Newborn Screening as a Public Health System: How Does it Work?

Michele Caggana, Sc.D., FACMG

January 30, 2017
Newborn Screening

Declared One of the Ten Great Public Health Achievements of the 21st Century by the CDC in 2011
Why Perform Newborn Screening?

Pre-symptomatic screening results in a change in health status

*World Health Organization Criteria – 1968*

- Prevalence in population, public health
- Marker in the blood
- Assay to detect the marker
- Therapy for the child
  - Legislation
  - Commissioner’s Declaration

The program cannot add diseases to the test panel
Why Does Newborn Screening Work?
Newborn Screening is Comprehensive

- A simple blood test used to identify many life-threatening illnesses before any symptoms begin.
- An **essential** program grounded in public health that prevents catastrophic health consequences through early detection, diagnosis and treatment.
- A **complex system** of testing, evaluation, and treatment that is dependent upon the dedication of persons working within the system.
Newborn Screening Is Not Diagnostic

- Partnership with families, providers, and specialists
- Risk assessment: Identify infants at increased risk
- High throughput
  - Identifies spectrum of disease
  - Case definitions essential!!
  - Takes all comers
Approximately 1 in 300 infants born in New York have a screened condition
POPULATION – BASED SCREENING
Phenylketonuria

Phenylpyruvic acid
FeCl3 test

Aspartame

http://138.192.68.68/bio/Courses/biochem2/AminoAcids/AminoAcidCarbonDeg.html
A Disorder, Treatment and Diagnostic Test

Dr. Asbjorn Folling
Dr. George Jervis
Dr. Horst Bickel
Dr. Willard Centerwall

Fig 6. The relationship between Dr Folling and the children first discovered to have PKU—a chance relationship through marriage and not genetically related.
The Perfect Storm

Niece had PKU; son with intellectual disability

Pictures Courtesy of Dr. Kenneth Pass
Jamestown, New York

- Fall 1961 talk for The Association for Retarded Children
- Began to receive newborn filter-paper specimens (29 states; 400K babies)
- “Thus, screening had its start in Jamestown, New York in 1961”

Picture Courtesy of Dr. Kenneth Pass
PHENYLKETONURIA IN PUBLIC HEALTH LAW

§ 2500 a

"It shall be the duty of (1) the administrative officer or other person in charge of each institution caring for infants twenty-eight days or less of age and (2) the person required ... to register the birth of a child, to cause to have administered to every such infant or child in its or his care a test for phenylketonuria in accordance with rules or regulations prescribed by the commissioner. ...

§ 2. This act shall take effect January first, nineteen hundred sixty-five. ""
MS/MS Phenylketonuria

Normal

Phenylketonuria

Data from Dr. Mark Morrissey
Carrier parents
No disease

Excludes HIV, ALD and Hypothyroidism in NY

Autosomal Recessive

FIGURE 1-8 Pedigree illustrating segregation of autosomal recessive trait. Allele A is dominant, a is recessive.
Newborn Screening

What is the Process?
NEWBORN SCREENING BLOOD COLLECTION FORM

Parents,

A blood specimen has been taken from your new baby for testing by the State Newborn Screening Program. This program is described in the brochure “For Your Baby’s Health.” To help hospital staff and the outcome of this important health service, take the pink copy to the baby’s doctor, who can obtain the test results and explain the procedure by calling (800) 535-3079. Under NY State law, test results are to be reported to your doctor and cannot be sent directly to parents.

Do your children have health insurance? If not, they may qualify for NYS’s health insurance program, Child Health Plus. Call 1 (800) 522-9006 for information.

Instructions to hospital:

After entering infant’s name, remove this pink copy and give it to the parents of this newborn, along with the educational brochure “For Your Baby’s Health.”

Lab I.D. 192718516

Newborn Screening Program
Serving New York Since 1965

Wadsworth Center
NYS Department of Health
http://www.wadsworth.org/newborn

PARENT COPY

(SEE REVERSE SIDE FOR INSTRUCTIONS)

Hospital

Mom
About 24 hrs after birth at each of 127 birth hospitals in NY.......
TIME SENSITIVE
NEWBORN SPECIMENS

We Ship Via UPS

Express envelope
We can process up to 2006 specimens (24 plates) daily
INVALID SPECIMENS

Require a repeat specimen

New sub-optimal category
96-WELL PLATES ARE LABELED FOR USE EACH DAY
SAMPLES ARE PUNCHED INTO 96-WELL PLATES
Texas Newborn Screening Laboratory

8 plates are distributed to 5 areas to test for 29 disorders.

