molecules to be packed into the subunit associated with the inner membrane or cristae. However, the possibility exists that the subunits are not all identical and that several combinations of a molecule of flavoprotein with a few molecules of cytochromes can occur.

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Hypoglycemia: A Potent Stimulus to Secretion of Growth Hormone

Abstract. *In normal subjects, hypoglycemia produces an abrupt and sustained rise in levels of human growth hormone in plasma. This effect is independent of insulin, glucagon, or epinephrine. Prolonged fasting is accompanied by a rise in the hormone level in plasma. Measurement of this hormone after induced hypoglycemia is a specific test for pituitary somatotropic function.*

The physiologic role of endogenous growth hormone in vertebrate carbohydrate metabolism has been deduced from indirect studies (*1*). Measurement of this hormone in plasma by bioassay and immunoassay techniques has been impeded by interfering substances in plasma and by lack of a sensitive method. With a new immunoassay method employing I^{131}-labeled human growth hormone (*2*), which is capable of detecting 0.25 mμg/ml of human growth hormone in unextracted plasma, acute physiologic changes in hormone levels have been demonstrated for the first time.

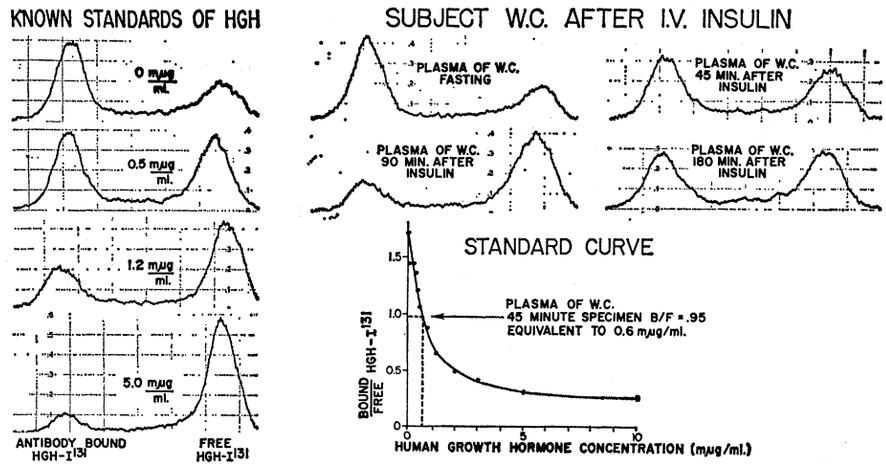

Fig. 1. Antibody-bound and free I^{131}-labeled human growth hormone (HGH-I^{131}) are separated by hydrodynamic flow chromatography on strips of filter paper and the strips are scanned for radioactivity. Shown are representative scans from known standard solutions (left) and from plasma samples of a normal subject (W.C.) before, during, and after insulin-induced hypoglycemia (upper right). All plasma samples were assayed at 1:10 dilution. Hormone values given in text and in subsequent figures are for undiluted plasma.

We measured endogenous human growth hormone in plasma by adapting, with modifications, methods previously employed for the immunoassay of plasma insulin (*3*). This method exploits the ability of purified and of endogenous growth hormone in plasma to inhibit competitively the binding of I^{131}-labeled growth hormone to growth hormone antibodies. Thus at fixed concentrations of antibody and labeled hormone, the ratio (B:F) of labeled hormone bound to the antibody (B) to unbound labeled hormone (F) decreases progressively with increasing concentration of unlabeled hormone. The concentration of endogenous hormone in a plasma sample is determined by comparison of the B:F ratio obtained from a solution containing the plasma with the B:F ratios obtained from standard solutions containing known concentrations of hormone (Fig. 1). No hormone was detected in plasma from several non-primate species or from totally hypophysectomized human subjects. Purified hormone, added to plasma, was recovered quantitatively.

In six normal subjects who were fasting, hypoglycemia, induced by insulin (0.1 unit/kg body weight, intravenously), was followed by an increase of at least 500 percent in plasma hormone concentration (Figs. 1 and 2) over fasting levels (0 to 3 mμg/ml) to values usually found in random plasma samples from acromegalic subjects (> 10.0 mμg/ml). Levels of hormone increased shortly after the onset of hypoglycemia, reached a peak about 30 minutes later, and persisted above fasting levels for several hours after the blood glucose level had returned to nor-

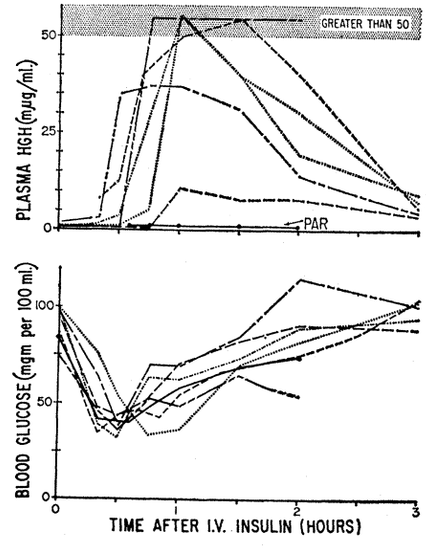

Fig. 2. Plasma human growth hormone (HGH) and blood glucose concentrations after insulin administered intravenously. (PAR, a hypophysectomized patient; other patients, normal.)

