2015 Alabama Newborn Screening Conference

Marriott Hotel and Conference Center
Prattville, Alabama
Friday, September 18, 2015

The Second Newborn Screen: Detection of Congenital Hypothyroidism and Congenital Adrenal Hyperplasia

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Objectives

- Background
- Perinatal trends in thyroid and adrenal tests
- Children's AI experience: 2nd NBS (2008-2014)
- Retrospective study 2015 (HHS – SACHDNC)
- Benefits and challenges

Background

- Second screen states (23% newborns in USA)
  - 9 states - mandated (AZ, CO, DE, NV, NM, OR, TX, UT, WY)
  - 3 states - recommended (Alabama, MD, WA) >85% included
  - Second screen states also use:

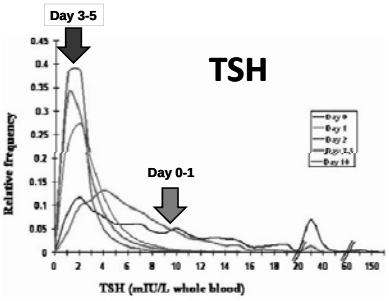
Background

- Targeted repeat screens (state specific)
- NICU premature and sick infant protocols
- One screen states (77% newborns)
  - Targeted repeat screens (state specific)
  - NICU premature and sick infant protocols

Background

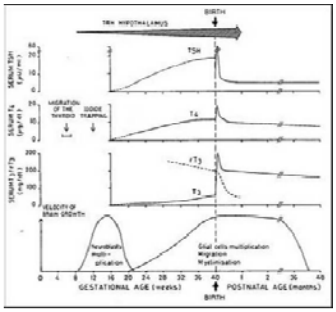
- Timing of first screen:
  - 1960's heel stick was collected @ 48-96 hours after birth
  - Later on, early discharges led to testing @ <24 hours to 48 hours
- European experience is
  - 4-6 days after birth (most screen at 3 days age)

Background



Pathology (2008) 40(2) pp 104-115. Newborn Screening

Perinatal Trends in Thyroid Levels (T4 And TSH)

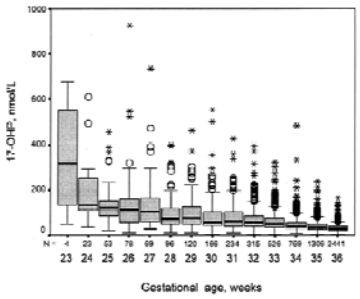


TSH

T4

Brain

Gestational Trends in CAH Labs (17-hydroxyprogesterone)



Postnatal Serum TSH Normal Infants

TSH (mU/liter)	-2SDS	-1SDS	0	+1SDS	+2SDS
Day of birth	2.43	3.84	6.44	11.75	24.03
1 day	1.90	3.21	5.54	9.76	17.58
2 days	1.40	2.61	4.64	7.94	13.10
3 days	0.94	2.03	3.75	6.24	9.65
4 days	0.60	1.48	2.85	4.63	6.82
1 wk	0.58	1.18	2.14	3.57	5.58
1 month	0.58	1.18	2.14	3.57	5.57
3 months	0.58	1.18	2.14	3.57	5.57
6 months	0.58	1.18	2.14	3.56	5.56
1 yr	0.57	1.17	2.13	3.55	5.54
2 yr	0.57	1.17	2.12	3.53	5.51
5 yr	0.56	1.15	2.08	3.47	5.41
8 yr	0.55	1.12	2.04	3.40	5.31
12 yr	0.53	1.09	1.98	3.31	5.16
15 yr	0.52	1.07	1.94	3.23	5.05
18 yr	0.51	1.05	1.90	3.16	4.93

Serum TSH <6 by 1-2 weeks

Case Example: Term Infant Diagnosed By 2nd NBS

Day collected	T4 (normal 5.1-25)	TSH (normal <25)
Day 2	T4 = 13	TSH = 16
Day 10	T4 = 10.7	TSH = 35
Day 30 (serum)	Free T4 = 0.54 (low)	TSH = 203

