tive inactivity of the *Ambystoma* PRL in this immunologic system is consistent with the results with rat glands and confirms the effectiveness of the electrophoretic system for separating amphibian GH and PRL. In contrast is the high immunoreactivity in the PRL zone of the polyacrylamide gels from the other amphibians, especially the two *Rana*. We cannot rule out the possibility that the immunoreactivity shown by most of the amphibian PRL's is due to contamination with GH. However, if such contamination occurs, it must represent a modified form of GH that does not migrate in the usual electrophoretic position. In order to account for this high degree of immunoreactivity by postulating GH contamination, the PRL region would have to contain up to 80 percent of the total GH present in the region identified as having GH bioactivity. Such levels of contamination seem unlikely since our bioassay failed to show significant somatotropic activity in the PRL region from *Necturus* and *Rana catesbeiana* when tested in the toad (*2*). Furthermore, when the PRL eluate was subjected to further electrophoresis under different conditions the *Rana* PRL was homogeneous.

On the basis of available information it appears that PRL from several anuran and urodele amphibia may have a high degree of immunochemical relatedness to amphibian as well as to mammalian (rat) GH. Since the actual amount of protein eluted from the GH and PRL regions has not been determined, it is not possible to compare the specific immunoreactivity of each hormone preparation. Our results provide further evidence of the structural similarities between these two pituitary hormones. In addition they emphasize the need for caution when attempting to use antibodies against mammalian hormones to measure hormones in nonmammalian species, even when the antiserum shows high specificity for the homologous mammalian hormone.

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Lack of Glucagon Response to Hypoglycemia in Diabetes: Evidence for an Intrinsic Pancreatic Alpha Cell Defect

Abstract. *Despite excessive glucagon responses to infusion of arginine, plasma glucagon did not rise in six juvenile-type diabetics during severe insulin-induced hypoglycemia, whereas glucagon in the controls rose significantly. Thus in diabetics pancreatic alpha cells are insensitive to glucose even in the presence of large amounts of circulating insulin. An intrinsic defect common to both alpha and beta pancreatic cells—failure to recognize (or respond to) plasma glucose fluctuations —may be operative in juvenile diabetes.*

Juvenile-type diabetes mellitus is generally thought to result mainly, if not exclusively, from deficient insulin secretion by pancreatic beta cells (*1*). Recent studies (*2–10*), however, suggest that pancreatic alpha cell dysfunction may also play an important role. Plasma glucagon levels are often elevated in diabetes (*3–5*). There is lack of suppression of glucagon by glucose (*6*), and glucagon responses to intravenous arginine are excessive (*7*). Nevertheless, it is unclear whether these abnormalities represent an intrinsic defect in alpha cells (*8*) or are merely the result of insulin deficiency (*9*). In dogs made

