CONGENITAL HYPOTHYROIDISM

IN PRETERM AND NEWBORN

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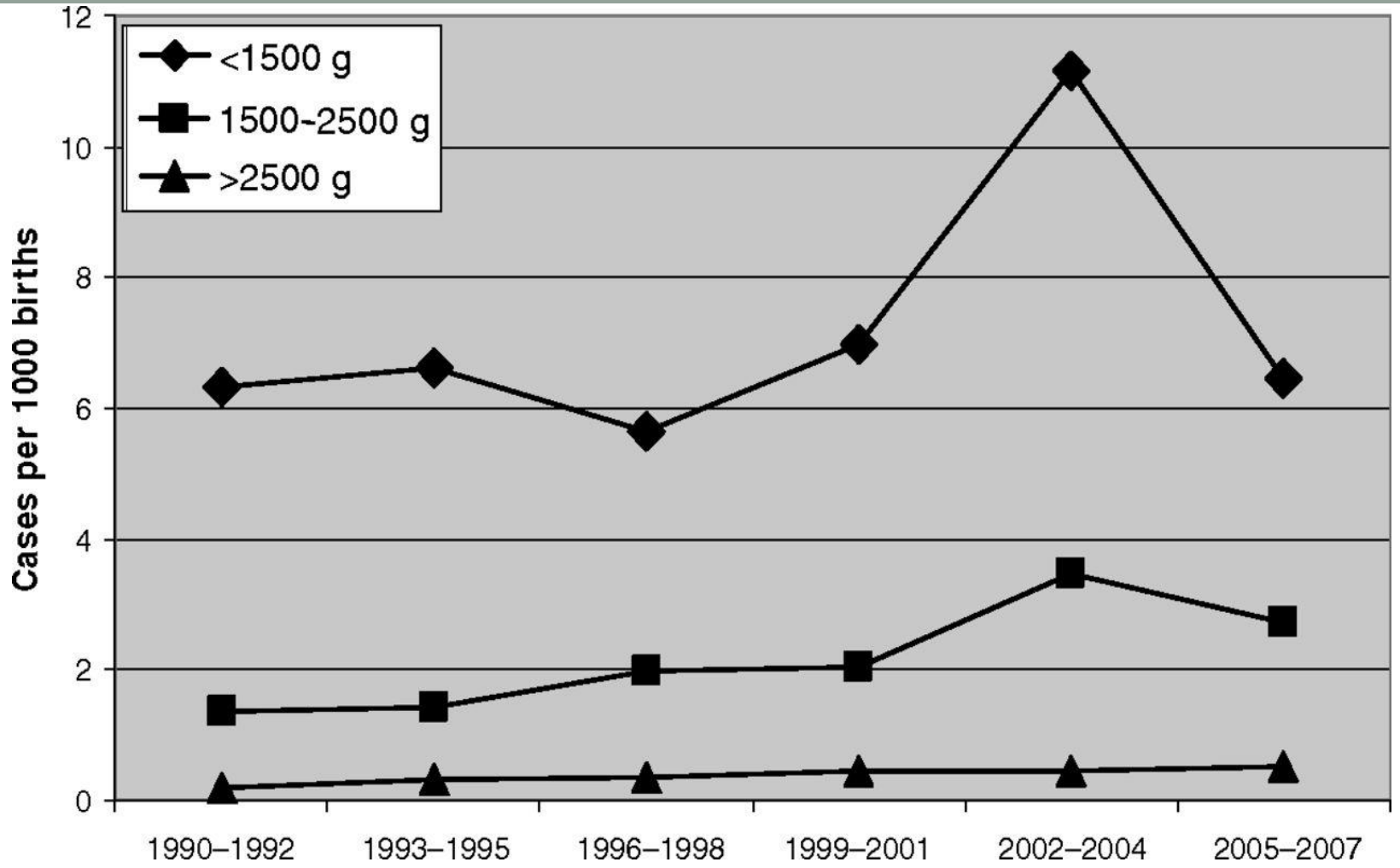
INTRODUCTION

- Congenital hypothyroidism (CH) is the most common congenital endocrine disease
- Cause of preventable mental retardation
- Endocrinologists and pediatricians recommend diagnosing CH as soon as possible
- L-thyroxine supplementation started within 2–3 weeks of age can prevent severe neurological damage

