History of Congenital Hyperinsulinism: Treatment and Research

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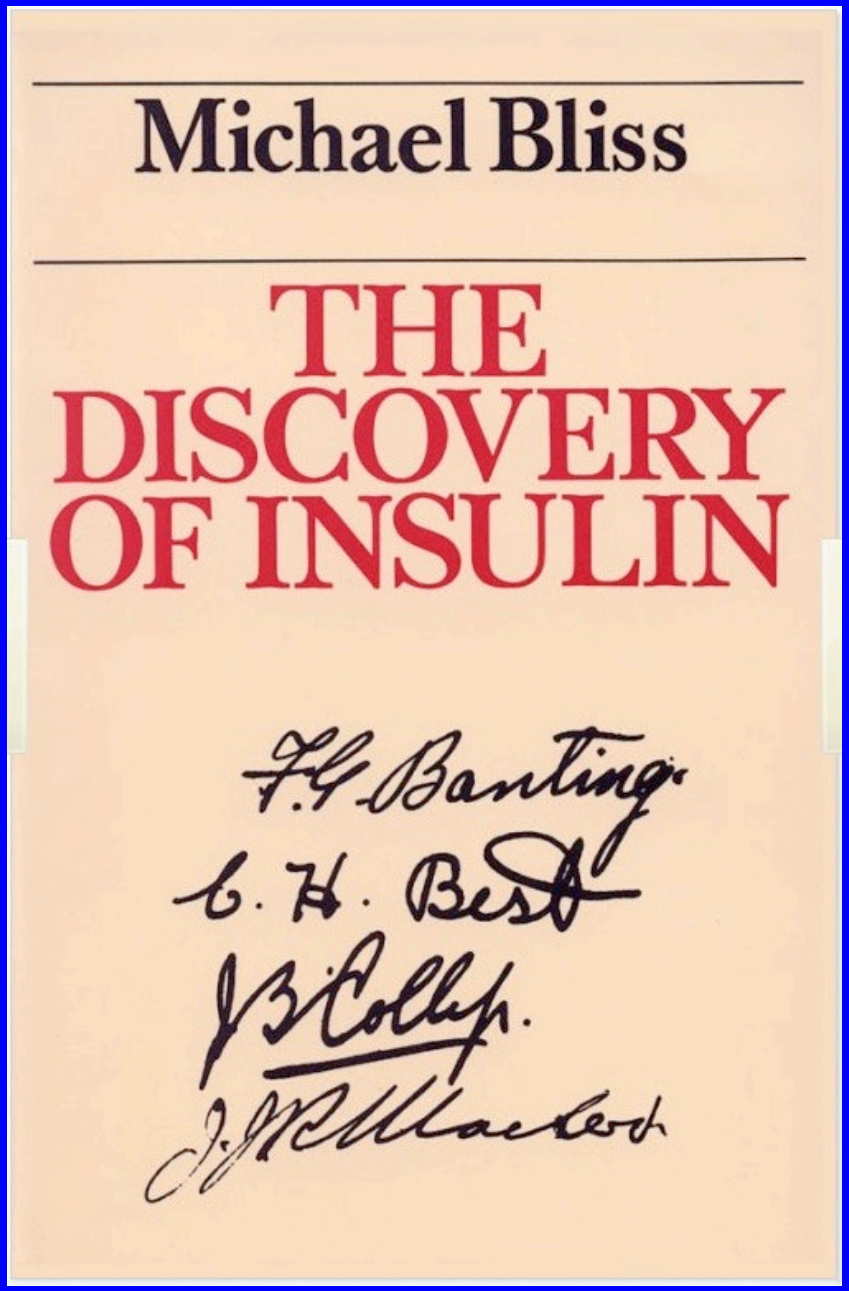
100 Years Ago

Hypoglycemia First Discovered

January, 1922:
one of the first diabetes patients treated with insulin starts "climbing the walls" …. symptoms caused by low blood sugar
(Dr. JB Collip)



75 Years Ago

Discovery of "Idiopathic Hypoglycemia of Infancy"

Fig. 3.—Photograph of J. G., aged 6 years, and B. G., aged 13 months. Taken two months after beginning of corticotropin therapy. Pancreatic resection scars visible.

