



Newborn Screening: The Future Is Here

.....

Ed McCabe, MD, PhD
Senior Vice President and
Chief Medical Officer
March of Dimes Foundation

Overview

- NBS and the March of Dimes
- Advocacy for Improving NBS
- NBS Deserves a “Culture of Safety”
- DNA Sequencing in NBS
- Summary



NBS AND THE MARCH OF DIMES



March of Dimes Mission

- To improve the health of babies by preventing birth defects, premature birth, and infant mortality
- NBS fits into the categories related to
 - Birth Defects
 - Infant Mortality



Newborn Screening (NBS)

- 4 million babies are born each year in the USA
- Every one of those babies has access to testing for a number of disorders
- NBS protects babies from disorders associated with disabilities and death by early identification and interventions
- NBS saves lives!



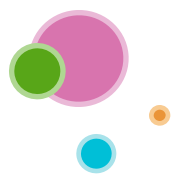
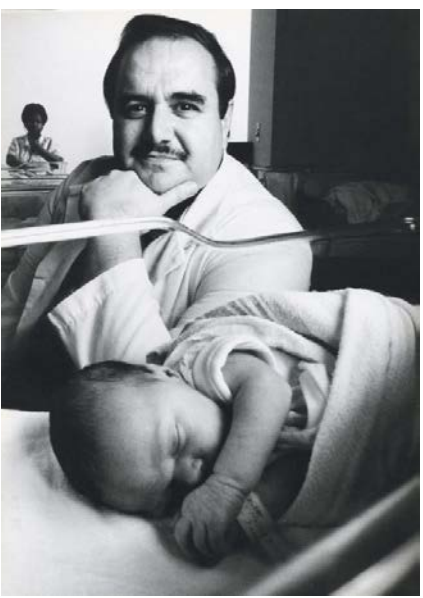
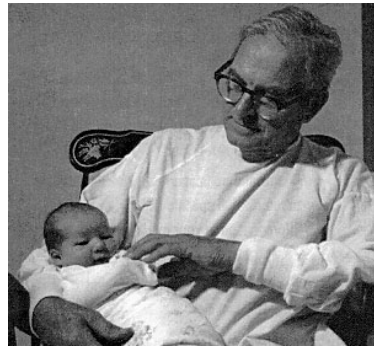
Newborn Screening (NBS)

- Was originally based on a heel stick blood sample taken before discharge from the nursery
- Now includes
 - Hearing testing for hearing loss
 - Pulse oximetry for critical congenital heart disease



Newborn screening tests developed through March of Dimes research

- 1961: PKU
- 1977: Congenital Adrenal Hyperplasia
- 1979: Congenital hypothyroidism
- 1984: Biotinidase Deficiency



ADVOCACY FOR IMPROVING NBS CONSISTENCY AND PARENT EDUCATION



NBS Advocacy

- Proliferation of tests led to a state-by-state patchwork
- MOD advocated for policies to promote more uniformity
- Developed annual NBS Report Cards



Newborn Screening For All Babies

Newborn Screening Tests by U.S. State 2004



0604

2004 Report Card

Newborn Screening Tests by U.S. States, 2008



Source: March of Dimes.
Data reported from NH&GHC as of December 31, 2008.
©2008 March of Dimes Foundation. All rights reserved.

2008 Report Card

March of Dimes Newborn Screening Report Cards Held States Responsible and Drove Change

*Green states are those offering: 9 or more tests in 2004
21 or more tests in 2008



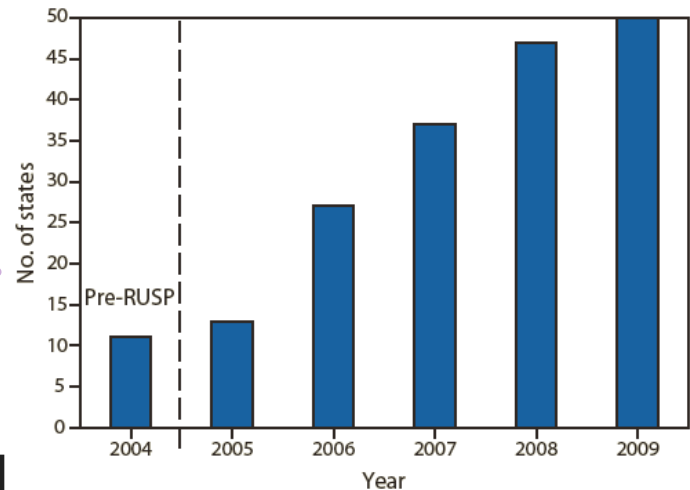
SDACHDNC

- Chartered in April 2013
 - “to advise the Secretary regarding... effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders”
 - Includes
 - “most appropriate application of universal newborn screening tests, technologies, policies, guidelines and standards”
 - Functions previously undertaken by SACHDNC



