

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



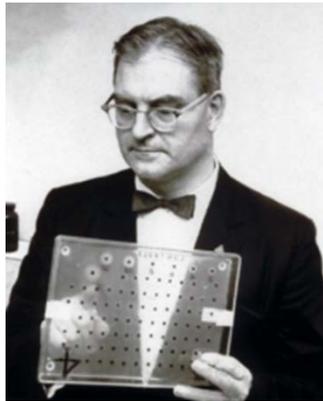
1965

- 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- The Guthrie test has been replaced by MS/MS (primarily) and other testing methods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

NET BENEFIT		FEASIBILITY	READINESS		
			Ready	Developmental	Unprepared
Significant Benefit	High Certainty	High or Moderate Feasibility	A1	A2	A3
		Low Feasibility	A4		
	Moderate Certainty		B		
Zero to Small Benefit	High or Moderate Certainty		C		
Negative Benefit			D		
	Low Certainty		L		



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!

