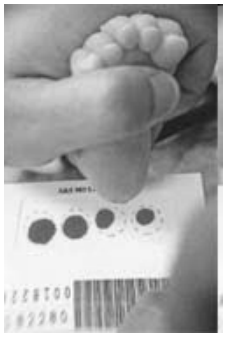
Review of Newborn Screening & Updates

Traci McDermott, MD

November 22, 2013



Objectives

#1 Review of Newborn Screening and its' national and local history

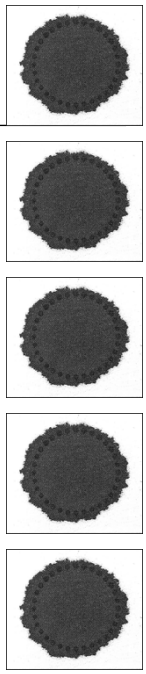
#2 The Numbers: Screening in Washington & Incidence of tested congenital disorders

#3 The importance of obtaining a second newborn screen & the research behind it

#4 Adding New Conditions to Recommended or Mandated Newborn Screening Panels & What's New

#5 Overview of services provided by Department of Health Newborn Screening Services & available resources

What is ***Newborn*** Screening?

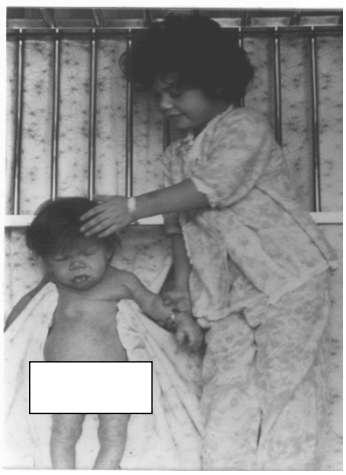


An integrated <u>system</u> that includes:

- Universal screening - all infants
- Follow-up to assure appropriate clinical response
- Diagnosis of affected infants
- Appropriate treatment and clinical care
- Evaluation of system effectiveness

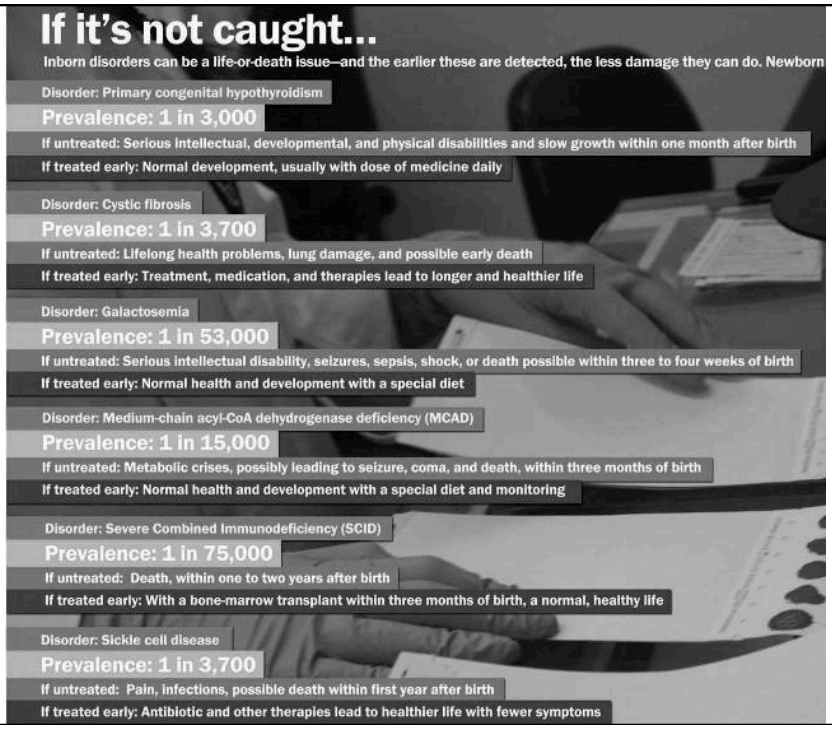
Why is Newborn Screening Important?