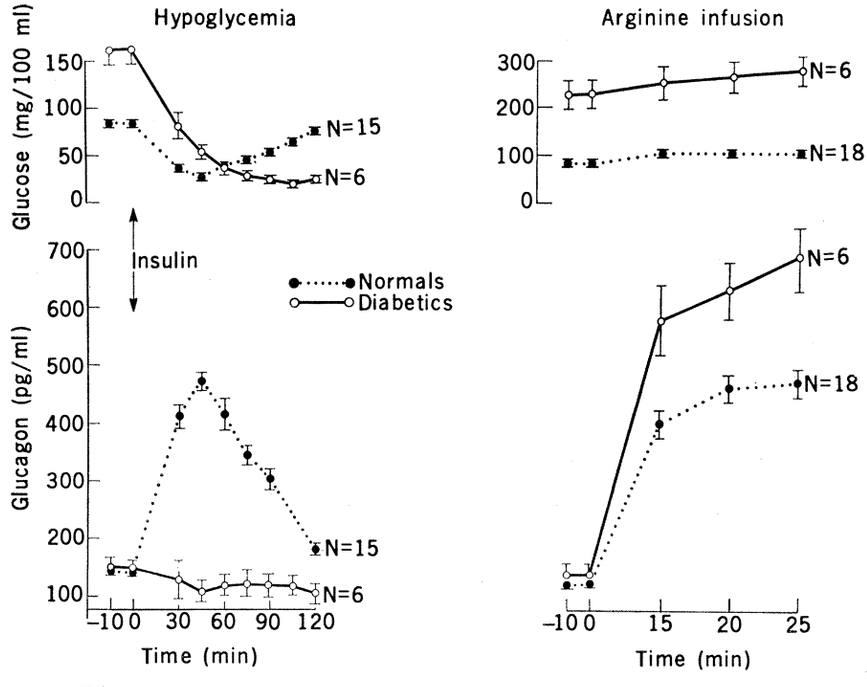

Fig. 1. Plasma glucose and glucagon responses to insulin-induced hypoglycemia (left) and to intravenous arginine infusion (right) in juvenile-type diabetics (——) and in normal controls (- - - -). Vertical bars indicate standard errors; N is the number of patients.

Table 1. Effects of insulin-induced hypoglycemia on glucose (mg/100 ml), glucagon (pg/ml), cortisol (μg/100 ml), and growth hormone (ng/ml) in 6 juvenile-type diabetics (insulin dose, 0.3 to 1.0 unit/kg) and in 15 normal controls (insulin dose, 0.15 unit/kg). Values are expressed as means ± standard errors of the means. "Basal" refers to the time (minutes) before and the time of insulin administration. Insulin was administered at time 0. N.S., not significant.

Subject	Basal		Minutes after first insulin administration						
	− 10	0	30	45	60	75	90	105	120
					Glucose (mg/100 ml)				
Controls	85 ± 2	85 ± 2	26 ± 2	36 ± 3	40 ± 2	45 ± 2	53 ± 3	61 ± 3	74 ± 3
Diabetics	163 ± 17	165 ± 17	80 ± 12	54 ± 8	39 ± 7	28 ± 4	25 ± 3	22 ± 1	26 ± 2
$P <$	.001	.001	.005	.005	N.S.	.005	.001	.001	.001
					Glucagon (pg/ml)				
Controls	144 ± 7	142 ± 7	391 ± 21	472 ± 15	415 ± 28	346 ± 26	304 ± 22		188 ± 8
Diabetics	154 ± 19	148 ± 15	130 ± 36	108 ± 13	120 ± 19	124 ± 24	119 ± 20	119 ± 13	105 ± 18
$P <$	N.S.	N.S.	.001	.001	.001	.001	.001		.001
					Cortisol (μg/100 ml)				
Controls	16 ± 5	15 ± 2		26 ± 2	29 ± 2	28 ± 3	28 ± 2		24 ± 3
Diabetics	20 ± 3	17 ± 3			24 ± 5	26 ± 6	27 ± 8	31 ± 8	34 ± 6
P	N.S.	N.S.			N.S.	N.S.	N.S.		N.S.
					Growth hormone (ng/ml)				
Controls	2.5 ± .5	2.7 ± .5		18 ± 2	35 ± 5	33 ± 4	31 ± 3		22 ± 6
Diabetics	2.6 ± .9	2.4 ± .9			21 ± 6	28 ± 6	30 ± 7	36 ± 8	29 ± 8
P	N.S.	N.S.			N.S.	N.S.	N.S.		N.S.

diabetic with alloxan, both hyperglycemia and hyperglucagonemia are rapidly reversed by insulin (*10*), but in human diabetes suppressibility of glucagon by glucose is not as readily reestablished by insulin (*8*).

The present studies were undertaken to further characterize the role of the pancreatic alpha cell in human diabetes. Since it had previously been shown that the pancreatic alpha cells of diabetics were insensitive to hyperglycemia (*6*), we were interested in whether these cells were also insensitive to hypoglycemia, normally a potent stimulus for glucagon release (*11*). Accordingly, the responses in plasma glucagon to insulin-induced hypoglycemia of six juvenile-type diabetics were determined by means of a radioimmunoassay specific for pancreatic glucagon (*12*). The diabetics (two males, four females), with a mean age of 43 years (range, 16 to 69 years), were all being treated with insulin and had had at least one documented episode of ketoacidosis. None were obese (mean weight, 95 percent of ideal body weight), acutely ill, or ketotic. The known duration of diabetes ranged from 2 weeks to 42 years (mean, 22 years). Despite fasting hyperglycemia, basal concentrations of plasma glucagon in the diabetics (154 ± 19 pg/ml) were similar to those in euglycemic controls (144 ± 7 pg/ml).