1. Risk of irreparable brain damage
   a) Delayed diagnosis
   b) Inadequate (early) therapy
2. Cause unknown!
3. Possibly Genetic?
4. Treatment options:
   Pancreatectomy or Cortisone

A. M. A.
American Journal of Diseases of Children
VOLUME 87 APRIL 1954 NUMBER 4

IDIOPATHIC SPONTANEOUSLY OCCURRING HYPOGLYCEMIA IN INFANTS

Clinical Significance of Problem and Treatment

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IN KEEPING with tradition concerning the choice of subject for a presidential address, I originally prepared a semiphilosophical dissertation for this occasion. Now, I must apologize to you for the sin of "deviation," because I suddenly decided only a few days ago to scrap that laboriously composed oration and substitute a résumé of some observations that my associates and I have made during the past few years in dealing with the clinical problem of spontaneous hypoglycemia in infants.

My seemingly impulsive decision to change to the latter title was the direct result of my seeing the seventh young child, among a series of cases recently examined in our clinic, who had suffered irreparable brain damage from severe hypoglycemia. Three of these were children who were victims of the misuse of insulin in the treatment of diabetes mellitus. The remaining four were examples of severe spontaneous hypoglycemia in infants who were victims of delayed diagnosis and inadequate early therapy.

The tragedy of permanent brain damage resulting from therapeutically induced hypoglycemia * is too well known and the precautions necessary for its avoidance are too obvious to justify special consideration at this time. The situation is quite different, however, in regard to the special group of infants with spontaneous hypoglycemia which I have felt compelled to discuss here today. There have been well-documented cases of brain damage associated with spontaneous hypoglycemia.†

65 Years Ago

Discovery of Insulin Radioimmunoassay

First demonstration that plasma insulin levels are elevated in infants with "Idiopathic Hypoglycemia of Infancy".

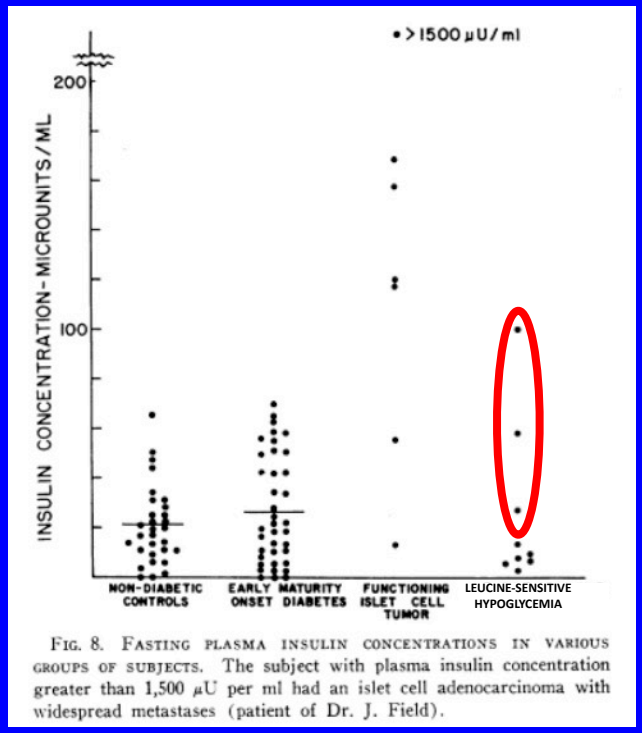
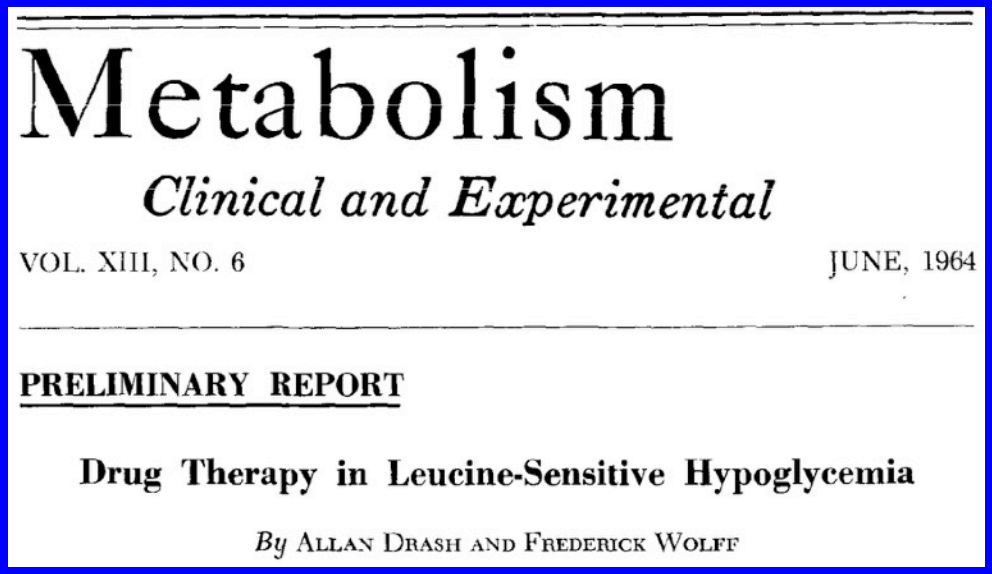


