Missed Cases of Primary Congenital Hypothyroidism in NICU Babies in California

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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

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>29mIU/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; 2nd 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

NICU babies constitute 8% of all babies screened, and 76% of missed PCH cases
# Missed NICU PCH Cases by Birth Weight

N=16

<table>
<thead>
<tr>
<th>Birth Weight Range</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1500 gm</td>
<td>5</td>
<td>31%</td>
</tr>
<tr>
<td>1500-2499 gm</td>
<td>6</td>
<td>38%</td>
</tr>
<tr>
<td>&gt;2500 gm</td>
<td>5</td>
<td>31%</td>
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</tbody>
</table>
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