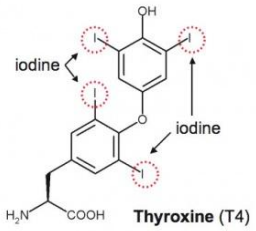
Carlo Corbetta, Clinical Endocrinology (2009) 71, 739–745
Screening of congenital hypothyroidism in preterm, low birth weight and very low birth weight neonates: A systematic review



Incidence rate of CH in Massachusetts, 1990–2007, for 3-year intervals, stratified according to birth weight category. The scale does not show the 2.5-fold increase in the incidence rate that occurred for newborns born at >2500 g.

PEDIATRICS Volume 125, Supplement 2, May 2010

PHYSIOLOGY



TH supply from the mother HCG exhibits a weak TSH

First trimester

10-12 weeks

Thyroid begins to collect and store iodine

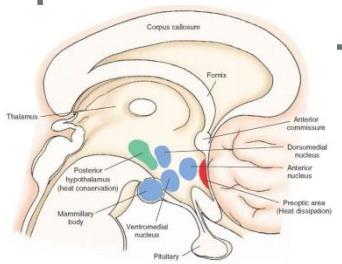
begins to secrete hormones

16 week

Second trimester

24-33 weeks

The hypothalamus take on an adult-like



FT4 serum concentrations continue to rise until 36 week

Third trimester

TSH, T3, and FT4 levels rapidly rise within the first postnatal half-hour

Monika Chaudhari, Thyroid Function in the Neonatal Intensive Care Unit

THYROID HORMONE TESTING

- The test should be collected after 24-hours postnatal age
- Preterm infants are at high risk for hypothyroidism with delayed TSH rise because of hypothalamic pituitary thyroid axis immaturity
- Rescreening should be collected at 2-weeks postnatal age or 2 weeks after the first screen was obtained
- Measuring both FT4 and TSH in primary screening tests and following tests

Monika Chaudhari, Thyroid Function in the Neonatal Intensive Care Unit

Artifacts and conditions that may affect thyroid function test interpretation

- **Iodine**

  (Wolff-Chaikoff is not typically mature)
- **Nonthyroidal Illness**

  (Respiratory distress syndrome, sepsis, …)
- **Medications**

  (Dopamine, Steroid, Metoclopramide, Caffeine, Heparin)
- **Maternal Factors**

  (Maternal TSH receptor blocking antibodies, thyroid medications)

Monika Chaudhari, Thyroid Function in the Neonatal Intensive Care Unit

Mengreli et al studied 311390 screened infants in Greece

TSH ≥ 20 mU/L: missing 40% of pre-term infants with CH

TABLE 1. Infants with CH and the recall rate in relation to various cutoff points of TSH in 311,390 screened newborns during a 3-yr period (January 2000 to December 2002)

TSH cutoff (mU/liter whole blood)	Newborns recalled, n	Recall rate (%)	Infants with CH, n
30	173	0.05	114
20	376	0.12	144
10	3784	1.20	200

Chryssanthi Mengreli, Screening for Congenital Hypothyroidism: The Significance of Threshold Limit in False-Negative Results, *The Journal of Clinical Endocrinology & Metabolism*, Volume 95, Issue 9, 1 September 2010, Pages 4283–4290

Carlo Corbetta

Retrospective study of 629,042 newborns screened with b-TSH cutoffs of 12 (years 1999–2002) or 10 mU/l (2003–2005)

