Expansion of Newborn Screening in Wisconsin and Beyond

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NEWBORN SCREENING
Outline

1. Review the criteria used in Wisconsin to expand NBS
2. Describe how SCID was added to NBS in Wisconsin in 2008
3. Describe the process that is required today to expand NBS
Newborn Screening in Wisconsin

- Most commonly practiced form of genetic screening
- 68,000 Wisconsin newborns per year
- 15,000 non-Wisconsin screens
- Detection of 46 genetic or metabolic conditions in newborns
NBS Process

- Obtain NBS/DBS Guthrie cards
- Education of mother and health care providers
- Collection of blood – heel stick
- Completion of test request form
- Submission of DBS to laboratory
- Data entry and punching of DBS
- Laboratory analysis
- Reporting hospital and health care provider
- Public health follow up
Appropriate Situations of Screening

– Health problem important to individual and community
– Diagnostic follow-up and intervention available
– Favorable cost-benefit ratio
– Public acceptance must be high

Appropriate Situations of Screening

– History of condition should be well understood
– Identification before symptoms occur
– Clear case definition of the condition
– Effective treatment plan is available
– Prevalence of the condition is “high”

Appropriate Situations of Screening

– Suitable and acceptable tests for screening and diagnosis
– Effective methods of prevention are available
– Evidence that screening can alter the natural history of the condition in a significant proportion of those screened

Elements of a Genetic Screening Program

- Universality – all babies should be included
- Education of parents, care providers
- Specimen quality must be assured
- Reliable lab screening tests
- Data integrity
- Timely notification and follow up

Elements of a Genetic Screening Program

- Appropriate diagnostic work up
- Appropriate treatment referral and care
- Education of family with false positive tests
- Continuous monitoring of program
- Cost-effectiveness assessments
- Acquisition of new knowledge

Laboratory Characteristics of a Good Screening Test

- Simple
- Rapid
- Inexpensive
- Safe
- Acceptable
Evaluation of Laboratory Screening Tests

• Reliability = Precision

• Validity = Accuracy
  – Sensitivity
  – Specificity
  – Predictive value positive
  – Predictive value negative
Ethics and Newborn Genetic Screening

- Should genetic screening be conducted?
- Should you or your child be tested?
- Should NBS be mandatory?
- Can screening specimens or DNA taken from specimens be saved for later use?
- Who should pay for NBS?
- Use and misuse of genomic technologies
Ethical Issues – Population Screening

• Unintended targets revealed by testing
• What must be reported
• Screening without follow up
  – Unsatisfactory specimens
  – Inconclusive test results
  – Lack of confirmatory testing
  – Lost to follow up
• Who pays – cost and benefit to society
• Who decides
• Risk for discrimination
Severe Combined Immunodeficiency (SCID)

- SCID is often called "bubble boy disease". SCID became widely known during the 1970's and 80's, when the world learned of David Vetter, a boy with X-linked SCID, who lived for 12 years in a plastic, germ-free bubble.

- "What we're saying is that essentially every baby with SCID could be cured if diagnosed early enough. SCID should be considered a pediatric emergency."

Dr. Rebecca Buckley,

Chief of Duke's Division of Pediatric Allergy and Immunology
Does SCID fulfill NBS criteria?

- **Prevalence of the disease (1:100,000 or greater)**
  - 1:66,000 (conservative estimate)
- **Can the disorder be detected by routine physical exam?**
  - SCID baby appears normal at birth.
- **Does the disorder have a short asymptomatic period after birth?**
  - SCID baby can be protected by passive maternal immunity.
- **Does the disease cause serious medical complications?**
  - Universally fatal within the first year of life
- **Is there potential for successful treatment?**
  - Hematopoietic stem cell transplantation
- **Is there a confirmatory test?**
  - Lymphocyte subpopulation analysis by flow cytometry
- **Does early intervention lead to better outcome?**
  - Yes! >97% survival if transplanted within 90 days
- **Is there a screening test?**
  - Measurement of TRECs using real-time PCR
Adding SCID to NBS Panel

• Reviewed clinical and scientific justification
• Input from experts and constituents
• Statutory or regulatory change
• Consider conducting a pilot study
• Public and professional education
• Validation of screening method
Emergency Public Health Rule

• Secretary Department of Health
• Administrator Division of Public Health
• Retired State Laboratory Director

• Emergency Public Health rule to allow screening for SCID beginning on January 1, 2008
Implementing Routine Testing for Severe Combined Immunodeficiency within Wisconsin’s Newborn Screening Program

**SYNOPSIS**

Severe combined immunodeficiency (SCID) is the result of genetic defects that impair normal T-cell development. SCID babies typically appear normal at birth, but acquire multiple life-threatening infections within a few months. Early diagnosis and treatment with a bone-marrow transplant markedly improves long-term outcomes.

On January 1, 2008, the newborn screening (NBS) program in Wisconsin became the first in the world to routinely test all newborns for SCID. A real-time quantitative polymerase chain reaction assay measures T-cell receptor excision circles (TRECs), which are formed during the maturation of normal T-cells. A lack or very low number of TRECs is consistent with T-cell lymphopenia. The development and validation of the TREC assay and the results of the first year of screening have been published. This article describes the process used to add SCID to the NBS panel, the establishment of follow-up capacity, and the integration of SCID screening into routine NBS workflows. The development of this expanded NBS program is described so that other states might benefit from the processes used in Wisconsin.
Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children
January 21, 2010

- Reviewed existing scientific literature on SCID
- Invited experts to testify before committee
- Unanimously voted to recommend adding SCID to the core screening panel for all newborns in the United States
- Adopted by HHS Secretary on May 21, 2010
Addition of SCID - 2008

- Research Collaboration - MCW, JMF, WSLH
- Assay validation and automation
- Pilot screening project
- Emergency rule approved by Secretary of Health
- Began screening January 1, 2008
- Funding for 3 year project from CDC
- Shared results with SACHDNC
- Increased NBS fees to cover costs
Addition of SCID - 2012

• Research Collaboration
• Assay validation and automation
• Pilot screening project- IRB review
• Funding for pilot project needed
• Department of Health rule to add test
  – Governor and legislative approval
  – 18-24 months
• Recommendation from Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children
• Increased NBS fees to cover costs - unlikely
What’s Next?

- Critical cyanotic congenital heart disease
- Fragile X syndrome
- DiGeorge syndrome (22q11.2 deletion)
- Congenital cytomegalovirus (CMV)
- Lysosomal storage diseases
Conclusions

• Expansion of NBS raises many technical and ethical issues
• New screening programs should be based on sound scientific and ethical principles
• Any broad screening should be widely supported and available to all infants
• Pilot screening programs are often useful
• Education and follow up activities are critical when expanding NBS
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Readings