Hemoglobinopathy Screening:
One test is used to identify:
- Sickle Cell Anemia
- Sickle Hemoglobin C Disease
- Sickle/Beta Thalassemia Disease
- Other hemoglobinopathy diseases and traits

Galactosemia & Biotinidase Screening:
Two tests are used to identify:
- Galactosemia
- Biotinidase Deficiency

Endocrine & Cystic Fibrosis Screening:
Three tests are used to identify:
- Congenital Hypothyroidism
- Congenital Adrenal Hyperplasia
- Cystic Fibrosis

SCID Screening:
One molecular test is used to identify:
- Severe Combined Immunodeficiency

Tandem Mass Spectrometry Screening:
One test is used to identify:
- 6 amino acid disorders (e.g. PKU)
- 5 fatty acid disorders (e.g. MCAD)
- 9 organic acid disorders (e.g. glutaric acidemia type 1)
SPECIMENS ARE BUNDLED FOR REPEATS
Staff notify specialists and physician of record
Newborn Screening Program
Wadsworth Center
New York State Department of Health
120 New Scotland Ave
Albany, NY 12208
Phone: (518) 473-7552  FAX: (518) 474-0405
Web: NYSDOH HCS  E-mail: nbsinfo@health.state.ny.us

Welcome Michele X Caggana - NYSDOH Wadsworth

Laboratory Announcements

To View Newborn Screening Results, select Secure Remote Viewer (icon on your left)

Specimens older than 2003 are not available from the Secure Remote Viewer

The Secure Remote Viewer is compatible only with Internet Explorer 8+ or Firefox

**POSTED 03/21/2014**

Our Program has moved. Effective March 24, 2014, our address is David Axelrod Institute, Newborn Screening Program, 120 New Scotland Avenue, Albany, NY 12208. Our main phone number, fax number and email have not changed. All mail already sent to our previous location will be forwarded. Please use our new address going forward.
Newborn Screening

How Are New Conditions Added?
Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

January 2005 Meeting Notice

Federal Register: December 15, 2004 (Volume 69, Number 240)

In accordance with section 10(a)(2) of the Federal Advisory Committee Act (Public Law 92-463), notice is hereby given of the following meeting:

Name: Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (ACHDGDNC).

Dates and Times: January 13, 2005, 9 a.m. to 5 p.m. January 14, 2005, 9 a.m. to 5 p.m.

Place: Ronald Reagan Building and International Trade Center, 1300 Pennsylvania Avenue, NW, Washington, DC 20004.

Status: The meeting will be open to the public with attendance limited to space availability.

Purpose: The Advisory Committee provides advice and recommendations concerning the grants and projects authorized under the Heritable Disorders Program and technical information to develop policies and priorities for this program that will enhance the ability of State and local health agencies to provide for newborn...
From: Newborn Screening: Toward a Uniform Screening Panel and System
American College of Medical Genetics for the Maternal Child Health Bureau
http://mchb.hrsa.gov/screening/
<table>
<thead>
<tr>
<th>Acylcarnitines</th>
<th>Amino acids</th>
<th>Hematology</th>
<th>Others</th>
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<td>FAO (5)</td>
<td>AA (6)</td>
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<td>GA-I</td>
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Establishes the “RUSP”

SACHDNC
Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children

- Chartered in February, 2003
- First meeting June 7, 2004
- Newborn Screening Saves Lives Act, 2007
  - Section 4 reads:
  - “(3) make systematic evidence-based and peer-reviewed recommendations that include the heritable disorders that have the potential to significantly impact public health for which all newborns should be screened, including secondary conditions that may be identified as a result of the laboratory methods used for screening”
SACHDNC

• Provides guidance to the Secretary, HHS, about the conditions that should be included in newborn screening
• If endorsed by the Secretary, the conditions become part of the RUSP
• Although newborn screening programs are operated at the state level, many strive to follow the RUSP
Composition of SACHDNC

- Members approved by HHS
- 1/10 Committee members is from a State NBS Program
- Liaisons from AAP, ASTHO, AAFP, ACMG, ACOG, AMCHP, APHL, Genetic Alliance, MOD, NSGC, SIMD, even DOD
- Ex Officio members: AHRQ, CDC, FDA, HRSA, NIH, designated federal official
Nominate a Condition

The RUSP is a list of disorders that are screened at birth and recommended by the Secretary of the Department of Health and Human Services (HHS) for states to screen as part of their state universal newborn screening (NBS) programs. Disorders on the RUSP are chosen based on evidence that supports the potential net benefit of screening, the ability of states to screen for the disorder, and the availability of effective treatments. It is recommended that every newborn be screened for all disorders on the RUSP. Most states screen for the majority of disorders on the RUSP; newer conditions are still in process of adoption. Some states also screen for additional disorders. Although states ultimately determine what disorders their NBS program will screen for, the RUSP establishes a standardized list of disorders that have been supported by the Committee and the Secretary of HHS.