Table 1. Global results of newborn screening programme for congenital hypothyroidism (CH) in Lombardy between 1999 and 2005

b-TSH cutoff (mU/l)	Screened newborns	Positive cases at 1st b-TSH	Recall rate after 1st b-TSH (%)	Positive cases detected by screening	Positive cases with hyperTSH	Positive CH cases on therapy	CH incidence per 10,000 births
12	348,715	2463	0·71	452	260	192	5·51 (1:1816)
10	280,327	3012	1·07	561	318	243	8·66 (1:1154)
Overall 99-05	629,042	5475	0·87	1013	578	435	6·91 (1:1446)
20 (virtual)	629,042	523	0·08	280	45	237	3·77 (1:2654)

b-TSH cutoff values for the first determination on blood spot were 12 mU/l in the period 1999–2002 and 10 mU/l in the period 2003–2005. A total of 435/1013 candidate newborns (43%) were found to be hypothyroid and started L-T4 treatment (true CH). The category of positive newborns with hyperthyrotropinaemia (hyperTSH) includes the cases positive at the 2nd TSH determination in whom L-T4 treatment was not started because hypothyroidism was not confirmed by the follow-up centres. The results of the screening that would had been obtained in the same period 1999–2005 with the virtual cutoff of 20 mU/l are reported in the last row for comparison.

 Clinical Endocrinology, **71**, 739–745

Sirinvasan et al, the North-East and North Cumbria region of England (3 years)

- Cutoffs TSH 6 mU/L
- TSH 6-20 mU/L: suspicious => repeat the test in gestational age at 36 weeks in newborns

➢ Increases false positives by 28-folds, while some cases were still misses

➢ Causing financial and psychological burden

Srinivasan R, Harigopal S, Turner S, Cheetham T. Permanent and transient congenital hypothyroidism in preterm infants. *ActaPaediatr*. 2012 ;101:e179_82

European Society for Paediatric Endocrinology Consensus Guidelines

Juliane Léger, Antonella Olivieri, Malcolm Donaldson, Toni Torresani,Heiko Krude, Guy van Vliet, Michel Polak, and Gary Butler; on behalf of ESPEPES-SLEP-JSPE-APEG-APPES-ISPAE, and the Congenital Hypothyroidism Consensus Conference Group

RECOMMENDATIONS

1	Strong recommendation
2	Weak recommendation
A	High quality
B	Moderate quality
C	Low quality

RECOMMENDATIONS (European Society for Paediatric Endocrinology Consensus Guidelines)

If venous free T4 (FT4) concentration is below norms for age, treatment should be started immediately	**1A**
If venous TSH concentration is ≥20 mU/L, treatment should be started, even if FT4 concentration is normal	**2B**
If venous TSH concentration is ≥6 to 20 mU/l beyond 21 days in a well baby with a FT4 concentration within the limits for age, we suggest a) investigation, which should include diagnostic imaging, to try to obtain a definitive diagnosis; b) consideration, in discussion with the family, of either initiating thyroxine supplementation immediately and retesting, off treatment, at a later stage; or with holding treatment but retesting twoweeks later	**2B**

RECOMMENDATIONS (European Society for Paediatric Endocrinology Consensus Guidelines)

L-T4 alone is recommended as the medication of choice for treating CH	**1B**
L-T4 treatment should be initiated as soon as possible and no later than 2 weeks after birth or immediately after confirmatory serum test results in infants in whom CH is detected by a second routine screening test	**1B**
An initial L-T4 dose of 10–15 μg/kg per day should be given	**1B**
Infants with severe disease, as defined by a very low pretreatment TT4 or FT4 concentration, should be treated with the highest initial dose	**1B**

RECOMMENDATIONS (European Society for Paediatric Endocrinology Consensus Guidelines)

Serum or plasma FT4 (or TT4) and TSH concentrations should be determined at least 4 hours after the last L-T4 administration	**1B**
TSH concentration should be maintained in the age specific reference range; TT4 or FT4 concentration should be maintained in the upper half of the age-specific reference range	**1B**
The first follow-up examination should take place 1–2 weeks after the start of L-T4 treatment	**1C**
Subsequent evaluation should take place every 2 weeks until a complete normalization of TSH concentration is reached; then every 1 to 3 months thereafter until the age of 12 months	**1C**

CONCLUSIONS

- Congenital hypothyroidism (CH) is the most common congenital endocrine disease, cause of preventable mental retardation
- Newborn should receive TSH and T4 based screening for congenital hypothyroidism in the first several days after birth
- Screens should be collected after 24-hours postnatal age in preterm
- Rescreening should be collected at 2-weeks postnatal age or 2 weeks after the first screen was obtained
- L-T4 treatment should be initiated immediately after confirmatory serum test results in infants in whom CH

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THANK YOU!