RUSP

- 31 Disorders
 - 29 Blood spot-based
 - 2 Functional tests
- Recommendations for uniformity
- Brings a discipline to addition of disorders to NBS



2012 MMWR 61;390-3

Newborn Screening Consumer Education



Newborn Screening Consumer Education

[march of dimes](#)
 working together for stronger, healthier babies

[select a category](#) Search [go](#) news: [March Of Dimes Honors Arizona With First](#)

Home > Videos > Learning about newborn screening

Learning about newborn screening

Learn more about newborn screening at [babysfirsttest.org](#)

00:00

Description | Related videos | Most played video

Learning about newborn screening 2:58

Learning About Newborn Screening



[march of dimes](#)
 working together for stronger, healthier babies

[select a category](#) newborn screening [go](#) news: [John Rainey Named Chair of 2015 March of Dimes](#)

Home > Search results

[donate now!](#)

Search results
 Newborn screening
 Showing 1-10 of 79 results

Show All
 Articles
 FAQ
 Features
 News
 PDFs
 Videos

Newborn screening
[www.marchofdimes.org/baby/newborn-screening.aspx](#)
 Your baby gets newborn screening tests before he leaves the hospital after birth. These tests look for rare but serious and mostly treatable health disorders that affect how the body works...

Newborn screening funding
[www.marchofdimes.org/advocacy/newborn-screening-funding.aspx](#)
 , Shire, The Arc and United Cerebral Palsy call on Congress to fund the Newborn Screening Saves Lives Act (P.L. 110-204). Newborn screening is a successful preventive public health activity. In...

Newborn Screening Saves Lives Reauthorization Act
[www.marchofdimes.org/advocacy/newborn-screening-saves-lives-reauthorization-act.aspx](#)
 , H.R. 1281, the Newborn Screening Saves Lives Reauthorization Act was introduced in the U.S. House of Representatives and referred to the House Committee on Energy and Commerce. A companion bill, S. 1417...

Newborn screening tests for your baby
[www.marchofdimes.org/baby/newborn-screening-tests-for-your-baby.aspx](#)
 Before your baby leaves the hospital, he has some special tests called newborn screening. Newborn screening checks for serious but rare conditions at birth. It includes blood, hearing and...

Newborn screening: What caregivers need to know online course
[www.marchofdimes.org/professionals/newborn-screening-what-caregivers-need-to-know-online-course.aspx](#)
 To view the course, go to the collaborator's website. The purpose of the course is to enable caregivers to raise expectant parents' awareness of newborn screening. Although state-mandated...

Newborn care in the delivery room
[www.marchofdimes.org/baby/newborn-care-in-the-delivery-room.aspx](#)
 eyes will be treated with medicated drops or ointment. This protects her eyes from bacterial infections that can be contracted during delivery. Newborn screening tests Your...

Levels of medical care for your newborn

Join us on Facebook
 Show your friends you are helping to end premature birth. [go](#)

My location

News Moms Need
BRACE yourself – The
 BRACE yourself for your new normal. This is the acronym that keynote speaker Kevin Bracy imparted to [more ...](#)

4 of 4

Stay informed
 Get the newsletter and find out how you're helping babies. [sign up](#)