Blood spot TSH x 2 = serum TSH

2nd NBS Data (2008-2014) Children's Hospital Alabama

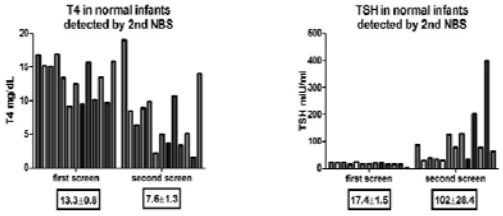
- **Congenital hypothyroidism (total 30-35 / year)**
  - **Term infants**
  - **Infants with congenital heart disease**
  - **Premature infants**

2nd NBS Data (2008-2014) Children's Hospital Alabama

- **Congenital adrenal hyperplasia (total 3-4 / year)**
  - **Term infants**

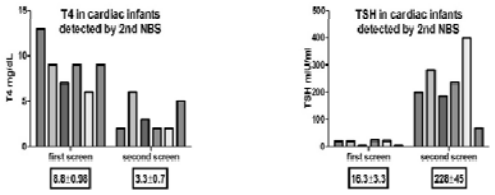
2nd NBS Data (2008-2014) - Congenital Hypothyroidism

- **13 term infants detected by 2nd screen**

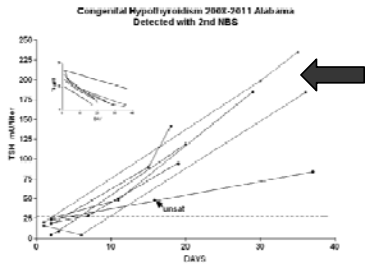


2nd NBS Data (2008-2014) - Congenital Hypothyroidism

- **6 cardiac infants detected by 2nd screen**

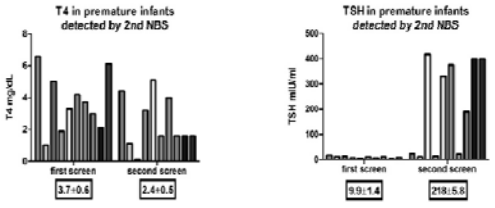


Congenital Heart Disease Newborns: Late Onset Congenital Hypothyroidism



2nd NBS Data (2008-2014) -Congenital Hypothyroidism

- **10 premature infants detected by 2nd screen**



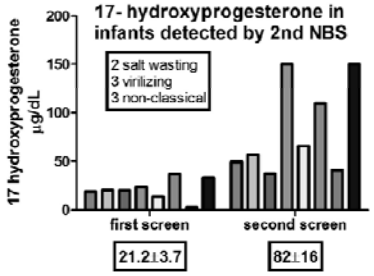
SUMMARY: 2nd NBS Data (2008-14) - Congenital Hypothyroidism

	Number	TSH range
Term infants	13	25-400
congenital heart disease	6	68-400
Premature infants	10	12-417
TOTAL	29	

- **29 infants detected by 2nd newborn screen**
- **~12 % of the all infants detected by both screens over the 7 year review**

2nd NBS Data (2008-2014) - Congenital Adrenal Hyperplasia

- 8 term infants detected by 2nd NBS



SUMMARY: 2nd NBS Data (2008-14) – Congenital Adrenal Hyperplasia

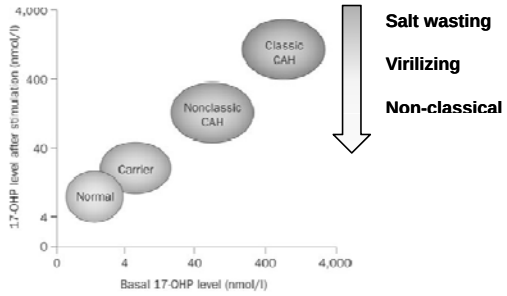
- 8 infants detected by 2nd newborn screen

	Number	Clinical
salt-wasting	2	life threatening
virilizing	3	preventable morbidity
non-classical	3	long-term variable impact
TOTAL	8	