FIG. 8. FASTING PLASMA INSULIN CONCENTRATIONS IN VARIOUS GROUPS OF SUBJECTS. The subject with plasma insulin concentration greater than 1,500 μU per ml had an islet cell adenocarcinoma with widespread metastases (patient of Dr. J. Field).

(Berson & Yalow, J Clin Invest, 1960)

60 Years Ago

Discovery of diazoxide (Proglycem)
as a treatment for hyperinsulinism



Metabolism
Clinical and Experimental
VOL. XIII, NO. 6 JUNE, 1964

PRELIMINARY REPORT

Drug Therapy in Leucine-Sensitive Hypoglycemia

By ALLAN DRASH AND FREDERICK WOLFF

50 Years Ago

"Idiopathic Hypoglycemia of Infancy" becomes "Congenital Hyperinsulinism"

(CHI or HI for short)

Other names (*best forgotten*)

- **Idiopathic hypoglycemia**
- **Leucine-sensitive hypoglycemia**
- **PHHI (Persistent Hyperinsulinemic Hypoglycemia of Infancy)**
- **Nesidioblastosis**

Hyperinsulinism in Infants and Children: Diagnosis and Therapy*

CHARLES A. STANLEY, M.D., AND LESTER BAKER, M.D.

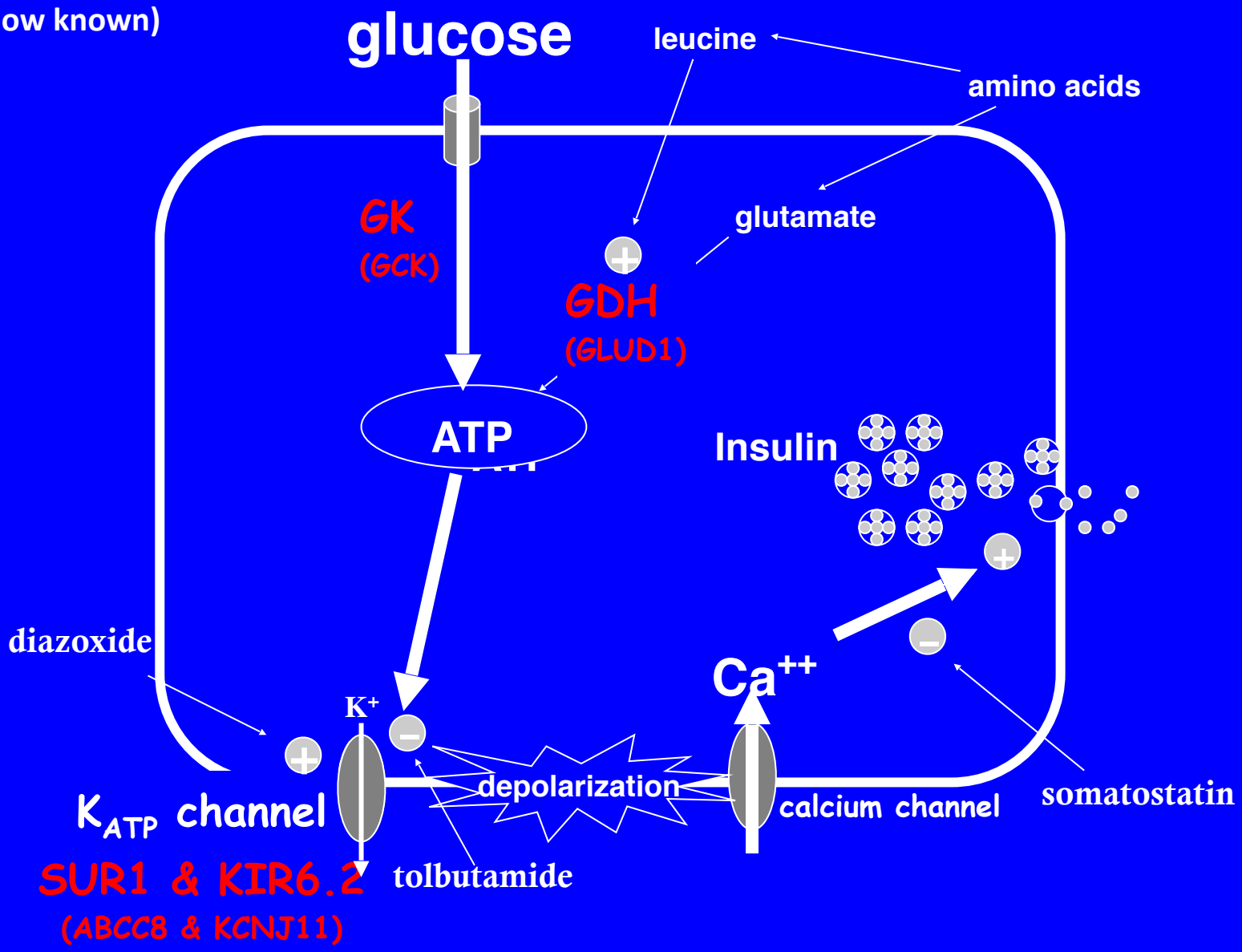
Division of Endocrinology, Children's Hospital of Philadelphia, and the Department of Pediatrics, University of Pennsylvania School of Medicine

