(HGH). L. BAKER, A. I. WINEGRAD, H. L. VALLET, R. S. CLEMENTS, G. MORROW and A. M. BONGIOVANNI. *Univ. of Pennsylvania Sch. of Med., Philadelphia, Pa.*

A 9½ year old girl has had severe reactive hypoglycemia since age 11 months. No evidence of a pancreatic adenoma was found on laparotomy. On recent re-evaluation, abnormalities of CHO metabolism were documented in both the fed and fasting states. Oral GTT consistently demonstrates a slightly elevated fasting level, a 2 hour value in excess of 140 mg.%, and a 5 hour value less than 40 mg.%. Plasma insulin concentration peaked at 1½ to 3 hours (50–80 μU/ml) but are still elevated at the 5th hour. This pattern was unaltered by therapy with Diazoxide or Tolbutamide. Symptomatic hypoglycemia consistently develops on prolonged fasting (20–24 hours). The plasma FFA, ketone and amino acids fail to show an appropriate response to fasting. Fasting hypoglycemia is rapidly corrected by the administration of glycerol, a substrate for gluconeogenesis. Despite normal growth, plasma HGH was undetectable following spontaneous hypoglycemia or exercise, or during sleep. Maximal stimulation with sequential insulin-arginine tolerance tests gave a subnormal response (5 mμg/ml). Acute HGH therapy prevented fasting hypoglycemia, and plasma FFA and ketones rose appropriately. Reactive hypoglycemia was also corrected. This appears to be a new hypoglycemic syndrome.

Direct "adrenergic" activity of diazoxide on insulin release. IAN M. BURR, ERROL B. MARLISS, and ALBERT E. RENOLD (Intr. by David Karzon). *Vanderbilt Univ. Med. Sch., Nashville, Tenn., and Inst. de Biochim. Clin., Geneva, Switzerland.*

The direct effects of the hyperglycemic agent diazoxide (D), on dynamic insulin (IRI) release from rat pancreas in vitro have been compared with those of epinephrine (E). Like E, D produces dose dependent suppression of the primary (I) and secondary (II) phases of glucose (G) induced IRI release, an effect partly reversed by α adrenergic blockade. Conversely, continuous stimulation with 10 μg/ml + 20 μg/ml phentolamine produces a biphasic pattern of IRI release similar to that observed with β adrenergic stimulation with l-isopropylnorepinephrine, either agent alone being ineffective. As for E, prestimulation with low doses of D selectively enhances subsequent G induced I, an effect abolished by β adrenergic blockade during prestim. In contrast to E, prestim. with higher concentrations of D enhances both phases of G induced IRI release, an effect which is not abolished by α adren. blockade during prestim. Conclusions: (a) D can stimulate both α and β adrenergic receptor activity in B cells which may explain both the direct inhibition of IRI release by D and the apparently paradoxical enhancement of IRI release on cessation of D therapy. (b) Some effects of D are not realized through direct effects on adrenergic receptors.

Immunoassay of glucagon-like activity in infants and children. D. Y. MURTHY and ELEANOR COLLE. *Montreal Children's Hosp.-McGill Univ. Research Inst., Montreal, Que., Can.*

Glucagon levels were assayed with a guinea pig antisera which cross reacts minimally with an extract of dog gut. Column chromatography of pools of plasma revealed three peaks. Peak I, which behaved like gut reacting glucagon-like activity accounted for less than 20% of glucagon-like activity in the fasting and post-arginine infusion pools. Peak II is the major peak and behaves like pancreatic glucagon on dilution. Peak III reveals minor differences on dilutional studies. With this antisera, the mean level in normal fasting prepubertal children was 669 ± 62 pg/ml and in fasting adolescent diabetic children in good control 333 ± 46 pg/ml. Following intravenous arginine infusion a 2 fold or greater rise was seen in glucagon-like activity in 5 children without abnormalities in carbohydrate tolerance, in 5 newly diagnosed diabetics, in 5 children with asymptomatic hyperglycemia, in 5 children with small stature secondary to intrauterine growth retardation, and in 1 child with growth hormone deficiency. Two children treated with chlorpropamide for 1 year for diabetes insipidus also had normal rises despite impaired insulin release. Values for glucagon-like activity were elevated in cord blood (mean 1288 ± 146 pg/ml) and in plasma from normal newborn infants before feeding (mean 1412 ± 55 pg/ml). Three of five infants of diabetic mothers and three of six infants with blood group incompatibility had levels greater than 2000 pg/ml.

Hormonal aspects of post-hypoglycemic hyperglycemia (Somogyi effect) in diabetic children. ERIKA BRUCK and MARGARET MACGILLIVRAY. *State Univ. of N. Y. at Buffalo, Sch. of Med., Children's Hosp. of Buffalo, Buffalo, N. Y.*

The causes of hyperglycemia and acetonuria which may alternate with hypoglycemia in diabetic children are poorly understood. To evaluate the hormonal basis of the "Somogyi effect" in 3 "brittle" diabetic children, glucose, growth hormone (HGH) and cortisol levels in blood were measured hourly or half-hourly, and urinary catecholamine excretion in 2-hourly collections, for several 24–48 hour periods. Profound hypoglycemia (7–40 mg%) alternating with prolonged hyperglycemia was demonstrated at unpredictable times, even though fasting glucose was normal or elevated. HGH levels increased sharply, sometimes to as much as 30–75 mμg/ml, with hypoglycemia or following every sharp fall in glucose, even when the latter remained in the hyperglycemic range. These peaks of HGH were usually followed by marked hyperglycemia. Plasma cortisol levels varied erratically without consistent relationship to glucose levels. Rises in catecholamine excretion (to 4–12 μg/hr) occurred following hypoglycemia and also independently of it, but did not always cause elevation of glucose. With gradual reduction of insulin dosage, the control of the diabetes improved, and in one patient who was profoundly stuporous, the mental state improved dramatically. These studies emphasize the importance of determining blood sugar concentration at frequent intervals since hypoglycemia may go unrecognized for years if the standard sampling times are adhered to. The hormonal data support the concept that growth hormone release in response to hypoglycemia in the diabetic is an important factor in producing hyperglycemia and insulin resistance.

Generalized lipodystrophy (lipoatrophic diabetes): Evidence for abnormal pituitary function. C. CHARLTON MABRY and DOROTHY R. HOLLINGSWORTH. *Univ. of Kentucky, Lexington, Ky.*

Long term observations and studies on two unrelated children with generalized lipodystrophy suggest a pituitary-endrocrine disorder with abnormal melanotropic growth-hormone-like secretion as the probable cause. Our patients have the advanced characteristics of generalized lipodystrophy which include loss of all body fat, skeletal and muscle overgrowth, hepatomegaly due to neutral fat infiltration, insulin resistant hyperglycemia, hyperlipemia, hyperpigmentation and greatly elevated levels of immunoreactive insulin.

We subjected a 13-year-old girl with generalized lipodystrophy to total surgical hypophysectomy. The pituitary gland was nor-