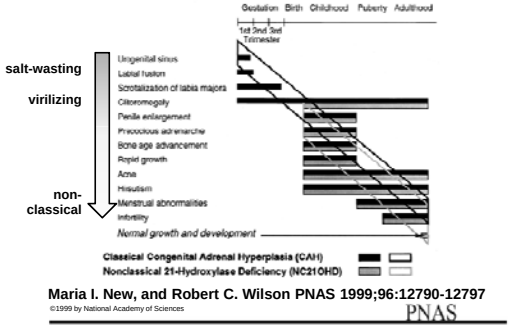
SUMMARY: 2nd NBS Data (2008-14) – Congenital Adrenal Hyperplasia

- ~40% of the all infants detected by both screens over the 7 year review

CAH Enzyme Deficiency is a Spectrum



Clinical Spectrum of Steroid 21-OHD

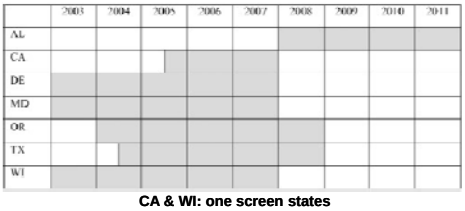


Maria I. New, and Robert C. Wilson PNAS 1999;96:12790-12797

PNAS

Retrospective Study (2003-2011) CH & CAH in One – and Two Screen States

- Commissioned by SACHDNC 2006 – coordinated by CDC and APHL and others



CA & WI: one screen states
AL, DE, MD, OR, TX: two screen states

Retrospective Study (2003-2011) Congenital Adrenal Hyperplasia

Detection rate of congenital adrenal hyperplasia cases.

CAH type	One-screen states	Two-screen states	p-Value[a]
Cases identified on the first screen and detection rates			
Salt wasting	69	125	0.225
	1/25,226	1/21,017	
Simple virilizing	12	20	0.788
	1/145,049	1/131,481	
Non-classical	5	17	0.101
	1/348,117	1/154,684	
Total number of cases identified and detection rates			
Salt-wasting	75	139	0.153
	1/23,208	1/18,918	
Simple virilizing	14	45	**0.012**
	1/124,328	1/58,436	
Non-classical	8	81	**<0.001**
	1/217,573	1/32,465	

[a] Based on Z-test for 2 proportions; significant p-values are shown in bold font.

All data from Alabama & Texas

	Two-screen states	
	# First screen	# Second screen
salt wasting	125	9
virilizing	20	23
non-classical	17	60
total	165	99 (36%)

Retrospective Study (2003-2011) Congenital Hypothyroidism

- **2251 cases / 4.64 million births**
- **11.5 % CH detected by 2nd NBS**
- **Detection rates similar: 1:1904 vrs 1:2201 (one vrs two screen states)**
- **Multivariant analysis: ethnicity important**

  (Hispanic & Asian / PI more likely detected on 2nd versus 1st NBS)

Conclusions - difficult retrospective analysis

Benefits and Challenges 2nd Newborn Screening

- **New, clinically important cases are identified**
- **Early treatment averts mortality |and morbidity**
- **Reveals broader disease spectrum**
- **Acts as safety net regarding first screen deficits:**

Benefits and Challenges 2nd Newborn Screening

- **Screens that are too early, inadequate, missed**
- **Ethnic trends detected for CH by 2nd screen**
- **Alabama was the only southeastern state represented in the 2015 CDC retrospective study**

Benefits and Challenges 2nd Newborn Screening

- **Mild disease variants are identified**
  - **More extensive diagnostic testing often required**
  - **Unclear therapeutics (? to follow or treat)**
- **Long term outcome studies are lacking**
  - **Local state programs are ideal models**

Benefits and Challenges 2nd Newborn Screening

- **Extra expense (versus cost of delayed diagnosis)**
- **2nd screen not adjusted to post-natal TSH norms**
- **Prospective studies are needed**

Acknowledgements

- **Leslie Pitts, CRNP**
  - **Endocrine Newborn Screening**
  - **Consultant Children's Hospital Alabama**
- **Alabama Newborn Screening Program and Laboratory - for their collaboration and support in the care of children with congenital endocrine disorders**

Faculty

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