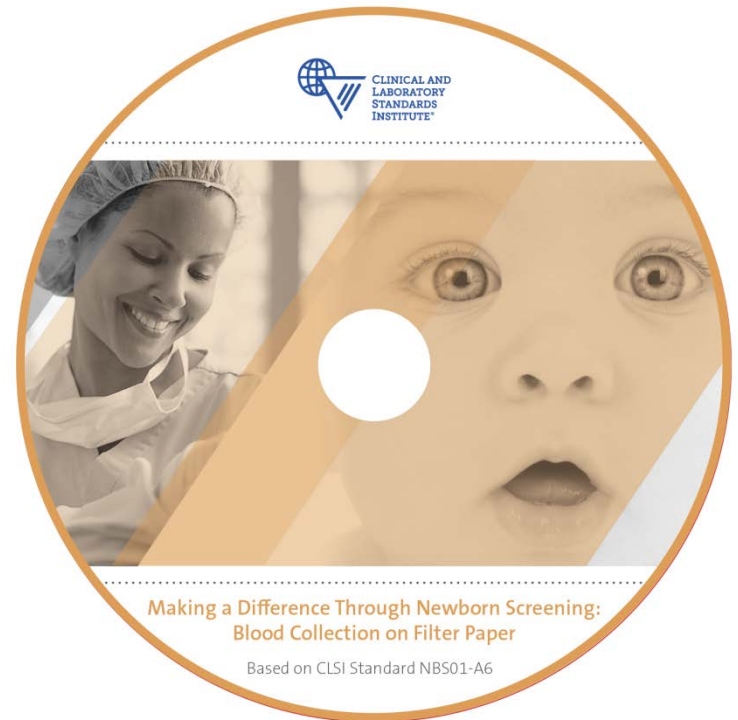
Learn more about the new March of Dimes coin! [go](#)

CLSI Education

Based on CLSI Standard NBS01



**Making a Difference Through Newborn Screening:
Blood Collection on Filter Paper**



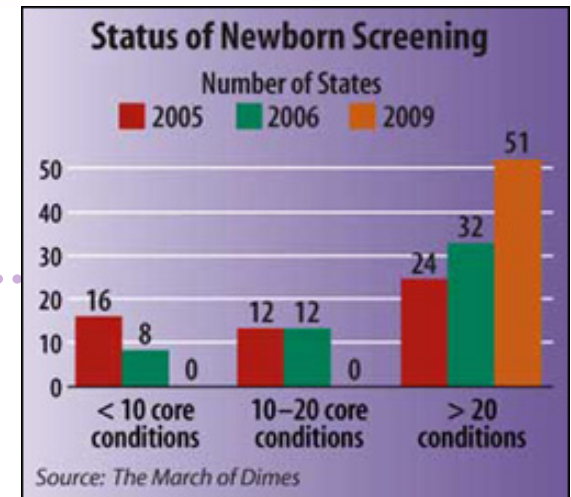
Newborn Screening Saves Lives Reauthorization Act of 2013

- Introduced into the
 - House: H.R. 1281 - Passed May 2014
 - Senate: S. 1417 - Passed January 2014
- Renews federal programs and state grants
- Supports parent and provider education
- Ensures laboratory quality and surveillance activities
- Reauthorizes the SACHDNC for 5 years
- MOD nominated

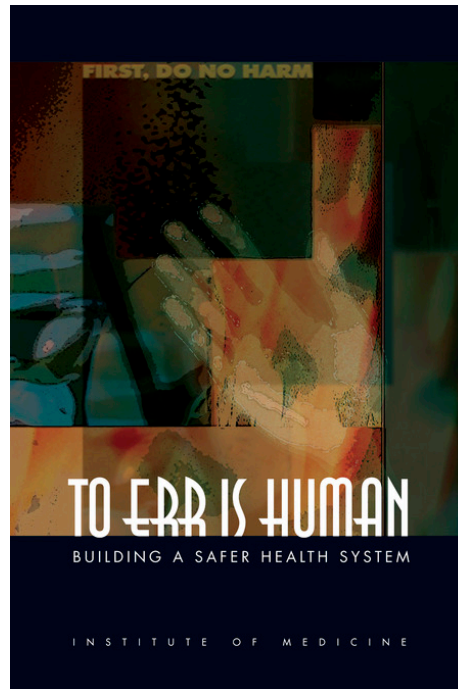


NBS: MOD Approach

- Select a Bold Problem
 - Reduce death and disability from birth defects
- Plan Strategically
 - Develop advocacy initiatives
 - Hold states accountable
- Solve Effectively
 - More robust and uniform NBS system



NBS DESERVES A “CULTURE OF SAFETY”



