

The Benefits of Early Treatment of Severe Congenital Hypothyroidism (CH) Prior to Serum Thyroid and Technetium (Tc) Scan Results

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Thyroid Screening in WA State

- Two screen state
- Thyroid screening began in 1977:
Primary T4
- Switch to Primary TSH in July 2004
- Cut-offs stratified according to age
at collection



Current Cut-off Table

TSH (IU/mL) serum	1 to 12 hrs	13 to 24 hrs	25 to 36 hrs	37 to 48 hrs	49 to 504 hrs 2-21 days	>504 hours >21 days
0 – 14.99	Normal	Normal	Normal	Normal	Normal	Normal
15.00 – 19.99	Normal	Normal	Normal	Normal	Normal	Borderline
20.00 – 24.99	Normal	Normal	Normal	Normal	Borderline	Borderline
25.00 – 29.99	Normal	Normal	Normal	Borderline	Borderline	Borderline
30.00 – 44.99	Normal	Normal	Borderline	Borderline	Borderline	Borderline
45.00 – 54.99	Normal	Borderline	Borderline	Borderline	Borderline	Borderline
55.00 – 59.99	Borderline	Borderline	Borderline	Borderline	Borderline	Borderline
60.00 – 99.99	Borderline	Borderline	Presumptive	Presumptive	Presumptive	Presumptive
≥100.00	Presumptive	Presumptive	Presumptive	Presumptive	Presumptive	Presumptive



Protocol In Follow-up for Severe CH

- Call PCP and fax a memo
- Serum thyroid studies
- Initiate treatment after work-up
- Consult with pediatric endocrinologist





CLINICAL REPORT

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Susan R. Rose, MD, and the Section on Endocrinology and Committee on Genetics

AMERICAN THYROID ASSOCIATION

Rosalind S. Brown, MD, and the Public Health Committee

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“... the infant should be examined immediately and have confirmatory serum testing to verify the diagnosis. Treatment with replacement levothyroxine should be initiated as soon as confirmatory tests have been drawn and before the results of the confirmatory tests are available.”

Supporting Journal Articles:

1. **Rastogi MV and La Franchi SH. Congenital Hypothyroidism. Orphanet J Rare Dis. 2010; 5: 17.**
2. Selva KA, La Franchi SH, et. al. Neurodevelopmental Outcomes In Congenital Hypothyroidism: Comparisom of Initial T4 Dose and Time to Reach Target T4 and TSH. J Pediatrics 2005; 147: 775-80.
3. Huo K, Zhu C, et. Al. Risk Factors for Neurodevelopmental Deficits in Congenital Hypothyroidism After Early Substitution Treatment. Endocrine Journal Advance Publication 2011; 10: 1-7.
4. Selva KA, La Franchi SH, et. al. Initial Treatment Dose of L-Thyroxine In Congenital Hypothyroidism. J Pediatrics 2002; 141 (6):786-792.
5. La Franchi SH: Should the Levothyroxine dose be Tailored to Disease Severity in Neonates with Congenital Hypothyroidism? Nature Clinical Practice: Endocrinology & Metabolism 2008; 4 (12): 658-659.



Dilemma in Recommendation Compliance



Wait for the
official
**Technetium
Scan** results
before
treatment ??

Demographics of True CH Cases

Year	Total Cases	Severe	Mild
2004	30	14	16
2005	54	39	15
2006	43	32	11
2007	48	32	16
2008	83	53	30
2009	72	44	28
2010	74	56	18
TOTAL	404	270	134



CH Prevalence in WA State

Year	# Screened	# True	Prevalence
2005	77,299	54	1: 1,431
2006	82,609	43	1: 1,921
2007	84,925	48	1: 1,769
2008	86,058	83	1: 1,037
2009	84,780	72	1: 1,176
2010	82,930	74	1: 1,120

*Median TSH for Severe CH on 1st NBS=210



TSH Thresholds – What is *Urgently* Presumptive?

TSH Level (\geq)	True (+)	False (+)	PPV
411	111	0	100%
300	150	4*	97%
200	188	9	95%
150	208	29	88%
125	229	60	79%
100	258	172	60%
75	296	587	34%
55	348	1985	15%
25	535	3736	13%
15	666	4308	13%
ALL	780	8007	9%