Adv Pediatr 1976

30 Years Ago

Genetic Causes of HI

(39 genes now known)



25 Years Ago

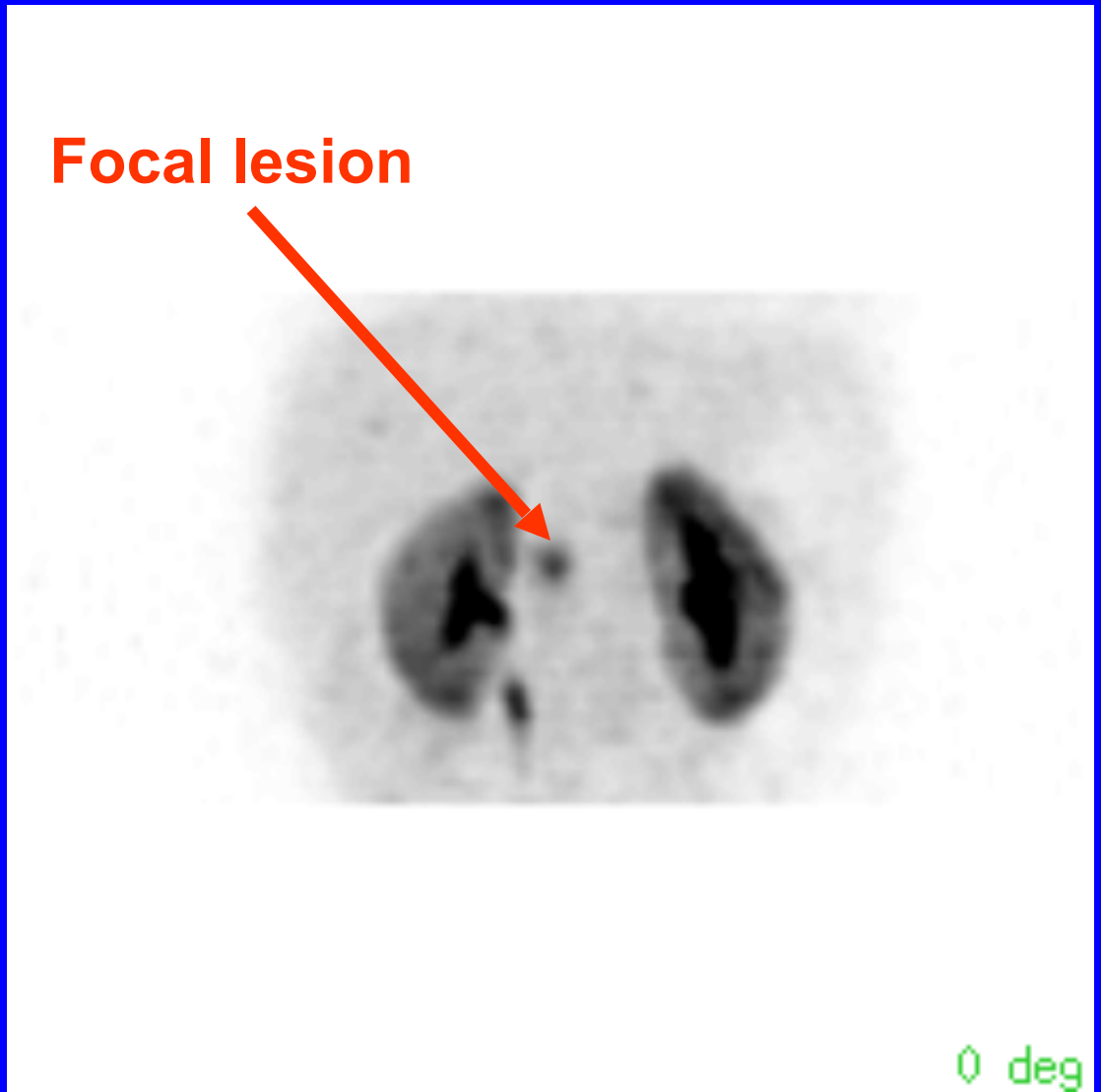
Genetic Testing