- It prevents death and disability to affected infants by providing early treatment
- It benefits the public through savings in health care costs and institutional care

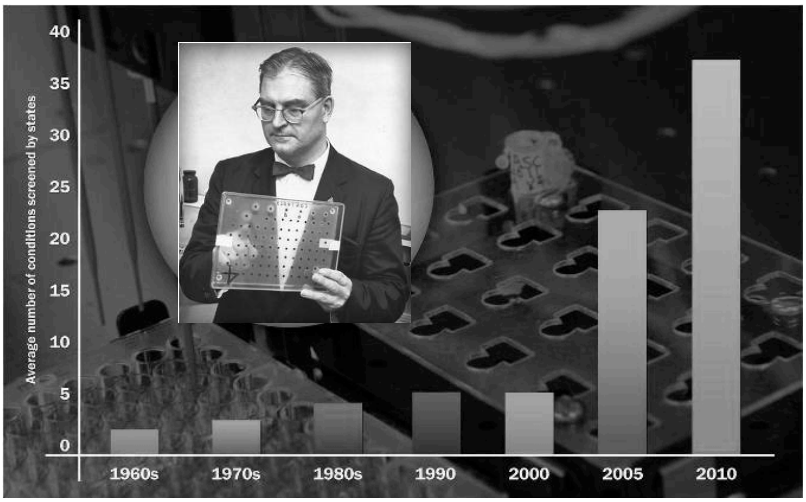


NBS Goal:

Correctly identify babies with congenital disorders and assure that they receive treatment as soon as possible.



History of Newborn Screening



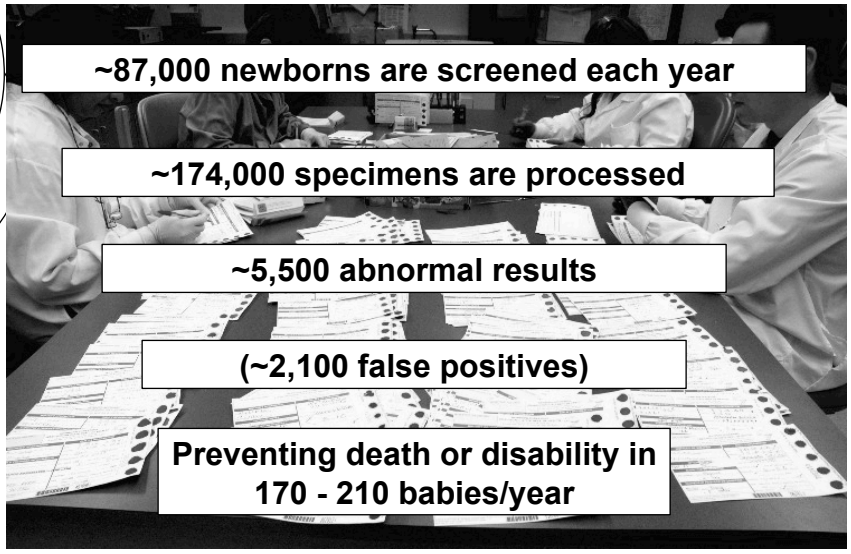
History of Screening in Washington

YEAR	DISORDERS ADDED
1963	PKU - test available - voluntary
1967	- Statute adopted, promotes screening
1976	- Statute revised, MANDATES screening - DOH given authority to add conditions; rules adopted
	to carry out intent of statute
1978	Congenital hypothyroidism (CH)
1984	Congenital adrenal hyperplasia (CAH)
1991	Hemoglobinopathies (Hb)
2004	Biotinidase deficiency (BIO)
	Galactosemia (GALT)
	Homocystinuria (HCY)
	Maple syrup urine disease (MSUD)
	Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency
2006	Cystic fibrosis (CF)
2008	Amino acid (AA) disorders: 3
	Fatty acid oxidation (FAO) disorders: 4
	Organic acid disorders (OA): 8

Objective # 2

The Numbers: Screening in Washington & Incidence of tested congenital disorders

How is Newborn Screening Done ?