Conditions for consideration by the Committee for the Recommended Uniform Screening Panel (RUSP) must be nominated.

The Committee encourages individuals and organizations to form multi-disciplinary teams to submit nominations for conditions to be considered for inclusion on the RUSP. Teams should include researchers and/or clinicians with expertise on the condition being nominated, advocacy and/or professional organizations with knowledge of issues relevant to newborn screening, and interested consumers/individuals.

To apply, the lead nominator or proponent should submit a Nomination Package that includes:

- Cover letter by the lead nominator that identifies all multi-disciplinary team members and their organizational affiliation(s), if applicable;
Nomination Process


• Condition, Treatment, NBS information
• Confirmatory testing information
• Pilot data
• References

Generally advocacy, clinicians, and scientists work together
Condition Review Process

• Based on 3 reports:
  o Systematic evidence review
  o Assessment of the bounds of benefit and harm
  o Evaluation of the capability of states to implement comprehensive
Principles for Making Recommendations

• Evidence based
• Health benefit to screened individual is the chief outcome that matters
• Account for feasibility and readiness of State Programs for screening
• Recommendations not impacted or modified based on insurance, medico-legal liability or legislation
# Evaluation of Magnitude and Certainty of Net Benefit; State Capability

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<thead>
<tr>
<th>Rating</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>There is high certainty that adoption of screening for the targeted condition would lead to a significant net benefit.</td>
</tr>
<tr>
<td>B</td>
<td>There is moderate certainty that adoption of screening for the targeted condition would lead to a significant benefit.</td>
</tr>
<tr>
<td>C</td>
<td>There is high or moderate certainty that adoption of screening for the targeted condition would lead to a small to zero net benefit.</td>
</tr>
<tr>
<td>D</td>
<td>There is high or moderate certainty that adoption of screening for the targeted condition would lead to a negative net benefit.</td>
</tr>
<tr>
<td>L</td>
<td>There is low certainty regarding the net benefit from screening.</td>
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# SACHDNC Decision Matrix

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<tr>
<th>NET BENEFIT</th>
<th>FEASIBILITY</th>
<th>READINESS</th>
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<td>Low Feasibility</td>
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<td>Moderate Certainty</td>
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<tr>
<td>Zero to Small Benefit</td>
<td>High or Moderate Certainty</td>
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<tr>
<td>Negative Benefit</td>
<td>Low Certainty</td>
<td></td>
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</tbody>
</table>

- **A1**: Significant Benefit with High or Moderate Feasibility
- **A2**: Significant Benefit with Low Feasibility
- **A3**: Significant Benefit with Low Certainty
- **A4**: Significant Benefit with Low Certainty
- **B**: Moderate Certainty
- **C**: Zero to Small Benefit with High or Moderate Certainty
- **D**: Zero to Small Benefit with Low Certainty
- **L**: Negative Benefit with Low Certainty
When A State Mandate Speeds Implementation

- QA/QC
- CLRS/CLIA
- IRB
- Screening Laboratory
- Facilities
- Clinical Medical
- Purchasing

Joseph J. Orsini
ALD Screening

Sequence of Events 1 – Legislated

- Aidan Seeger, a 7 year old from Brooklyn passes 4/29/2012
- Mrs. Seeger called me in May 2012 to discuss screening
- Family garnered support: NY politicians; website; billboards
- Bill submitted August 2012
- Approved by Health Finance Committee 02/28/2013
- Became law 03/31/2013; start 01/01/2014 (actual 12/30/2013)

aidanhasaposse.org
State of New York

2386

2013-2014 Regular Sessions

In Senate

January 17, 2013

Introduced by Sen. ADAMS -- read twice and ordered printed, and when printed to be committed to the Committee on Health

AN ACT to amend the public health law, in relation to requiring adrenoleukodystrophy screening of newborns

The People of the State of New York, represented in Senate and Assembly, do enact as follows:

Section 1. This act shall be known and may be cited as "Aidan's Law".

