Plasma Growth-Hormone Response to Glucocorticoids in Diabetics[1] (35002)

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The plasma human growth-hormone (HGH) response to hypoglycemia (1) is blunted by the daily administration of glucocorticoids (2). The effect on the HGH response of single-dose corticoid given every other day as recommended by Harter *et al.* (3) has not been studied extensively.

Despite the accepted diabetogenic potential of growth hormone, disagreement exists in the literature as to growth-hormone levels in diabetics. Glick *et al.* (4) and Hunter *et al.* (5) have noted no significant differences between diabetics and normals. Powell *et al.* (6) have indicated that the HGH levels in diabetics are inappropriately high when compared to the elevated blood glucose levels. Hunter *et al.* (5) noted in some diabetics, during induced hypoglycemia, a rise in HGH occurring at a higher glucose level than usual while Fatourechi *et al.* (7), using continuous monitoring, noted no such deviation.

The following studies are designed to show, in diabetics, the effects on HGH of glucocorticoid administered as a single dose every other day.

Methods. The subjects consisted of three groups; (1) nondiabetic subjects, (2) maturity-onset diabetics not requiring insulin

[1] Supported by U.S. Public Health Service Grant RR67.

[2] Clinical Trainee in Metabolism; supported by U.S. Public Health Service Grant AM5054.

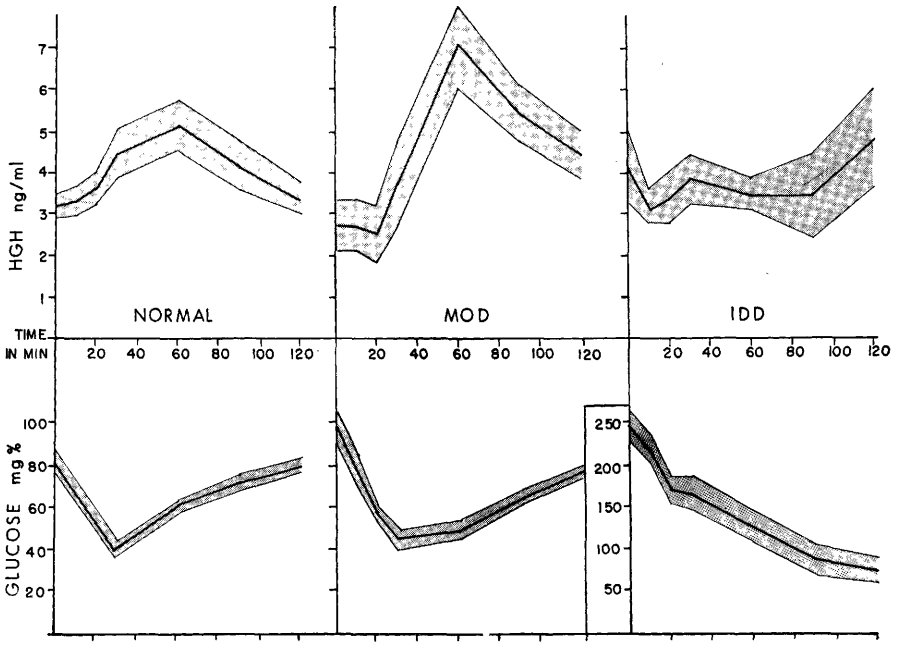

FIG. 1. Human growth-hormone and blood-glucose response to iv insulin is shown for normals, maturity-onset diabetics, and insulin-dependent diabetics. The mean values and standard error are shown.

(MOD), and (3) insulin-dependent diabetics (IDD).

Fasting HGH levels and insulin tolerance tests were carried out after an hour of bed rest. HGH was determined by the double-antibody radioimmunoassay (8). Test insulin was given intravenously in a dose of 0.1–0.3 U/kg. Blood was sampled for 120 min for HGH and glucose. Some of the subjects in Group 3 (IDD) were restudied after a period of 3 weeks of prednisone given in a single dose of 50–75 mg every other day by mouth.

HGH response to hypoglycemia. The effect of an insulin-tolerance test on the blood glucose and HGH is shown in Fig. 1 for the three groups. The difference in the glucose response occasioned by the higher fasting glucose in the diabetics is evident and renders interpretation of the HGH response difficult. In spite of similar glucose curves, the MOD Group showed a greater response in HGH than did the normals. The IDD Group showed a later response in HGH than the others, corresponding to the more gradual fall in the blood glucose.

Of importance was the striking difference in the HGH response of a group of normal, ambulatory young males compared to the hospitalized normals (Fig. 2). Although they were both kept at bed rest for 1 hr before the test and during the test, the fasting values were lower than the hospital normals, but rose to much higher levels during the test.

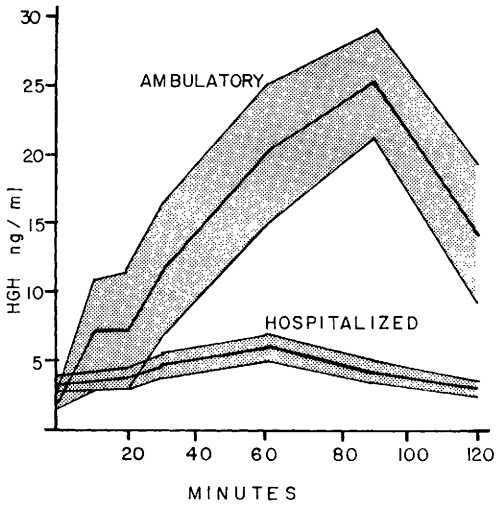

FIG. 2. Human growth-hormone response to hypoglycemia is shown for hospitalized and nonhospitalized normals after 1 hr of bed rest for each.