Symptomatic insulin-induced hypoglycemia (Table 1, Fig. 1) did not stimulate glucagon secretion in any of the diabetics. However, in 15 controls comparable hypoglycemia caused plasma glucagon concentrations to rise to 472 ± 15 pg/ml ($P < .001$). Failure of the diabetics to respond to hypoglycemia was specific for the pancreatic alpha cell, since both growth hormone and cortisol responses of the diabetics were similar to those of the controls (Table 1), and symptoms of sympathetic discharge (sweating and tachycardia) in the diabetics were also similar to those in controls. Neither antecedent hyperglycemia nor a slower decline of plasma glucose explain the lack of glucagon response in the diabetics, since glucagon responses did occur in controls made comparably hyperglycemic by glucose infusion when hypoglycemia was induced at a similar slow rate (see Table 2).

Because it had been reported that in subjects with long-standing juvenile-type diabetes the pancreatic islets are hyalinized (*13*), glucagon responses to intravenous arginine (250 mg per kilogram per 25 minutes) were also studied to investigate the possibility that failure of the diabetics to respond to hypoglycemia might be due to an absence of pancreatic alpha cells. In all diabetics, including two with diabetes of over 42 years duration, plasma glucagon rose during arginine infusion (Fig. 1). Moreover, mean glucagon responses in diabetics exceeded those of controls ($P < .01$).

The present study thus demonstrates that there is no glucagon response to hypoglycemia in juvenile-type diabetes despite the fact that excessive glucagon responses to arginine occur. This abnormality does not appear to be secondary to insulin deficiency per se since all diabetics were on long-term insulin therapy. Moreover, the defect occurred with insulin present at concentrations sufficient to cause profound hypoglycemia.

Table 2. Effects of prior glucose infusion (5 to 6 mg kg^{-1} min^{-1} for 1 hour) on plasma glucose (mg/100 ml) and glucagon (pg/ml) responses to insulin-induced (0.15 unit/kg administered at time 0 and again 30 minutes later) hypoglycemia in three normal controls. Values are expressed as means ± standard errors of the means. "Basal" refers to the time (minutes) before glucose infusion.

Basal	Glucose infusion				Insulin ↙ 0	Insulin ↘ 30	Minutes after insulin administration					
− 70	− 60	− 45	− 30	− 15			45	60	75	90	105	120
						Glucose (mg/100 ml)						
85 ± 7	87 ± 5	177 ± 8	186 ± 22	182 ± 19	187 ± 21	113 ± 33	70 ± 29	44 ± 14	34 ± 6	31 ± 3	36 ± 4	45 ± 6
						Glucagon (pg/ml)						
150 ± 26	156 ± 13	130 ± 30	107 ± 19	58 ± 27	81 ± 13	193 ± 14	279 ± 18	356 ± 97	390 ± 90	427 ± 96	470 ± 117	569 ± 146

It is also unlikely that this abnormality resulted from long-standing insulin deficiency, since it was demonstrable as early as 2 weeks after the acute onset of diabetes in a 16-year-old subject.

In conclusion, plasma glucagon in the juvenile-type diabetic neither rises during hypoglycemia nor falls with hyperglycemia. Thus the diabetic pancreatic alpha cell appears to be insensitive to changes in the concentration of plasma glucose. Since there are data indicating diminished sensitivity to glucose for the diabetic beta cell (*14*), an intrinsic functional defect common to both alpha and beta pancreatic cells may be operative in juvenile diabetes mellitus. The site of such a lesion is speculative but may involve either loss of glucose recognition because of a defective glucose receptor or aberrant transmission of a perceived glucose signal due to a defective intracellular messenger system. The fact that glucagon responses to arginine still occur in diabetes would seem to exclude a common defect in the secretory apparatus. Current models for islet cell secretion which emphasize the role of a glucose receptor (*15*) and of Ca^{2+} (*16*) and cyclic adenosine monophosphate (*15*) as intracellular messengers are compatible with these possibilities.

