Newborn Screening
What Do You Do With the Results?

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Disclosure Statement
• I have no actual or potential conflict of interest in relation to this program.

Objectives
– Describe the rationale behind newborn screening for selected disorders.
– List the number of disorders screened for in Missouri and Kansas
– Explain how results are relayed to the physician and what steps need to be taken for low, moderate and high risk results
– Identify additional screens that are being mandated and how they might have an impact on the practice of medicine

Newborn screening
• Newborn screening is the process of testing newborn babies for treatable genetic, endocrinologic, metabolic and hematologic diseases

History
• Robert Guthrie
  – Pioneered early screening
  – Phenylketonuria (late 1960s)
  – Blood spot
  – Bacterial inhibition test
• Congenital hypothyroidism
  – Second test
  – Added 1970s
• Edwin Naylor and others
  – Tandem mass spectrometry 1990s
  – Large expansion of potentially detectable congenital metabolic diseases that affect blood levels of organic acids.
• Additional tests added to many programs over last two decades.
• Newborn screening
  – adopted by most countries around the world
  – lots of screened diseases vary widely

Wilson and Jungner Criteria
1. The condition should be an important health problem.
2. There should be an accepted treatment for patients with recognized diseases
3. Facilities for diagnosis and treatment should be available
4. There should be a recognizable latent or early symptomatic stage
5. There should be a suitable test or examination
6. The test should be acceptable to the population
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process, not just a ‘once and for all’ project.


Robert Guthrie

Blood spot

Tandem mass spectrometry

Blood sample
Pros and Cons

- "Expansion of NBS to untreatable diseases stems from the admirable desires of parents, researchers, and physicians to help children . . . but such screening runs counter to the principles of evidence-based medicine and the judicious use of healthcare resources."


Pros and Cons

- Mandatory newborn screening for treatable disorders is accepted.
- Mandatory NBS for untreatable disorders is on the horizon
- Mandatory NBS for untreatable diseases is not always benign or ethical
- The shift has been away from the traditional focus on providing specific benefits to individual children to an emphasis on providing potential benefits to families and society at large.

Current Screening in Missouri

- **Organic Acid Disorders**
  - 2-Methyl-3-hydroxybutyric aciduria
  - 2-Methylbutyryl-CoA dehydrogenase deficiency
  - 3-Hydroxy 3-methylglutaric aciduria
  - 3-Methylcrotonyl-CoA carboxylase deficiency
  - 3-Methylglutaconic aciduria
  - Beta ketothiolase
  - Glutaric acidemia type I
  - Isobutyryl-CoA
  - Isovaleric acidemia
  - Malonic acidemia
  - Methylmalonic acidemia
  - Methylmalonic acidemia
  - Multiple carboxylase deficiency
  - Propionic acidemia

- **Hemoglobinopathies**
  - Sickle cell diseases and thalassemias

- **Others**
  - Hearing
  - Biotinidase Deficiency (BIO)
  - Classical galactosemia (GALT)
  - Congenital adrenal hyperplasia (CAH)
  - Congenital primary hypothyroidism (CH)
  - Cystic fibrosis (CF)
  - Amino Acid Disorders
    - Argininemia
    - Argininosuccinate acidemia
    - Citrullinemia type I
    - Citrullinemia type II
    - Defects of biopterin cofactor biosynthesis (BIOPT-BS)
    - Defects of biopterin cofactor regeneration (BIOPT-RG)
    - Homocystinuria
    - Hyperphenylalaninemia
    - Hypermethioninemia
    - Maple syrup urine disease
    - Phenylketonuria
    - Tyrosinemia type I
    - Tyrosinemia type II
    - Tyrosinemia type III

- **Fatty Acid Disorders**
  - Carnitine acylcarnitine translocase deficiency
  - Carnitine uptake defect
  - Carnitine palmitoyl transferase deficiency I
  - Carnitine palmitoyl transferase deficiency II
  - Dienoyl-CoA reductase deficiency
  - Glutaric acidemia type II
  - Long-chain hydroxyacyl-CoA dehydrogenase deficiency
  - Medium-chain acyl-CoA dehydrogenase deficiency
  - Medium-chain ketoacyl-CoA thiolase deficiency
  - Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase deficiency
  - Short-chain acyl-CoA dehydrogenase deficiency
  - Trifunctional protein deficiency
  - Very long-chain acyl-CoA dehydrogenase deficiency

Current Screening in Missouri

- 44 Inborn errors of metabolism
  - aminoacidopathies, organic acidurias, fatty acid oxidation defects, bioinfands deficiency and galactosemia
- 2 Endocrinopathies
  - Hypothyroidism, CAH
- Cystic fibrosis
- The Hemoglobinopathies
  - SS, thalassemia: (18 types)
- Hearing

Chain of Command-Missouri

Follow-up: The Genetic Tertiary Center also contacts the primary care provider to discuss necessary follow up tests.

There is an option of the Genetic Tertiary Center contacting the family and arranging for testing.

The Genetic Tertiary Center will contact the family and arrange for tests if (1) a care provider has not been identified and/or (2) the results are medium/high risk and the PCP has difficulty arranging for timely follow up.

Current Screening-Missouri

- Missouri Newborn Screening Contact Information
  - NBS Laboratory
    - Patrick Hopkins
    - patrick.hopkins@dhss.mo.gov
  - Follow up Program 573-751-2662
    - Julie Raburn-Miller
    - julie.raburn-miller@dhss.mo.gov

- Missouri Statutes

- Screening Requirements
  - Required by law on all infants, with a second test required if initial screen is done prior to 24 hrs.