NBS Is a Complex System

- Many targeted disorders are rare
- Large number of individuals are involved in the NBS system
 - But most will not be involved in identification of an affected individual
 - Do not understand the NBS system and their impact
- Unusual events in a complex environment provide the opportunity for errors at the many steps in the system

High Reliability Organization

- HRO paradigm is a key feature of system safety
- HROs exist in “target rich” environments
 - Inherently risky and unsafe
 - Where consequences of errors are enormous and prevent experimentation



Mort et al. 2013. Acad Med 88:1099-1104

Ruchlin et al. 2004. J Healthc Manag 49:47-58

Sutcliffe. 2011. Best Pract Res Clin Anaesthes 25:133-144

NBS: Adverse Events and System's Failures

- Many disorders targeted by NBS can strike the affected neonate within days of birth
 - Delays can result in death or disabilities
- Therefore, many states require NBS samples to be sent to the laboratory within 24 hours of collection
- MJS reported that delays occurred even when insurance or the state would have covered more timely delivery

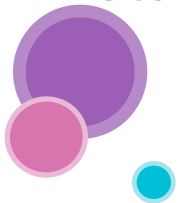


Newborn Screening: “Deadly Delays”

Milwaukee Journal Sentinel

Reasons for delays:

- Hospitals collecting multiple specimens over days before sending them to the laboratory
 - Process known as “batching”
- State NBS laboratories closed on weekends and holidays
- Lack transparency about transit times
- State programs vary widely



High Reliability Organizations



- Provide reliability through infrastructure that
 - Prevents adverse events by anticipation
 - Examples: to identify, map and mitigate risk in an anticipatory manner
 - Is resilient by containing these events
 - Examples: to recognize and contain errors before they spread and cause failure
- Provide optimally reliable outcomes by continuous quality improvement (CQI)

NBS and Culture of Safety

Continuous Quality Improvement



- Example from California reported in MJS
 - California newborn screening program visited each hospital and reviewed practices every 2 years
 - Visit of one hospital identified NBS sample batching as a problem
 - Immediately corrected according to subsequent data monitoring
- Shows value of having CQI practices in place to identify errors, providing for prevention and resilience, characteristics of an HRO and a culture of safety

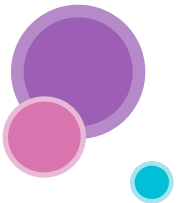
Newborn Screening Quality Improvement

- Publications on “Culture of Safety” in NBS
- NBS Quality Improvement Work Group
- NBS Quality Awards to State Health Officials:
 - ✓ Establish policies of full transparency and 95% transit times of 72, 48 or 24 hours
 - ✓ Robert Guthrie NBS Award for full transparency and 95% transit goal of 24 hours



Improving Newborn Screening in Your State

- If your State Health Official has established a policy of full transparency and 95% transit by 72, 48 or 24 hours:
 - ✓ **Nominate for a NBS Quality Award**
 - Will be vetted by ASTHO
 - ✓ **Additional Awards will be announced in December 2014**
- Encourage your hospitals to set their own goals to prevent “Deadly Delays” for their babies



Inaugural Newborn Screening Quality Award – 72 Hours



Will Humble, MPH
Director, Arizona Department of
Health Services



Estimate of Missed Children

- We estimated the number of children missed by NBS
 - Using data from Holtzman et al. (Pediatrics 1986)
 - A minimum of 80-120 babies missed per year
 - Resulting in unnecessary morbidity and mortality

NBS Culture of Safety

- NBS is a complex system prone to errors
- Errors represent
 - Missed babies
 - Avoidable morbidity and mortality
 - Human factors problems
- We have known these issues since at least 1986

DNA SEQUENCING IN NBS



Incorporating DNA Sequencing into NBS

- The Human Genome Project is leading to cheaper DNA sequencing
- DNA is present in the NBS dried blood spots (DBS)
McCabe et al. 1986
- NIH has funded four grants to determine if DNA in the DBS can be sequenced and the implications of this



NICHD and NHGRI Grants

- Each of these sites will consider three areas of interest
 - Genomic sequencing from the NBS dried blood spots (DBS) and analysis of the sequence data
 - Investigation of impact of these data on patient care
 - Ethical, legal and social implications of the use of genomic sequence information in newborns