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Sphaeroma terebrans: A Threat to the Mangroves of Southwestern Florida

Abstract. Sphaeroma terebrans, *a wood-boring isopod, is destroying the prop roots of red mangroves along the southwestern coast of Florida to such an extent that the Ten Thousand Islands and mangrove fringes of the mainland are steadily shrinking. Mangroves of the Florida Keys apparently are free of this wood borer.*

For an undetermined number of years, a wood-boring crustacean of the order Isopoda, *Sphaeroma terebrans* Bate (*S. destructor* Richardson), has been destroying the prop roots of the red mangroves, *Rhizophora mangle* L., along the southwestern coast of Florida (*1*). The attack of *Sphaeroma* is centered in the Ten Thousand Islands region in the midst of the greatest stand of mangroves in North America and one of the greatest in the world. The result is that the shoreline of the mainland and of the mangrove islands is gradually shrinking. An ecocatastrophe of serious magnitude to the seaward fringe of the Everglades National Park and adjacent areas appears to be in progress. *Sphaeroma* has already eliminated much of the protective outer edge of this great mangrove stand. It threatens to eliminate much more and to alter those features of the Everglades environment that depend upon the red mangrove barrier.

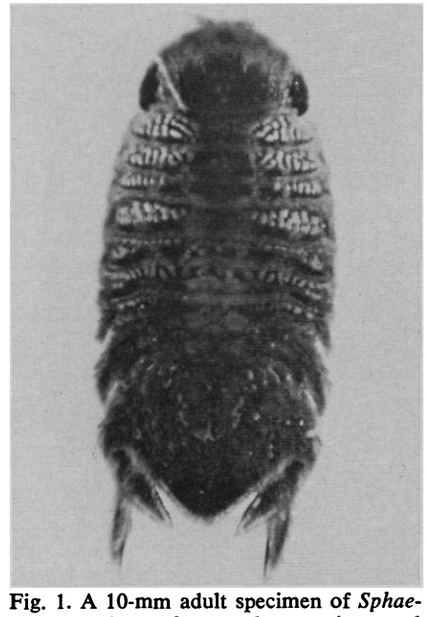

Fig. 1. A 10-mm adult specimen of *Sphaeroma terebrans* from a burrow in a red mangrove prop root. [Photograph by N. J. Eiseman]

About 70 years ago Richardson (*2*) reported that *Sphaeroma terebrans* (Fig. 1) had been observed boring into pier pilings at the mouth of the St. Johns River near Jacksonville. Apparently the only reported occurrence of this species on the Gulf coast of Florida (*3*) involved its capture in a plankton net.

In connection with a study of the benthic algal epiphytes of red mangrove prop roots throughout southern Florida, we discovered that a major portion of the trees in the Ten Thousand Islands area had their prop roots cut off at approximately the level of mean high water so that their normal benthic algal epiphytes were not present. Those prop roots that remained were perforated on their shaded (concave) side and exhibited all stages of destruction accompanied by secondary decomposition by bacteria and fungi. Inside these prop roots were numerous individuals, both juveniles and adults, of *Sphaeroma*.

We were able to demonstrate that this isopod is a rapid borer into living mangroves by placing pieces of uninfected prop roots and seedlings 20 to 30 cm long in a container of seawater with a few adult *Sphaeroma*. The isopods bored into the mangrove material within 24 hours and produced extensive hollowing within a few days.

Depredations of *Sphaeroma* are extensive in northern Florida Bay and in Whitewater Bay in the Cape Sable area, and are extremely severe among the Ten Thousand Islands north to Naples (Fig. 2). The isopod has infested red