

# Missed Cases of Primary Congenital Hypothyroidism in NICU Babies in California


Heidi Lerner, MPH, MS, RN  
Genetic Disease Screening Program  
California Department of Public Health



# Objectives

- Review possible reasons why babies in neonatal intensive care units (NICU) constitute the majority of missed primary congenital hypothyroidism (PCH) cases in California.
- Explore strategies for reducing the risk of missing PCH in NICU babies.





# California screens for primary congenital hypothyroidism (PCH) by measuring thyroid stimulating hormone (TSH)

- PCH constitutes 90% of all cases of congenital hypothyroidism
- PCH is defined by low thyroxine (T4) and elevated TSH





# January 2008-September 2011

## 1.94 million babies screened in California

21 reported diagnosed cases of PCH that had negative newborn screens, i.e., were false negatives (FN). Of those:

- 16 (76%) were in NICU when screened
- 6 (28%) had Down Syndrome (DS)
- 4 (19%) had cardiac anomalies

Mean age at specimen collection: 55.3 hours

Mean age at initiation of treatment: 46 days





# Standard of Care

American Academy of Pediatrics (2006):

Thyroid therapy started within 2 weeks of age can normalize cognitive development

By this standard, there was a delay in treatment, placing these 21 babies at risk of impaired physical and mental development.



## Risk Factors for Undetected PCH

- PCH is more prevalent in very low birth weight (VLBW) babies (<1500 g) than in non-VLBW babies (Woo, et al, 2011)
- PCH is more prevalent in babies with DS than in general population (Coleman, 1994)
- The probable reason DS, VLBW and sick babies are at risk for having missed PCH is delayed rise in thyroid stimulating hormone (TSH) i.e., an initial specimen that had a normal TSH level and an elevation detected on subsequent test(s)



## Risk Factors for Undetected PCH (Cont.)

### Risk factors for delayed TSH rise:

- Immaturity of the hypothalamic-pituitary-thyroid axis (HPT) in preterm babies
- HPT axis affected with non-thyroidal illness, congenital anomalies (especially cardiac), and DS (Van Trotsenburg, et al, 2002)
- Some drugs commonly used in NICU (dopamine, steroids) suppress TSH (Larson, et al, 2003)
- Exposure to iodine-containing agents used as cleansing agent for procedures (surgical prep) or as a contrast agent for radiological procedures can cause transient hypothyroidism (Gruniero-Papendieck, et al, 2005)





# CALIFORNIA'S CURRENT PRACTICES

- Measures TSH using a fluoroimmunoassay
- TSH > 29 mIU/L is reported out. Primary care providers are instructed to have confirmatory testing done, advised to consult with an endocrinologist
- Babies are routinely screened once
- Specimen to be collected between 12-144 hours of age, and ideally 24-48 hours
- Specimen collected prior to transfusion, regardless of age; 2<sup>nd</sup> spec. collected at least 24 h post-transfusion





# January 2008-September 2011

Diagnosed PCH cases:	963
PCH cases in NICU babies:	128 (13%)
% PCH cases in NICU that were missed (16/128):	12.5%
% PCH reported cases missed by NBS (21/963)	2.2% (?)
Overall PCH prevalence:	1:2018
PCH Prevalence in NICU babies:	1:1241
<b>NICU babies constitute 8% of all babies screened, and 76% of missed PCH cases</b>	