Section 2. Subdivision (a) of section 2500-a of the public health law, as amended by chapter 863 of the laws of 1986, is amended to read as follows:

(a) It shall be the duty of the administrative officer or other person in charge of each institution caring for infants twenty-eight days or less of age and the person required in pursuance of the provisions of section forty-one hundred thirty of this chapter to register the birth of a child, to cause to have administered to every such infant or child in its or his care a test for phenylketonuria, homozygous sickle cell disease, hypothyroidism, branched-chain ketonuria, galactosemia, homocystinuria, ADRENOLEUKODYSTROPHY and such other diseases and conditions as may from time to time be designated by the commissioner in accordance with rules or regulations prescribed by the commissioner. Testing, the recording of the results of such tests, tracking, follow-up reviews and educational activities shall be performed at such times and in such manner as may be prescribed by the commissioner. The commissioner shall promulgate regulations setting forth the manner in which information describing the purposes of the requirements of this section shall be disseminated to parents or a guardian of the infant tested.

Section 3. This act shall take effect on the one hundred eightieth day after the date of its approval.
3 Families Impacted by ALD
After the Vote......
September 25, 2015

The Honorable Sylvia Mathews Burwell
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Secretary Burwell:

The Advisory Committee on Heritable Disorders in Newborns and Children (Committee) is charged with making systematic evidence-based recommendations on heritable disorders that have the potential to significantly impact public health for which all newborns should be screened.

During the Committee's August 2015 meeting, we reviewed the evidence-based report for the nominated heritable disorder – Adrenoleukodystrophy (X-ALD). Based on this report and deliberations on all associated clinical data, testing platforms, available treatments, benefits and harms, public comment, and the public health impact assessment, the Committee voted to recommend to you the following:

1. Expand the Recommended Uniform Screening Panel (RUSP) to include the addition of X-ALD.
2. Provide federal funding to State newborn screening programs to implement the screening of X-ALD, including funding to collect data and disseminate information that further defines short and long term follow-up procedures for pre-symptomatic and symptomatic detection.
Joseph A. Bocchini, Jr., M.D.
Committee Chairperson
Advisory Committee on Heritable Disorders in Newborns and Children
5600 Fishers Lane
Room 18W68
Rockville, MD 20857

Dear Dr. Bocchini:

Thank you for your letter on behalf of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) regarding the ACHDNC’s recommendations to add X-linked Adrenoleukodystrophy (X-ALD) to the Recommended Uniform Screening Panel (RUSP) and to provide federal funding to state newborn screening programs to implement the screening of X-ALD.

I would like to commend the ACHDNC on your evidence review that included an analysis of the benefits and harms of newborn screening for X-ALD as well as the capability of state newborn screening programs to offer comprehensive testing and follow-up services for infants identified with X-ALD. After reviewing the ACHDNC’s report, *Newborn Screening for X-Linked Adrenoleukodystrophy (X-ALD): A Systematic Review of Evidence*, and taking into consideration the utility of current screening technologies, treatment for X-ALD, and the impact on public health systems, I accept the ACHDNC’s recommendation to expand the RUSP to include the addition of X-ALD. As you may know the Affordable Care Act requires that most health plans cover newborn screening for heritable disorders, and screening for X-ALD is essential to ensure early diagnosis and treatment for affected infants.
What Else is Being Discussed for Addition on the RUSP?

- Spinal muscular atrophy – deletion of exon 7 in SMN1 gene (pilot in NY hospitals)
- Fragile X syndrome – CGG repeat (>200); AGG
- Duchenne muscular dystrophy – creatine kinase followed by deletion/duplication; DNA sequence – specificity; other conditions
- Other LSDs (Gaucher disease/Niemann-Pick disease, Fabry disease – mild/severe mutations, frequency issues)
- Guanidinoacetate methyltransferase deficiency
Spinal Muscular Atrophy

- 1 in 6,000 frequency
- Four types, type I is most severe
- Deletion (most often) of SMN1
- #copies of SMN2 important
- No treatment, but early diagnosis useful; some data on efficacy in affected children
- Dr. Tom Prior developed a molecular assay
SMA Pilot Study

SMN1 – 2 copies
SMN1 – 1 copy
Blanks

Combining with TRECks and KRECks

3,705 screened
3,484 2 normal copies of SMN1
57 1 normal copy of SMN2 (1/57)
1 homozygous deletion (sample 116)