Annual WA NBS Numbers

2011 WA DOH Birth Data

Facility	Hospital	Birth Center	Home	Total
# of Births	80,377	1,006	1,674	86,956
Percent	92.4 %	1.2 %	1.9 %	

Attendant	Certified Midwife	Licensed Midwife	Other Midwife	All Midwife	Total Births
# of Deliveries	7,484	2,404	113	10,001	86,956
Percent	8.6 %	2.8 %	0.1 %	11.5 %	

2012
Newborn Screening Annual Report

86,180 Babies Screened
- 115 severe disorders (1 in 749 babies)
- 94 mild forms (1 in 917 babies)

209 Total disorders (1 in 412 babies)

1,244 Hemoglobin traits (1 in 69 babies)

Disorders Detected This Year

2013 Statistics (3rd Quarter July through September)		
3rd Quarter	**2013**	**General**
23,133	66,076	Hospitals, Birth Centers & Home Births*
43,950	124,340	Specimens Tested (most infants have two newborn screens performed)
3rd Quarter	**2013**	**Infants Diagnosed**
4	5[a]	Amino Acid disorders
0	1	Biotinidase Deficiency
0	5	Congenital Adrenal Hyperplasia
21	56	Congenital Hypothyroidism
2	12	Cystic Fibrosis
0	1[b]	Fatty Acid Oxidation disorders
2	5	Galactosemia
1	2[c]	Organic Acid disorders
7	15	Sickle Cell Disease and Other Clinically Significant Hemoglobinopathies
37	**102**	**All Dried Blood Tests Combined**
29	59	Early Hearing Loss
66	**161**	**All Disorders Combined**

*Excludes babies born at Bremerton and Whidbey Island Naval hospitals
a Includes 2 infants with phenylketonuria (PKU), 2 infants with maple syrup urine disease (MSUD), and one infant with tyrosinemia type 1 (TYR-1)
b Infant with medium chain acyl-CoA dehydrogenase (MCAD) deficiency
c Includes one infant with isovaleric acidemia (IVA), and one infant with methylmalonic acidemia (MMA), but excludes two infants with 3-methylcrotonyl CoA carboxylase (3-MCC) deficiency (a condition not on our mandatory screening panel)

Objective # 3

The importance of obtaining a second newborn screen & the research behind it

Timing is Critical

- Day 1 - Baby born at a local birthing hospital (< 25 miles from lab) NBS specimen collected at 26h
- Day 3 - Patient was admitted at tertiary hospital because of high blood ammonia levels
- Day 4
  - Received a call from a metabolic specialist inquiring about NBS results - specimen not received in NBS lab
  - Specimens sent via courier to Seattle Children's lab confirming diagnosis of Propionic Acidemia
  - Patient underwent dialysis
- Day 5 - NBS specimen received, STAT testing revealed elevated C3 (propionyl carnitine)
- Day 8 - recovered from metabolic crisis

Benefits of the 2nd Newborn Screen

- Identify conditions that may not be evident in the first 48 hrs
- Identify mild forms of conditions on the NBS panel
- Rule out conditions on the NBS panel
  - Cutoffs are tailored on the 1st screen to reduce the # of borderline abnormal results & unnecessary referrals (decrease false positives)
- Resolve interfering substances (e.g. mom's levels, administered medications)
- Confirm disease/trait – without need for further testing in some cases

WASHINGTON STATE NEWBORN SCREENING PROGRAM

LIST OF DISORDERS TESTED BY THE NEWBORN SCREEN (AKA HEELSTICK):

Amino Acid Disorders

*Argininosuccinic acidemia (ASA)
*Citrullinemia (CIT)
Homocystinuria (HCY)
*Maple syrup urine disease (MSUD)
Phenylketonuria (PKU)
Tyrosinemia type I (TYR-I)

Fatty Acid Disorders

Carnitine uptake deficiency (CUD)
*Long-chain L-3-hydroxy acyl-CoA (LCHAD) deficiency
*Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency
*Trifunctional protein (TFP) deficiency
*Very-long chain Acyl-CoA dehydrogenase (VLCAD) deficiency

Organic Acid Disorders

3-hydroxy-3-methylglutaric aciduria (HMG)
Beta-ketothiolase deficiency (BKT)
Glutaric acidemia type I (GA-I)
*Isovaleric acidemia (IVA)
*Methylmalonic acidemias (CblA,B and MUT)
Multiple carboxylase deficiency (MCD)
*Propionic acidemia (PROP)

Other Disorders

~~Biotinidase deficiency (BIOT)~~
*Congenital adrenal hyperplasia (CAH)
Congenital hypothyroidism (CH)
Cystic fibrosis (CF)
*Galactosemia (GALT)
Hemoglobinopathies (Hb)

