50+ Years of Improving Health Through Newborn Screening: A Model of Public Health Success

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Michigan Screens for 55 conditions!

- 14 Amino acid disorders
- 2 Endocrine disorders
- 13 Fatty acid oxidation disorders
- 5 Hemoglobin disorders
- 14 Organic acid conditions
- 2 groups of immunodeficiencies
- 3 “other” disorders: biotinidase deficiency, galactosemia, cystic fibrosis
- Hearing loss
- Congenital heart disease
Big Numbers

- 112,790 screened in 2014
- Leading to 259 diagnoses
Traditional Screening Criteria – Wilson and Jungner (1968)

- Condition – important health problem
- Natural history – understood
- Latent or early symptomatic stage
- Test – easy, acceptable, accurate, reliable
- Treatment – accepted, more effective if started early
- Diagnosis and treatment – cost effective
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SCREENING IS A PROCESS – NOT A TEST
1965

- Advances in nutrition
  - Cool Whip
  - Diet Pepsi
  - TGI Fridays opens
  - Poppin’ Fresh “born”
Early History

- 1957 – Robert Guthrie, MD, PhD, developed a method to monitor blood phenylalanine levels in blood on filter paper (bacterial inhibition test)
- 1961 – NBS began in two hospitals in NY; funding received from the Children’s Bureau to trial screening nationally
- 1967 – 37 states mandated NBS for PKU

https://www.nbstrn.org/about/spotlight/Guthrie
Dried-Blood Spot

- The Guthrie test has been replaced by MS/MS (primarily) and other testing methods
- Use of DBS has been central to linking in public health agencies
Past Two Decades of Newborn Screening

- Rapid expansion of conditions that can be detected
- New screening technology
- New treatments
- Harmonization across states
- Better coordination in public health agencies for short- and long-term follow-up
- Emergence of point-of-care testing
  - Screening for Congenital Hearing Loss
  - Screening for Critical Congenital Heart Disease
1965

- Top Movies
  - *The Sound of Music*
  - *Thunderball*
  - *Doctor Zhivago*
  - *For a Few Dollars More*
  - *Von Ryan’s Express*
DNA testing

• Most conditions are heritable
• However, testing is not primarily DNA based
  – Metabolic Products (MS/MS)
  – Sickle Cell Disease (HPLC or IEF)
  – Cystic Fibrosis (IRT, DNA)
  – Severe Combined Immunodeficiency (TREC assay [PCR])
  – CH (Hormone levels)
  – Hearing Loss (Functional)
  – CCHD (Indirect marker)
Current Status

• Largest coordinated genetic screening program in the US
• Individual state programs with input from the federal Department of Health and Human Services
• Challenges
  – What to include
  – How to screen
  – Short-term follow-up
  – Long-term follow-up
Federal Activity

- HRSA
- NIH
- CDC
- AHRQ
- Advisory Committee
- NCC
- RCC
- NewSTEPs
- Baby’s First Test
- NBSTRN
1965

- **Top TV shows**
  - *Days of Our Lives*
  - *F Troop*
  - *I Dream of Jeannie*
  - *Lost in Space*
  - *Hogan’s Heroes*
Intertwined questions:

• What if screening might be of benefit to the family but not necessarily the child?
• What if the screening might not benefit individual until much later in life?
• What if we do not know the natural history?
• What if there is no treatment?
• What is the role of public health?
• Is screening a function of the test or of the condition?
• What defines a target, a condition, a disease, or an outcome?
• How should costs be considered?
• Should opportunity cost be considered?
How can dried-blood spots be used?

- Quality Improvement / Evaluation
- Development of new screening approaches
- Surveillance
- Forensics
- Biomedical research
  - NBS related
  - Non-NBS related
Michigan BioTrust

- Run by the Michigan Department of Health and Human Services
- Oversees the storage and use of dried-blood spots
- Holds them “in trust” for future research
- Includes
  - Community Values Advisory Board
  - Scientific Advisory Board
  - Board of Directors (Michigan Neonatal Biobank)
The Advisory Committee

- Provides advice and recommendations to the Secretary, HHS, about the conditions that should be included in newborn screening
- If approved by the Secretary, the conditions become part of the RUSP
- Although newborn screening programs are operated at the state level, many follow the RUSP
Evolution of the RUSP

• 2006 – the American College of Medical Genetics recommended 29 core conditions based on expert panels

• The Advisory Committee next adopted an evidence-based approach, which led to
  – *Added to the RUSP: SCID, CCHD, and Pompe Disease*
  – *Recommended for addition: MPS 1 and X-ALD*
  – *Recommendations against adding: Hemoglobin H disease, Krabbe disease, and neonatal hyperbilirubinemia*
New Condition Review Process

• Based on 3 reports
  – Systematic evidence review
  – Assessment of the bounds of benefit and harm
  – Evaluation of the capability of states to implement comprehensive screening – Public Health System Impact Assessment
## Advisory Committee Decision Matrix

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<th>NET BENEFIT</th>
<th>FEASIBILITY</th>
<th>READINESS</th>
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<td>Ready</td>
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<td>Significant Benefit</td>
<td>High or Moderate Feasibility</td>
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<td>Low Feasibility</td>
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<td>Moderate Certainty</td>
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<td>Zero to Small Benefit</td>
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Point-of-Care Testing

- **Congenital Hearing Loss**
  - *Widely adopted*
  - *Follow-up (or at least documented follow-up is a major challenge)*

- **Critical Congenital Heart Disease**
  - *Rapid adoption, with variation across states in implementation*

- **Challenges**
  - *Determining the role of public health and NBS*
  - *What makes a service NBS versus good clinical practice?*
  - *What are the levers to support adoption and high-quality care?*
Screening and Short-Term Follow-up

- Efficiently maximizing laboratory-test accuracy
- Information systems and communication
  - *What goes out and to whom?*
  - *Carrier status?*
  - *Variants of unknown significance?*
  - *Late-onset disease*
- Time to analysis, reporting, and clinical management
- Identification of health care providers for short-term follow-up, especially of conditions that are challenging to confirm
- State boundaries
Long-Term Follow-up

• Availability of metabolic foods
• Uptake of new therapy, such as hydroxyurea for children with sickle-cell disease
• Access to expensive therapies
  – *Who is financially responsible? For how long?*
• Adherence
  – *Diets*
  – *Medication*
Back to Newborn Screening

• One of the most successful public health programs
• A system, not a test
• Relies on dedicated professionals in public health
• Increasing demand for comprehensive services, but limited resources
• Constant “disruption” by technology
1965

- **Top Music Hits**
  - *Wooly Bully* – Sam the Sham and The Pharaohs
  - *I Can’t Help Myself (Sugar Pie, Honey Bunch)* – The Four Tops
  - *(I Can’t Get No) Satisfaction* – The Rolling Stones
  - *You Were On My Mind* – We Five
  - *You’ve Lost That Lovin’ Feelin’* – The Righteous Brothers
The Future

“Prediction is very difficult, especially if it’s about the future.”

-Nils Bohr

“The future isn’t what it used to be!”

-Anonymous
The Future

• Increasing use of point-of-care tests
• Increase use of DNA-based tests
• Growing challenges
  – *Unknown variants, late-onset disease, carriers*
  – *Shortage of specialists*
  – *Access to care/treatment*
• Newborn screening programs and Public Health will continue to play a central role in newborn screening
1965

- **Cost of Living**
  - *Average Yearly Income* - $5,942
  - *First Class Stamp* – $0.05
  - *Local Call* - $0.10
  - *One Gallon of Gas* - $0.31
Thank you!