Types of Congenital HI

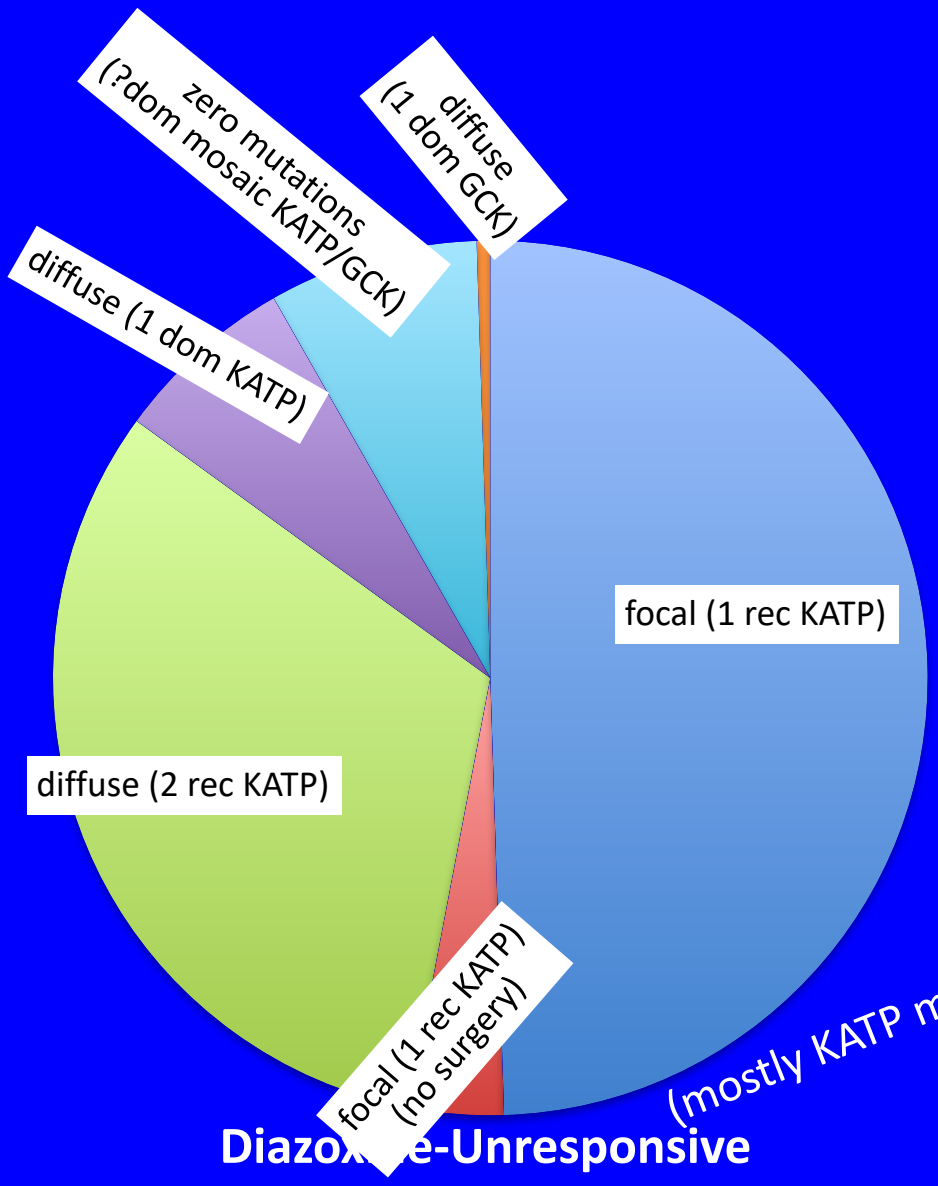
1. Genetic:
   - Diffuse vs. Focal
   - Recessive vs. Dominant Inheritance
   - Sporadic