Washington State Department of Health

2nd Screen & Adrenal Hyperplasia

- Sensitivity is increased
  - 73% sensitivity with 1 screen in Wisconsin Study – 2005
- False Negatives are reduced
  - 22% false negatives with 1 screen in Minnesota Study - 2012

Congenital Adrenal Hyperplasia (CAH)

	Salt Wasting	Simple Virilizing	Non Classical	Total
CAH cases	42 (71%)	13 (24%)	3 (5%)	58
Total # screened	1: 19,000	1:58,000	1:270,000	809,849
False Negative on 1st NBS	8 (19.0%)	10 (76.9%)	---	18 (33%)
Overall False Negative	1a (2.3%)	1b (7.1%)	---	2 (3.6%)

10 year review of CAH Data from Washington State Department of Health
a 724g baby, 17OHP=53.5 on the 1st NBS and was on steroid treatment for 2nd NBS (17OHP=23.26)
b 3941g baby, 17OHP=25.16 on the 1st NBS and did not have a routine 2nd NBS

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PEDIATRICS Vol. 125 Supplement May 2010, pp. S48-S53

Effect of Laboratory Practices on the Incidence Rate of Congenital Hypothyroidism

Vicki Hertzberg, PhD, Joanne Mei, PhD, Bradford L. Therrell, PhD

"… laboratories that used a TSH assay for initial screening reported a 24% higher incidence rate of CH than those that used a T4 assay."

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PEDIATRICS Vol. 76 No. 5 November 1985, pp. 734-740

Screening for Congenital Hypothyroidism With Specimen Collection at Two Time Periods: Results of the Northwest Regional Screening Program

Stephen H. LaFranchi MD, et al.

"… a routine second specimen led to an added detection rate of infants with hypothyroidism"

" … even very mild cases of congenital hypothyroidism which escape clinical diagnosis are at risk for neurologic damage."

Screening Practices for Congenital Hypothyroidism

State	Method /Cutoff	2nd Screen	Detected by 2nd Screen	# Infants /Year	Prevalence
California	TSH ≥100	No	- - -	275	1: 2,200
Oregon	T4<5; TSH>25	Yes	33%	25	1: 2,000
Idaho	T4 <5; TSH>25	Yes	42%	12	1: 2,000
Washington	TSH≥15	Yes	33%	65	1:1,300

"… after adjusting for screening methodologies and parameters, an increasing incidence rate still persisted."

2nd Screen & Hypothyroidism

Classification	1st Screen	Subsequent Screen	Total
Presumptive	41	7	48
Borderline	8	17	25
TOTAL	**49 (67%)**	**24 (33%)**	**73***

2010 Data from Washington State Department of Health

Picking up True Positive Cases on the 2nd Screen: **Homocystinuria**

- 4121g baby girl
- **1st screen at 69 hrs of life: Methionine = 64 µmol/L**
  - cutoff at the time was 80 µmol/L, now it would be < 72 µmol/L
- **2nd screen at 15 days of life: Methionine = 257 µmol/L**
  - cutoff at the time was 80 µmol/L, now it would be < 72 µmol/L
- Diagnostic tests confirmed baby has Homocystinuria:
  - **Methionine = 490 µmol/L** (blood drawn 14 days after 2nd NBS)
  - non-responsive Vitamin B deficiency
  - baby on formula and doing well clinically
  - baby has never been symptomatic; normal physical and mental development

Picking up True Positive Cases on the 2nd Screen: **MCADD**

- 2780g baby boy
- **1st screen at 55 hrs of life:** C8 = 0.08; C10:1 = 0.07; C8/C10 ratio = 0.79; C8/C2 ratio = 0.01; all normal results
  - note: baby was in the NICU and on antibiotics, HA/TPN, and steroids
- **2nd screen at 8 days of life: C8 = 0.72**; C10:1 = 0.25; **C8/C10 ratio = 2.23; C8/C2 ration = 0.06**
- Diagnostic labs confirmed MCAD deficiency:
  - Abnormal organic acids and abnormal acylcarnitine profile
  - Genotyping: Y67H/G267R (199T>C/799G>A)
- Baby on formula

So why the 2nd Screen?