Effect of prednisone on HGH of diabetic patients. The effect of a single dose of 50–75 mg of prednisone given every other day was studied in the IDD Group. The fasting values for the group (Table I) were significantly lower ($p<.02$) after prednisone. A comparison of the effect on the insulin-tolerance test in the group is more difficult because of the variation in the timing of the hypoglycemic response and in the fasting glucose levels.

TABLE I. Fasting Plasma HGH (mμg/ml).

Case no.	Before prednisone	On prednisone
1	2.48	2.06
2	4.80	2.12
3	6.96	6.24
4	3.16	3.16
5	2.52	3.16
6	5.90	3.54
7	3.94	3.70
8	4.60	5.20
9	2.12	1.36
10	4.00	3.60
11	7.40	5.40
12	6.00	5.80
13	5.60	4.80
14	9.80	2.80
15	1.40	2.80
16	5.40	2.80
17	2.00	1.40
18	3.80	2.00
19	5.40	1.80
Mean	4.59	3.35
σm	.49	.11

In Table II are shown the comparison of the maximum level of the HGH during the test compared with the minimum value of the glucose. The mean minimum HGH values are significantly lower after prednisone ($p<.01$) in spite of lower mean glucose levels. Five of nine subjects showed a decreased HGH response in the face of a comparable or increased response in the glucose (Fig. 3).

Discussion. The striking difference in the HGH response to insulin between the hospitalized normals and the previously ambulatory normals presents difficulty in comparing

TABLE II. Plasma HGH Response to Insulin.

	Before treatment		Prednisone	
	Max[a] HGH	Min[b] gluc	Max HGH	Min gluc
	2.2	46	5.2	50
	8.0	47	3.8	180
	6.0	170	3.8	84
	7.0	181	2.8	26
	7.6	50	2.6	14
	9.8	40	3.0	28
	10.4	40	3.2	72
	2.2	45	1.6	53
	5.2	41	2.0	28
	5.2	119	8.0	35
Mean	7.06	94	4.00	64
σm	5.59	13	.47	15

[a] Max HGH is the highest plasma human growth-hormone level after insulin injection.

[b] Min gluc is the nadir of the blood glucose value after insulin.

the curves for the pathological group. Frantz and Rabkin (9) have previously emphasized the influence of exercise after awakening in elevating the fasting levels. Frohman *et al.* (10) noted marked instability for 30 min after activity. Thus, most studies emphasize the influence of exercise immediately prior to obtaining fasting samples for HGH (11–13) but results reported herein show clearly that, even though fasting HGH levels are stabilized by fasting and a period of 1 hr rest, the subsequent HGH response to hypoglycemia is exaggerated and influenced by the greater activity of the ambulatory group on the previous day. When comparable hospitalized normals are used as a control group, then the maturity-onset diabetics (MOD) show an increased HGH response to a similar degree of hypoglycemia. In testing for the HGH response to hypoglycemia, it is clear that merely resting subjects until comparable basal HGH levels are attained is not a sufficient control since subsequent responses to insulin are still influenced by the state of activity at a remote time.

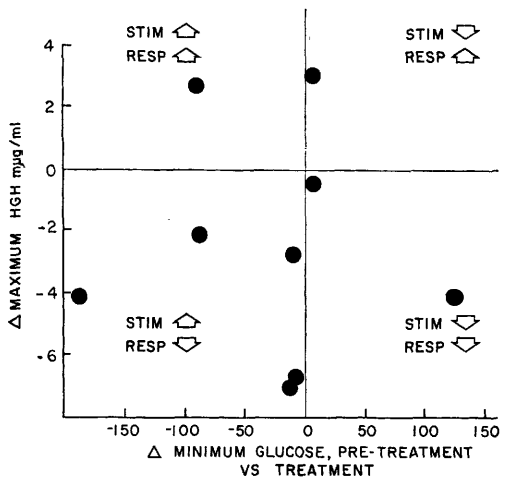

FIG. 3. The change in HGH and blood-glucose response to insulin is shown between pretreatment and treatment periods with alternating glucocorticoid therapy. The quadrants as shown by the arrows indicate the four possibilities of increased or decreased HGH response to increased or decreased hypoglycemic stimulus.

These results also show that a significant lowering of the fasting HGH levels and a blunting of the response to hypoglycemia can be induced in diabetics by a single dose of prednisone given every other day, although this is not to the extent reported for daily administration of glucocorticoids (2).

Summary. Plasma human growth-hormone (HGH) response to hypoglycemia was studied in normals, maturity-onset diabetics, and insulin-dependent diabetics. Interpretation of the response is valid only when equated to comparable levels of glucose. Hospitalized and nonhospitalized normals, although showing comparable basal HGH levels after 1 hr of rest, show significantly different responses to insulin. When hospitalized normals are used as controls, the maturity-onset diabetic group show a significantly higher peak response to a comparable degree of hypoglycemia.

Glucocorticoid administered as a single high dose every other day produces a significant lowering of the basal HGH levels and of the response to hypoglycemia in the insulin-dependent diabetic group.

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Received May 26, 1970. P.S.E.B.M., 1970, Vol. 135.