- NBS Fee: $50.00

- Approximate Annual Births: 76,400
- Major Racial/Ethnic Groups
  - White: 83%
  - American Indian: <1%
  - African American: 15%
  - Asian/Pacific Islander: 2%
  - Hispanic Ethnicity: 3% (may also be included in race categories above)
Mo. votes to add 5 diseases to newborn screenings

Monday, May 11, 2009

JEFFERSON CITY, Mo. (AP) — Missouri is poised to become one of the few states that test infants for certain kinds of rare and often fatal genetic disorders.

Krabbe, Pompe, Gaucher, Fabry and Niemann-Pick A/B

Current Screening-Kansas

- Amino Acid Disorders
  - Phenylketonuria (PKU)
  - Maple Syrup Urine Disease (MSUD)
  - Homocystinuria (HCY)
  - Tyrosinemia Type I (TYRI)
  - Argininosuccinic acidemia (ASA)
  - Citrullinemia (CIT)

- Fatty Acid Disorders
  - Medium chain acyl-CoA dehydrogenase deficiency (MCADD)
  - Very long chain acyl-CoA dehydrogenase deficiency (VLCADD)
  - Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD)
  - Trifunctional protein deficiency (TFD)
  - Carnitine palmitoyltransferase I deficiency (CPT I)

- Organic Acid Disorders
  - Isovaleric Acidemia (IVA)
  - Glutaric Aciduria Type I (GA-I)
  - 3-hydroxy-3-methylglutaryl CoA lyase deficiency (HMG)
  - Multiple carboxylase deficiency (MCD)
  - Methylmalonic Acidemia/Methylmalonyl-CoA Mutase (MUT)
  - Methylmalonic Acidemia/Vitamin B12 Disorders (Cbl A,B)
  - 3-methylcrotonyl-CoA carboxylase deficiency (3MCC)
  - Propionic Acidemia (PROP)
  - Beta ketothiolase deficiency (BKT)

- Hemoglobinopathies
  - Sickle Cell Anemia (SCA)
  - Sickle C Disease (SC C)
  - Sickle Beta Thalassemia (HB S/Th)

- Other Disorders
  - Hypophosphatemia (HYPOTH)
  - Biotinidase deficiency (BIO)
  - Congenital Adrenal Hyperplasia (CAH)
  - Transferrin Deficient Galactosemia (DAI)
  - Cystic Fibrosis (CF)

- Hearing (HEAR)

Current Screening-Kansas

- Starting July 1, 2008, Kansas newborns are screened for the core panel of 29 conditions recommended for inclusion in all state screening programs by the national American College of Medical Genetics. The state will utilize tandem mass technology (MS/MS), a major technological advance in newborn screening.

- The Kansas program encompasses all components of a comprehensive state system:
  - Screening - About 40,000 KS births/initial tests each year with about 2,000 needing repeat,
  - Follow-up - Appropriate health care providers are notified and staff track to assure repeat,
  - Diagnosis - Newborns with positive screens see medical specialists for a final determination,
  - Management - Families and their infants receive ongoing care through a medical team.
  - Education - Information and education are available to families and to providers.
  - Evaluation - Advisory council oversees program/systems to ensure effectiveness/efficiency.

Approximate Annual Births: 39,700

- Major Racial/Ethnic Groups
  - White: 89%
  - American Indian: 1%
  - African American: 8%
  - Asian/Pacific Islander: 2%
  - Hispanic Ethnicity: 12% (may also be included in race categories above)

Kansas Statutes

Screening Requirements
Requested by law on all infants, with a second test required if initial screen is done prior to 24 hrs.

NBS Fee: None

Current Screening-Kansas

Current Screening-Kansas

Kansas Statutes

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What You Might See and What You Should Do
Several tests are not reliable if the sample is obtained before 24 hours of age. If specimen is collected at less than 24 hours of age, a repeat specimen will be requested! Repeat filter paper sample/repeat testing.
TPN:
No result can be given for amino acids while on TPN.
Either repeat screen 48 hours after TPN has been discontinued or switch to D10 for 6-12 hours, repeat screen and then restart TPN.

- Low risk
  - Repeat NBS
- Moderate risk
  - Confirmatory labs
  - Immediate consultation/visit *
- High risk
  - Confirmatory labs
  - Immediate consultation/visit

Confirmatory labs:
- Serum acylcarnitine profile
- Urine organic acid profile
- BMP
- Serum total and free carnitine, LFTs, CK*
- DNA analysis

High Risk!!!
DO: Call the Newborn Screening Follow Up Center if their representative has not already contacted you!
DON'T: Assume this is a false positive and do a repeat newborn screen!!!

Repeat screen was again abnormal!!!
Patient had been started on soy-based formula but appropriate follow-up labs had not been obtained.
Delay in diagnosis—is this Classic Galactosemia or is it Duarte-Galactosemia?

Kansas-
Example of letter sent to parent
Objectives

- The participant will be able to describe the rationale behind newborn screening for selected disorders.
- The participant will recognize the number of disorders screened for in Missouri and Kansas.
- The participant will develop an understanding of the process for results reporting and will recognize the appropriate steps that should be taken for low, medium and high risk results.
- The participant will be able to identify additional tests that are being mandated and how they might have an impact on the practice of medicine.