Cook Children’s HI Center

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Cook Children’s HI Center

- Formed in Oct 2010
  - Mission: To provide excellence in medical care to patients with HI in the Southern United States, using a family centered care model.
  - Located in Fort Worth Texas
  - Cook Children’s Medical Center is a 400 bed not for profit stand alone children’s hospital
HI Team Physicians

- Pediatric endocrinologist
- Pancreatic surgeon
- Histopathologist
- Neonatologist
- Neurologist
- Gastroenterologist
HI team support staff

- HI Nurse
- Social Worker
- Psychologist
- Nutritionists
- Speech and language therapists
- Feeding therapists
- Child life specialist
- Family advisory council and support group
Clinical activities

• In patient service is located in our unique 100 private bed room NICU with special twin, triplet and quadruplet rooms

• Surgeries are performed in our main campus.

• Outpatient clinic is located in our new Endocrinology department but we also see patients in satellite clinics nearer home for the more routine interim visits.
Scholarly activity

• Education of physicians
  – Talks in all the major children’s hospital in Texas
  – Talks in Ca, NM, La, Mi, Fl, Ga
  – Talks to PESTOLA

• Book Chapters

• Presentations at the major and local meetings
Research

• Several IRB approved protocols
  – HI Database
  – Neurological outcomes study
  – Genotype – Phenotype study
  – PET Study under review
  – PET IND application
Advocacy

- Work with “HI Kids” to improve access to quality HI care for children in Texas and to increase awareness of this disease in the medical community
- Work with “CHI”
- Work with individual families who are not in centers of excellence to help them through the process of dealing with physicians not familiar with this disease
Surgeries

- Operate on patients with known diffuse disease
  - 2 mutations and AD HI
- Patients whose insurance (primarily medicaid) is not accepted by or will not allow transfer to CHOP
- Families who can not make the trip to CHOP
• Worked with the local neonatologists to implement policies for fasting all neonates who have hypoglycemia lasting > 48 hours or requiring IV fluids to resolve.
  – We are seeing approximately 15-20 patients a year with THI just in our local catchment area
Genetics 101

• Objectives
  – Explain why our children have HI
  – Explain why it is not your fault
  – Explain why it may not be a good idea for your children to date other children in HI clinics
Why are we all different

• Nearly everyone is different
• We have characteristics similar to our families
• These characteristics may be passed from generation to generation
• Genetic information
• Chromosomes
• Genes
• DNA
What are genes

• Genes carry information
• Some traits we have are carried on one gene
  – Red Hair
• Some traits need many genes
  – Height
• Some diseases are caused by many genes
  – Down Syndrome
How do genes cause disease

- Genes primarily make proteins
- Proteins have important functions
  - KATP channel made of 2 proteins
  - Responsible for making sure the right amount of insulin is released into the blood by the beta cell
  - If underactive or not there
    - Hyperinsulinism
Hyperinsulinism

- The secretion of insulin is very complex and there are many steps involved.
- Each step is regulated by proteins.
- Each protein has the potential to be made incorrectly.
- Thus there are many forms of hyperinsulinism.
- Each type of HI will cause different problems and require different treatments.
Different forms of HI

- There are 4 common forms of HI known, 4 more rare types and many more not yet characterized.
- The beta cells in KATP HI patients can not tell if the glucose is low or high so they just keep making insulin.
- The beta cells in GDH HI make insulin when you eat protein as well as sugar.
- The beta cells in Exercise induced HI make insulin when you exercise as well as when you eat sugar.
So why does my child have HI

• Because they have a broken gene involved in the secretion of insulin

• Genes are broken either by:
  – A mutation in the DNA: $GATT \rightarrow GATA$
  – A deletion of some DNA
    • $GATTAGTA \rightarrow GATA$

• Broken genes
  – May be inherited
  – May be acquired
So why is it not my fault

- We can not control our own genes
- There are different ways we pass mutations to our children
  - From generation to generation
    - Dominant mutations
  - No one in the family has the disease then one of the children has it
    - Recessive mutation
    - Spontaneous dominant mutation
Mendelian genetics

• A scientific description of how hereditary characteristics are passed to offspring
  – Dominant and recessive factors
• Each child has two copies of each gene
  – One from mother and one from father
• Most diseases require the child to have two broken genes
  – Neither mother nor father have the disease because they only have one broken gene
  – The parents are called “carriers”
Example of recessive disease

Mother

Hh

H

Hh

HH

Hh

Father

Hh

H

hh

Hh

Hh

Hh
Example of dominant disease
So what about Focal HI

- Focal HI which is caused by recessive mutations in ABCC8
- Only father carries mutation so the child looks like a “carrier”
- BUT
  - In the pancreas, during development of the early fetus, one cell loses the mother's ABCC8 good gene and only has the father's broken gene.
  - These cells grow to become a focal lesion
Focal $K_{ATP}$ HI: Two hit hypothesis of Knudson

(Maternal LOH & Paternal KATP Defect)
So why should my kids not date the other kids in the HI clinic (Statistically speaking)

- In the population 1 in every 100 people carries a gene for HI
  - The chances of marrying another carrier is 1:10,000 and the chances of a having a baby with Diffuse CHI is 1:40,000
  - If you have HI then the chances are 1:100 of marrying a carrier and 1:200 of having an affected child
- In the HI clinic 1:2 siblings will be a carrier and so the chances of marrying a carrier is 1:2 and the chances of having an affected child is 1:2
- If 2 affected kids marry there is 100% chance that the kids will be affected.
Conclusions

- Hyperinsulinism is a genetic disease
- There are many forms of HI
- There are many ways to inherit HI
- Each form has its own complexities
- The disease is not wonderful but our kids are