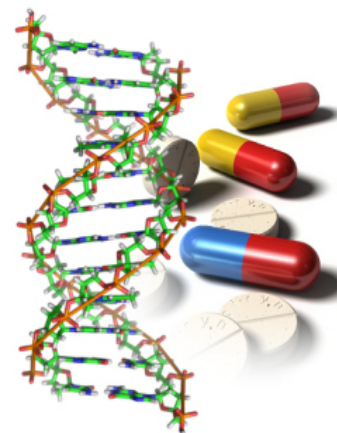


Examples from Funded Projects

- Identify and overcome technical challenges in sequencing DNA from DBS
- Determine optimal approaches for returning results to physicians and families
- Evaluate whether sequencing information complements NBS results and improves care
- Reduce sequencing results turnaround to 50 hours and determine impact on diagnosis and care in the NICU



Adverse Drug Events



- **ADEs have a significant impact**
 - Overall incidence in US hospitals estimated at 6.7% or >2MM/yr
 - Fatal ADEs estimated at 0.3% or >100,000 excess deaths/yr
Nussbaum et al. Genetics in Medicine, 6th & 7th editions, 2001 & 2007
- **Nearly 2% of US hospital admissions experience a preventable ADE**
 - Results in an increased cost of \$4,700/admission or ~\$2B
IOM, To Err Is Human: Building a Safer Health System, 2000
- **Therefore, there are sizable numbers in morbidity, mortality and healthcare costs attributable to ADEs**

Pharmacogenomics

- Uses genome-wide assessment technologies
 - To personalize therapeutic selection and dosage to improve drug
 - Safety
 - Efficacy
 - To reduce preventable adverse drug events (ADEs)
- Should NBS DNA sequencing include known ADE allele associations?
 - Would go beyond disease conditions



NBS & DNA Sequencing: Ethical, Legal and Social Implications

- Which sequence variants should be reported in the context of NBS?
 - All identified?
 - All with known associations for
 - Diseases?
 - Other sequence variants, e.g. ADEs?
 - Only those for which knowledge and intervention can impact morbidity and mortality in childhood?
 - Only those on the current NBS recommended uniform screening panel (RUSP)?



Should NBS Samples Be Analyzed in the Third Trimester?

- Even if samples can be analyzed routinely by 5 days of age
 - Some babies will become critically ill before that time
- Is there a way to prevent the inevitable “Deadly Delays” in NBS?

Should NBS Samples Be Analyzed in the Third Trimester?

- If high quality fetal DNA can be obtained for sequencing in the mother's third trimester blood
- If NICHD studies show DNA sequencing efficacious
- Then should fetal DNA be sequenced to determine appropriate services?

SUMMARY



Summary

- NBS is 51 years old
 - Incredibly powerful
 - Need to work as a community to
 - Improve the culture of safety
 - Reduce missed babies
- Adding new technologies will not prevent systems failures



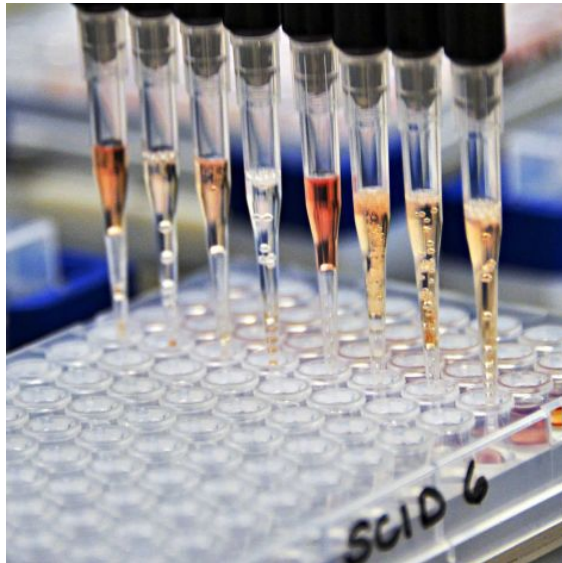
Summary

- We must be relentless advocates for NBS
 - Federal: NBS Reauthorization Act
 - State: Attacks on “privacy” grounds





THANK YOU



march  of dimes®