reported here was to determine the sensitivity of the fowl to the hyperglycemic effect of crystalline glucagon.

Materials and Methods

White Leghorn cockerels ranging in weight from 600 to 1100 grams, and in age from 8 to 12 weeks, were used in this study. The birds were raised in the laboratory from day old chicks on a constant diet of a commercial growing feed. Twenty-four hours before they were to be used, their food was withdrawn. After a 12 hour fast, the birds were weighed, marked and allowed to feed for the remaining 12 hours prior to treatment.

The crystalline glucagon[1] was dissolved in water after adjusting the pH to 9.0-9.5 with 0.1 N NaOH. The dosages of hormone used were 0.1, 1.0, 10 and 25μgm./kg. fasted body weight. Injection was into the right wing vein in a volume of 0.05 ml. per kg. Blood samples were taken, as previously described (2), from the left wing vein immediately before injection and at five minute intervals after treatment until the maximum response had been reached. Blood sugar was determined by the Folin-Malmros micro-method as adapted for the photoelectric colorimeter by Horvath and Knehr (3).

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Results

A significant hyperglycemia was obtained with the 0.1 μgm. dose. (Fig. 1) The maximum response to this dose was observed at 5 minutes

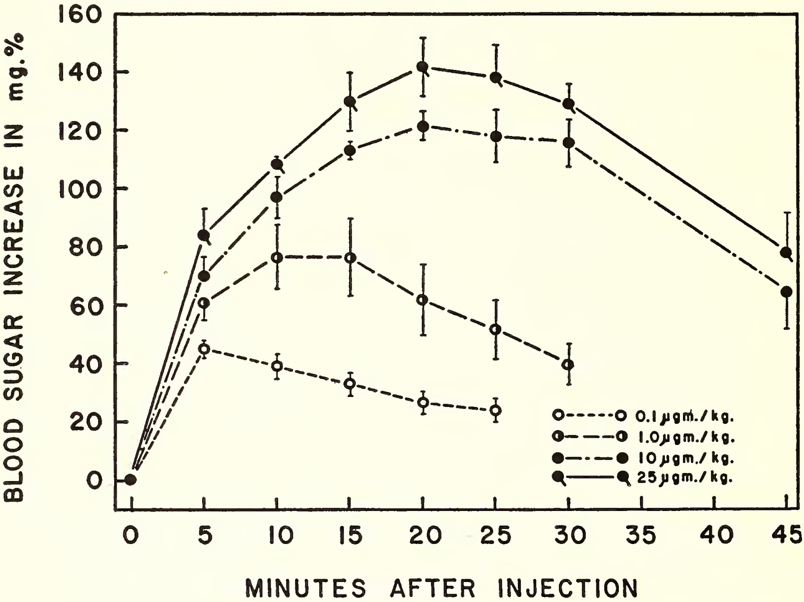

Figure 1: The mean hyperglycemic response of the White Leghorn chicken to crystalline glucagon administered i.v. at time 0 in 0.05 ml. water at pH 9.5. The standard error of the mean values is also shown.

after injection (Table 1). The interval between time of treatment and the time at which the maximum response for each dose was reached, was increased as the dosage was increased (Table 2).

When the log of the dose is plotted against its maximum blood sugar increase, one obtains a straight line for the dosage range used in this experiment. (Fig. 2)

Staub *et al.* (6) have reported that in the cat, a dose of 0.2 μgm. increases the blood sugar 45 mg.%. In the chicken this same response is obtained with one half that amount, or 0.1 μgm. The absolute maximum response in the cat is reached with 1-2 μgm. (6), whereas in the chicken the absolute maximum response would be obtained by a dose somewhere above 25 μgm.

This high sensitivity and wide dosage response range of the bird to glucagon, together with the report that the bird pancreas contains approximately six times as much glucagon as the mammalian pancreas (10), suggests that glucagon's role in the hormonal regulation of carbohydrate metabolism should not be overlooked when considering possible differences between birds and mammals in respect to this regulation.