*Mom was on thyroid medication in all 4 cases

2010 Presumptive Screens: Days from Referral to Treatment

Days	# of Cases
0	19
1	14
2	9
3	4
4	1
8	1
TOTAL	48



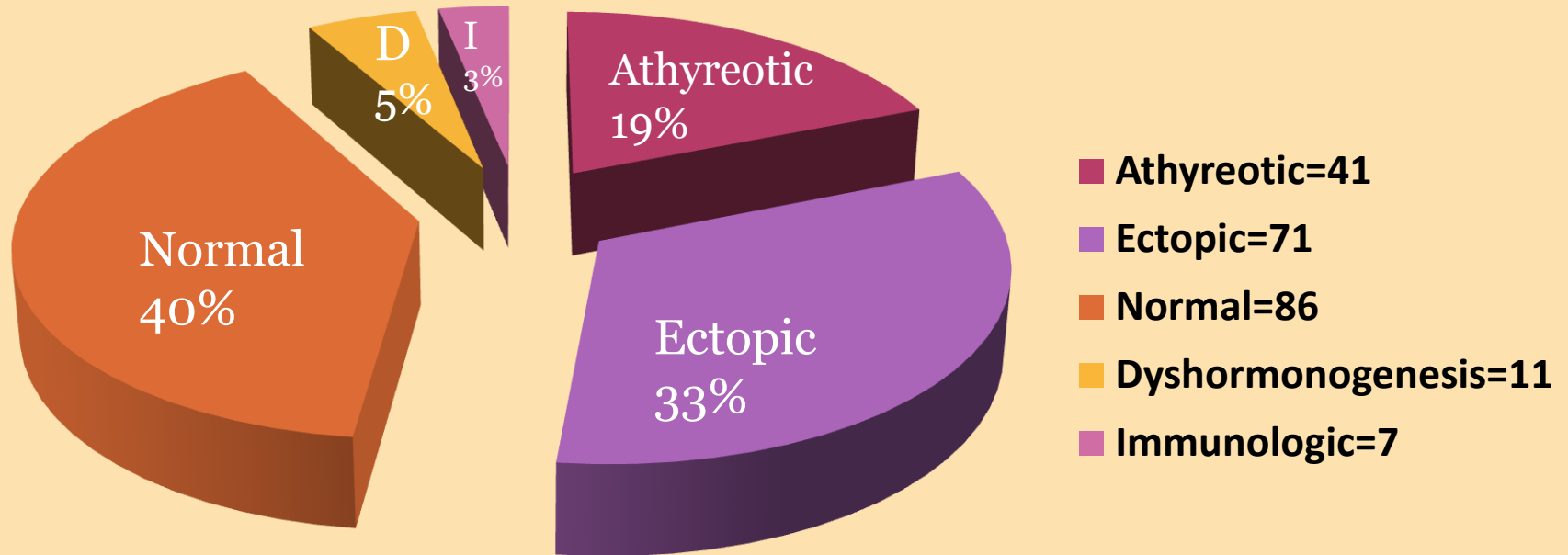
2004-2010 Confirmed CH Cases

Technetium Scan Results

SCAN DATA	TOTAL	Severe / Mild
Technetium Scans done	216	-
A) Scans <u>before</u> treatment (13%)	29	13 / 16
ABNORMAL scans before treatment	16 (55%)	-
Normal scans before treatment	13 (45%)	-
B) Scans <u>same day</u> treatment (25%)	54	37 / 17
ABNORMAL scans same day treatment	30 (56%)	-
Normal scans same day treatment	24 (44%)	-
C) Scans <u>post</u> treatment (62%)	133	106 / 27
ABNORMAL scans post treatment	79 (59%)	-
Normal scans post treatment	54 (41%)	-

*Scan is not required to confirm diagnosis of CH but is helpful in prognosticating and determining the etiology.

True CH (Scan Results: N=216)





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“Treatment need NOT be delayed to perform the scan. A thyroid scan can be performed within the first few days of treatment, because the elevated TSH found in patients with permanent CH rarely normalizes within this time period.”

Time to Normalization of TSH

Days to normal TSH	Total
0-15 days post Tx	63 (71%)
16-30 days post Tx	26 (29%)
Total	89 (100%)

*Available data from 89 (22%) of the 404 true positive cases 2004-2010



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- ❖ Regardless of normal Tc scan results, confirmatory serum results should guide initiation of treatment unless **TSH \geq 300** where immediate hormone replacement therapy is warranted.

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- ❖ NBS follow-up recommendations will be more aggressive for **TSH \geq 300**
- ❖ Regardless of early treatment, athyreotic & ectopic CH (severe forms) will still manifest in the thyroid scan
- ❖ Regardless of normal Tc scan results, confirmatory serum results should guide initiation of treatment unless **TSH \geq 300** where immediate hormone replacement therapy is warranted.
- ❖ Review of available progress notes and subsequent NBS revealed:
 - 71% treated early had normal TSH within 0-15 days,
 - 29% had normal TSH within 16-30 days post treatment.

Newborn Screening Follow-up

Recommendations when TSH \geq 300:

1. Draw baseline serum thyroid studies on the same day of referral (coordinate with PCP)
2. Inquire if mom is on PTU or other thyroid meds
3. Recommend starting Levothyroxine immediately (prior to serum results)
4. If possible, schedule Tc Scan on same day of lab draw. If not, schedule it as soon as feasible.



Bottom line: Benefits of Early Treatment

- ✓ Studies have shown inverse relationship between IQ and age at diagnosis
- ✓ Regardless of Tc scan results and prior to obtaining confirmatory serum results, patients with **TSH \geq 300** should start treatment to mitigate the loss of IQ points.
- ✓ **GOAL:** Early diagnosis, prompt and adequate treatment, appropriate long-term follow-up is essential to achieve the best neurodevelopmental outcome close to their genetic potential!



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Thank you!

*Washington State
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