2. Non-Genetic:
   - Transient Neonatal (“perinatal stress HI”)

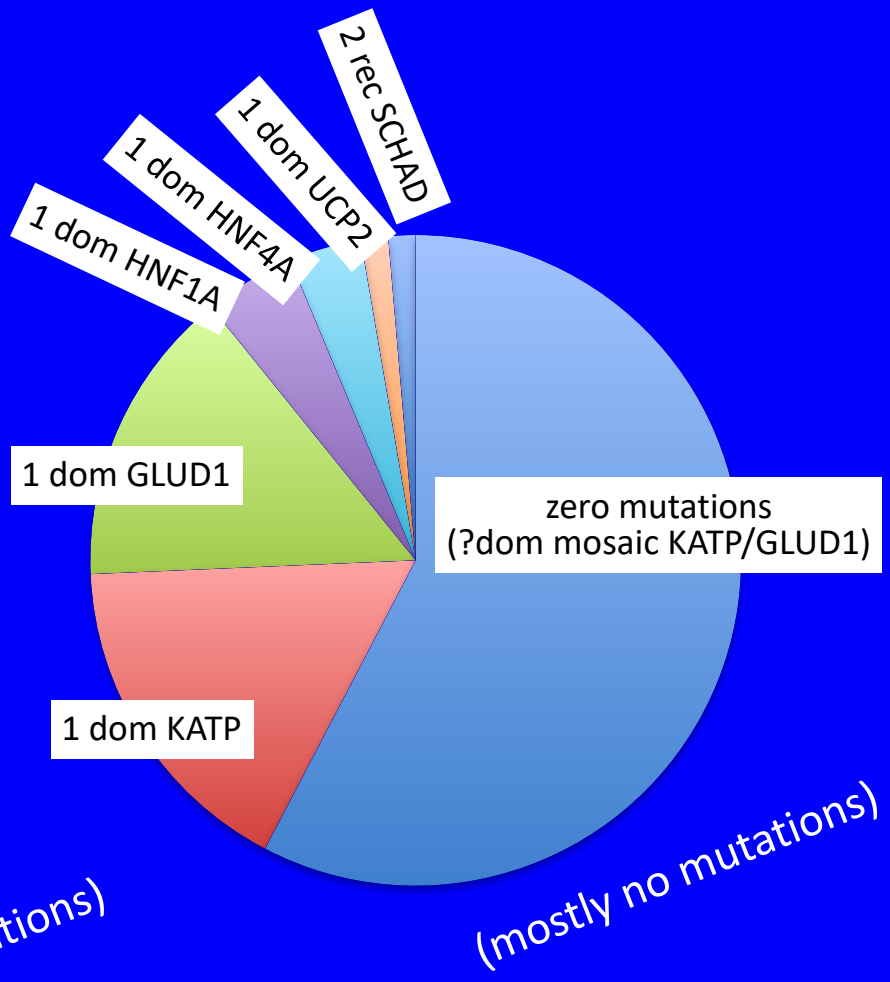
^{18}F-DOPA PET scan localization of focal adenomatosis HI lesion, 5 wk old neonate



Mutations in 705 Children with Congenital HI (1997-2014)



Diazoxide-Unresponsive (434)



Diazoxide-Responsive (219)

Now

Current Treatments for Hyperinsulinism

1. Surgery
   a) Sub-total pancreatectomy (1950s onward)
   b) Curative excision of focal lesion (1990s onward)

2. Medical
   a) Diazoxide (1964 onward)
   b) Octreotide (1980s onward)

The Future

Wish List

1) New and better HI treatment(s)
   (5+ potential therapies for HI now in clinical trails)

2) Universal newborn screening to detect HI earlier and prevent brain injury

3) Universal entry of all HI children in the HI Global Registry (HIGR)

The Children's Hospital *of* Philadelphia®

CONGENITAL
HYPERINSULINISM CENTER

end