

2015 Alabama Newborn Screening Conference



Marriott Hotel and Conference Center
Prattville, Alabama
Friday, September 18, 2015

The Origin of Newborn Screening

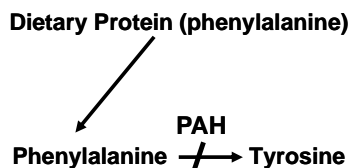
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Phenylketonuria (PKU)

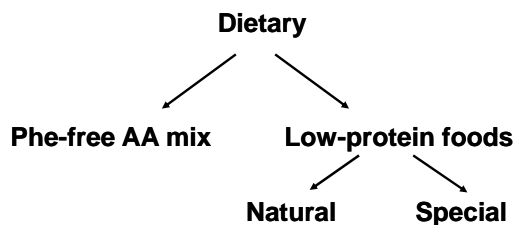
Clinical Phenotype

- Intellectual Disability (Moderate - Severe)
- Autism / Autism Spectrum
- Hyperactivity (often severe)
- Seizures
- Eczema

PKU



Treatment of PKU



1955 - 1962


- Several investigators discovered that newborn initiation of diet prevented ID in PKU

EARLY TREATED PKU

- Retarded brother
- Sister identified by newborn testing
- Early dietary treatment
- Good outcome


Newborn Screening

- Guthrie specimen
 - Heel stick
 - Filter paper
 - Dried blood
- Transport to Central Lab



Guthrie Test

- Bacterial assay
- Growth zone




Opposition to Mandatory Newborn Screening

- American Academy of Pediatrics, 1964
 - “The enthusiasts...without taking into account parents...unwilling or unable to maintain dietary treatment. Over-rigidity of dietary management has led to early death...Unrealistic claims for normalcy...have led to frustration and discouragement on the part of pediatricians and parents.”

Maple Syrup Urine Disease (MSUD)

- Neonatal disease
- Intellectual disability
- Ketoacidosis
- Maple syrup odor (ear)
- Increased leucine




Maple Syrup Urine Disease

Leucine	Isoleucine	Valine
↕	↕	↕
α-ketoisocaproic acid	α-keto-β-methylvaleric acid	α-ketoisovaleric acid
BCKA ↓		
Isovaleryl-CoA	α-methylbutyryl-CoA	Isobutyryl-CoA

BCKA= branched chain α-ketoacid dehydrogenase complex

Homocystinuria (CBS DEF)

- Intellectual disability
- Ectopia lentis
- Skeletal abnormalities
- Thromboembolism
- Increased methionine



Congenital Hypothyroidism

- Intellectual disability
- Coarse facies
- Hypotonia
- Growth delay
- Reduced thyroxine



Sickle Cell Disease

- * Bacterial infections, often fatal
- Hemolytic anemia
- Splenomegaly
- Bone disease
- Stroke

Glutaric Acidemia I

- Macrocephaly
- Encephalopathic episodes
- Dystonia



Tandem Mass Spectrometry (MS/MS)

- Single assay for multiple disorders
- Wide range
- Pattern analysis
- Increased efficiency



NBS in the U.S. < 2006

- Lack of uniformity
 - Some states 5 disorders
 - Other states 12 disorders
 - Several states 25-30+ disorders
- Baby in one state detected; baby in an adjoining state not detected

Cystic Fibrosis

- Chronic pulmonary disease
- Pancreatic insufficiency
- Positive sweat test
- High morbidity
- Eventual early death

Newborn Screening Advisory Committees

- **Pediatricians**
- **Biochemical (metabolic) geneticists**
- **Endocrinologists**
- **Public health personnel**
- **Ethicists**
- **Lawyers**

Family Support Organizations

- **National PKU Alliance**
- **National Urea Cycle Disorders Foundation**
- **Organic Acidemia Foundation**
- **Cystic Fibrosis Foundation**
- **Hunter's Hope Foundation**
- **FOD Family Support Group**

Faculty

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