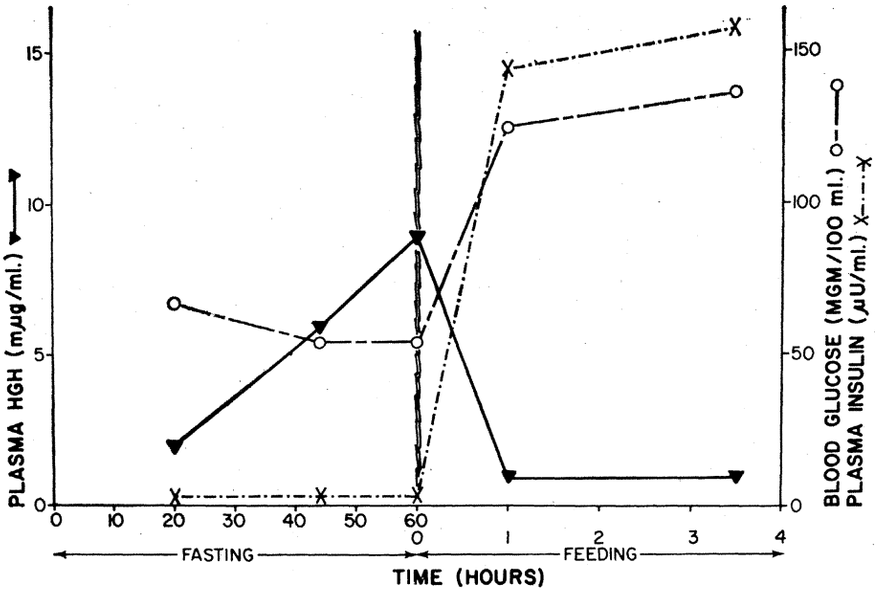

Fig. 3. Blood glucose, plasma insulin, and plasma human growth hormone (HGH) in a normal subject during prolonged fasting and subsequent feeding.

mal. When the hypoglycemia induced with insulin was terminated shortly after onset by the administration of glucose, or when hypoglycemia was prevented by simultaneous administration of glucose and insulin, the plasma hormone remained at the fasting level.

In two patients with tumors (reticulum-cell sarcoma and fibroxanthoma) associated with chronic hypoglycemia, multiple specimens of plasma showed glucose concentrations below 40 mg/100 ml and very high hormone levels (30 to 50 mμg/ml), although endogenous plasma insulin concentrations, measured by immunoassay (see *3*), were lower than normal fasting levels.

In two fasting normal subjects the level of the hormone in plasma did not rise after parenteral administration of glucagon or epinephrine in doses sufficient to produce significant hyperglycemia.

Insulin (0.05 unit/kg body weight) was administered intravenously to a patient totally hypophysectomized for carcinoma of the breast and maintained on replacement doses of adrenal steroids and thyroid hormone. With this dose of insulin, as with the higher dose in normal subjects, blood glucose fell rapidly to less than half the fasting level, but growth hormone was not detected in the plasma (Fig. 2, PAR).

Prolonged fasting (2½ days) of a normal subject was accompanied by a progressive rise in the level of the hormone in plasma, although the level of blood glucose fell only slightly, and the level of endogenous insulin in plasma was zero. Feeding was followed by rapid increases in the levels of blood glucose and plasma insulin and a fall in the plasma growth hormone (Fig. 3).

Thus, hypoglycemia is a potent stimulus to the release of growth hormone. This release is not mediated by insulin, glucagon, or epinephrine. Prolonged fasting also raises the growth hormone level, and the administration of glucose may result in decreased levels of the hormone in plasma. This is the first report of acute changes in endogenous human growth hormone in plasma in response to physiologic stimuli.

The repeated administration of growth hormone produces glucose intolerance (*4*). Appreciation that hypoglycemia and fasting markedly stimulate release of growth hormone may contribute significantly to the understanding of the following clinical phenomena: (i) the temporary glucose intolerance of poorly nourished or fasting subjects ("starvation diabetes"), (ii) the insulin resistance and impaired glucose tolerance of diabetic patients after attacks of insulin hypoglycemia ("Somogyi effect"), (iii) the impaired glucose tolerance of patients with chronic hypoglycemia secondary to functioning islet-cell adenomata.

Endogenous plasma hormone concentration may be properly interpreted only in relation to the subject's blood sugar, recent dietary intake, and perhaps other, as yet undefined, influences.

Measurement of plasma hormone level after hypoglycemia appears to be a specific, sensitive, and direct test of pituitary somatotropic function, which is useful in the differential diagnosis of pituitary disease in the adult. This test may also be valuable in distinguishing pituitary dwarfism from other conditions of retarded growth in children and thereby provide a guide for therapeutic administration of human growth hormone.

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Implanted Electrodes: Cable Coupler for Elimination of Movement Artifact

Abstract. *The wires in the recording cable are connected to stainless-steel tubes supported by a ball bearing. The tips of the tubes rotate freely in mercury-filled grooves connected to the recorder through stainless-steel screws. No attenuation or distortion of the signal appears on records obtained through the coupler.*

A frequent problem encountered in electrophysiological studies of brain-wave activity in unrestrained conscious animals is one of twisted and kinked recording cables. This results in electrical artifacts, rapid cable deterioration, and restriction of the animal. The device shown in Fig. 1 has proved to be a satisfactory solution to the problem.

It allows the recording cable to turn freely as the animal moves and, at