- Two Screens, the 2nd between 7-14 days is **standard of care*** in Washington, with >90% of infants having both screens performed
- We pick up 1/3 of one of the most common congenital conditions (CH) on the 2nd Screen, avoiding significant developmental & growth delays
- Offers parents & the child's medical provider increased reassurance that these conditions have been detected (increased sensitivity)

Objective # 4

Adding New Conditions
to Recommended or Mandated
Newborn Screening Panels
& What's New

Adding New Condition: - Criteria for screening

- Early identification benefits the newborn
- Treatment is available
- Nature of the condition justifies population-based screening
- A good screening test exists
- The benefits justify the costs of screening

SCID – "The Bubble Boy" Severe Combined Immunodeficiency

- Babies born with SCID lack immune cells, lymphocytes
- Early detection can avoid severe infections & prevent deaths
- With stem cell transplant, children can be 'cured'

David Vetter, Baylor College of Medicine Archives

2014 New Screening Addition

- 2010: SCID recommended nationally by HHS
- 2012: WA Newborn Screening Committee approved
- October 9, 2013: State Board of Health Meeting - unanimous approval to add SCID to Washington's required screening
- WAC 246-650-020 newborn screening rule will be revised to reflect this
- January 1, 2014: planned implementation

*Test done on same collected dried blood spot

Costs of Screening

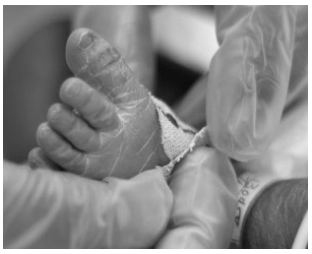
- $60.90 – per baby (2012 and current)
- $69.00 – per baby (post SCID implementation)

- Plus $8.40 per baby to help support clinic care

Critical Congenital Heart Disease (CCHD) – Pulse Oximetry Screening

"**The goal…** is to identify newborns with structural heart defects usually associated with hypoxia in the newborn period that could have significant morbidity or mortality early in life with closing of the ductus arteriosus or other physiologic changes..."

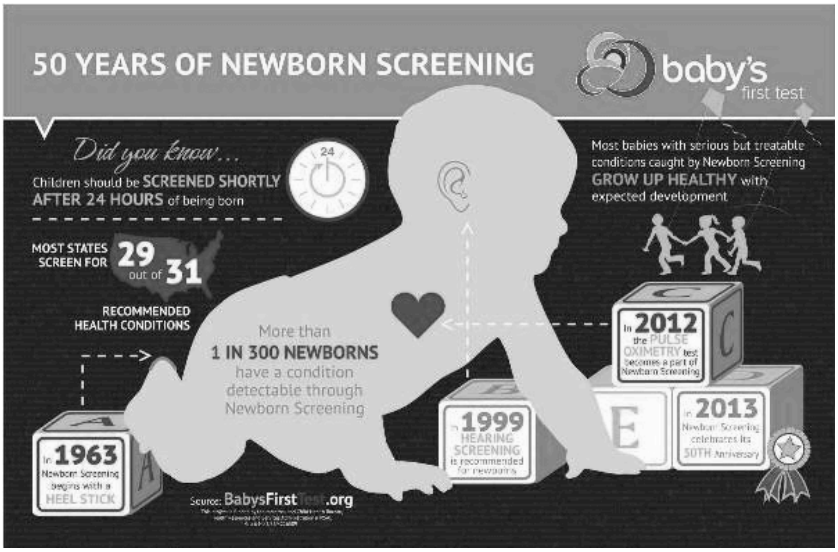
Kemper AR et al *Pediatrics* 2011



- Added to the recommended universal screening panel in 2012
- Adopted by the AAP in Jan 2013
- More Later Today…
  - Amy Schultz, MD

Objective # 5

Overview of services provided by Department of Health Newborn Screening Services & available resources



"The Newborn Screening Story:

How one simple test changed lives, science and health in America"

Learning Outcomes

- Participants will be able to provide information to their colleagues regarding the disorders screened for by Washington State's newborn screening program and those that have been universally recommended and adopted by many state hospitals.
- Participants will be able to discuss the incidence of disorders identified by newborn screening in relation to the percentage of births attended by midwives and infants born outside of hospitals in Washington State.
- Participants will be able to inform parents of the importance of newborn screening and how screening is conducted in Washington State.

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Washington State Department of Health

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