TABLE 1. The hyperglycemic response of the White Leghorn chicken to graded doses of crystalline glucagon.

Dose	Number of birds	Initial blood sugar[1]	Blood sugar increase from initial level in mg.% at: 5 Mins	10 Mins	15 Mins	20 Mins	25 Mins	30 Mins	45 Mins
0.1 μgm./kg.	6	187[2]	45	39	33	27	24		
		± 2[3]	± 3	± 4	± 4	± 4	± 4		
1.0 μgm./kg.	6	187	61	77	77	62	52	40	
		± 3	± 6	±11	±13	±12	±10	± 7	
10 μgm./kg.	6	182	70	97	113	122	118	116	65
		± 9	± 7	± 7	± 3	± 5	± 9	± 8	±13
25 μgm./kg.	6	180	84	108	130	142	138	129	78
		± 3	± 9	± 3	±10	±10	±11	± 7	±14

[1] mg./100 ml. whole blood.
[2] mean value.
[3] ± standard error of the mean.

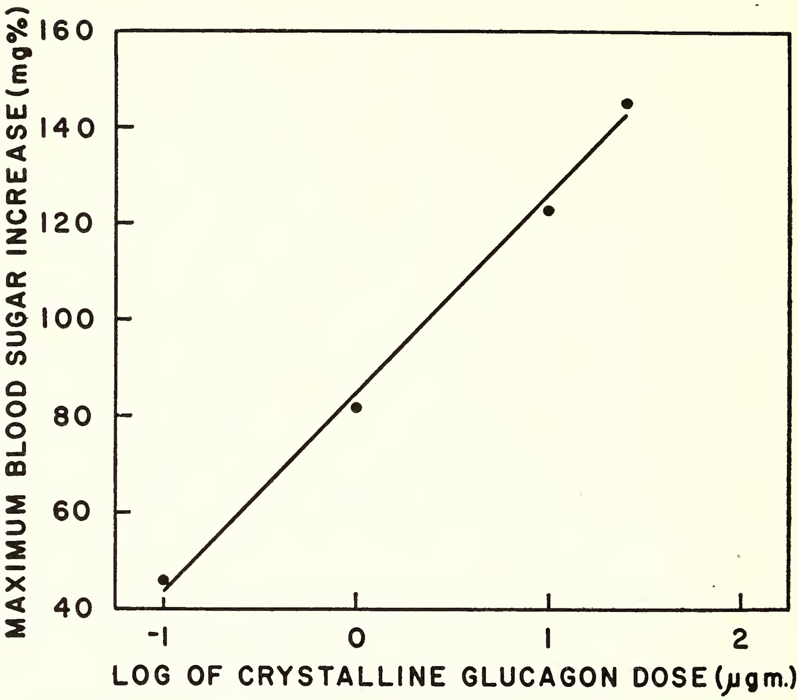

Figure 2: The log dose-mean maximum hyperglycemia produced by crystalline glucagon in the White Leghorn chicken. Hormone administered i.v. in 0.05 ml. water at pH 9.5.

TABLE 2. The maximum response of the White Leghorn chicken to graded doses of crystalline glucagon.

Dose	Number of birds	Initial blood sugar[1]	Maximum blood-sugar increase[1]	Time when maximum observed[2]
0.1 μgm./kg.	6	187[3] ± 2[4]	46 ± 4	5
1.0 μgm./kg.	6	187 ± 3	82 ±12	10
10 μgm./kg.	6	182 ± 9	123 ± 6	20
25 μgm./kg.	6	180 ± 3	145 ±12	20

[1] mg./100 ml. whole blood.
[2] mins. after treatment.
[3] mean value of six determinations.
[4] ± standard error of the mean.

Summary

A significant hyperglycemia is produced with 0.1 μgm. of crystalline glucagon in the White Leghorn cockerel. The log dose-maximum response curve is linear for the dosage range used (0.1 μgm.-25 μgm.). An increase in dosage increases the interval between treatment and the time when the maximum response is reached. The sensitivity of the chicken to glucagon appears to be higher than that of mammals.

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