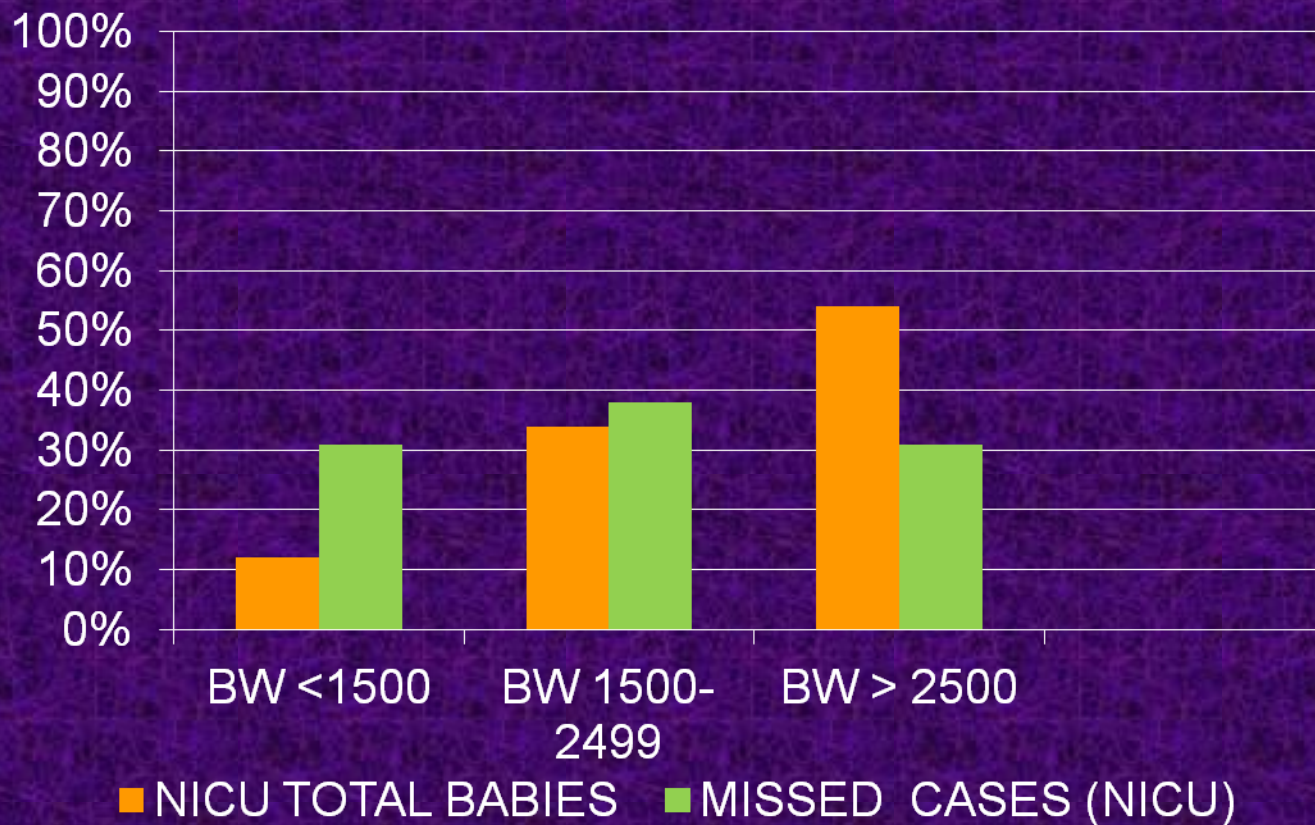


# # Missed NICU PCH Cases by Birth Weight

## N=16

<b>&lt;1500 gm</b>	<b>1500-2499 gm</b>	<b>&gt;2500 gm</b>
5 (31%)	6 (38%)	5 (31%)

# Total NICU Babies by Weight vs. Missed NICU PCH Cases by Weight







# Approaches to Reducing Number of Missed PCH Cases in NICUs

## ➤ **Serial screening**

Clinical and Laboratory Standards Institute recommends screening x 3 while in NICU: on NICU admission, at 48-72 hours, and at 28 days or discharge (CLSI, 2009) *While most babies' HPT axis is functioning by 1 month, it can take up to 171 days* (Larson, et al, 2006)

## ➤ **Single screen with a lower cutoff for NICU babies** (Korada, et al, 2008)

## ➤ **Full thyroid function evaluation (by neonatology-endocrinology team) at discharge or at 30 days, whatever comes first** (Kugelman, et al, 2009)





\$



# Conclusion

No screening program will detect all babies with primary congenital hypothyroidism.

However, the data indicate that by adopting a different screening strategy for NICU babies that addresses their risk factors, there would likely be a significant reduction in false negatives.







# Acknowledgements

Fred Lorey, Ph.D., Chief, Program & Policy,  
Genetic Disease Screening Program, CDPH

Erica Gordon, MS, Chief, Newborn Screening  
Clinical Services Branch, Genetic Disease  
Screening Program, CDPH

Tracey Bishop, BS, Program Specialist, Genetic  
Disease Screening Program, CDPH

