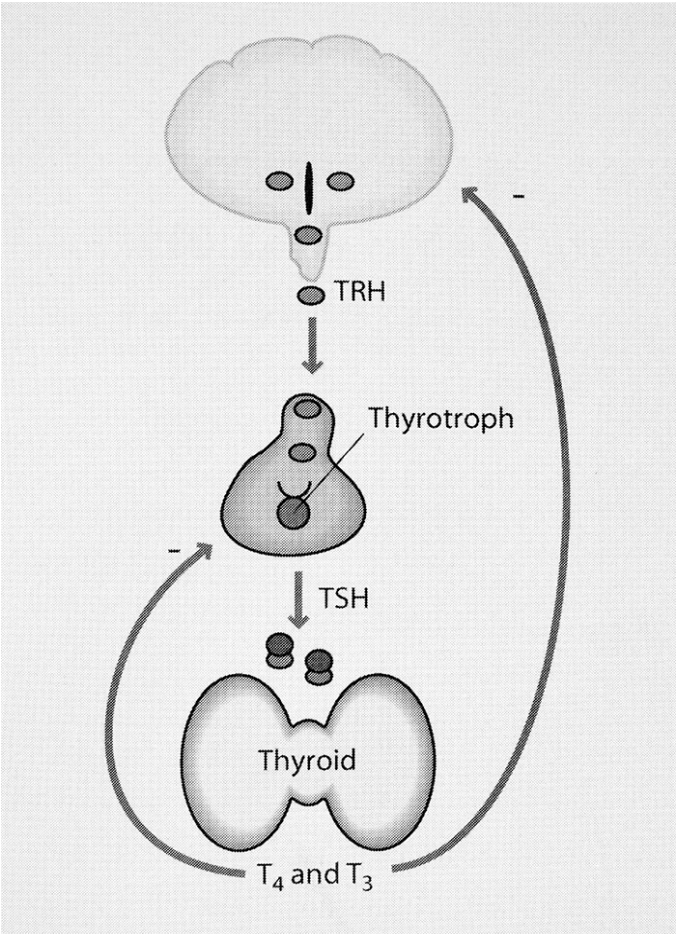
WHEN SUSPECTING A THYROID DISORDER:
WHAT TESTS TO ORDER AND WHEN?
WHAT DO THE RESULTS MEAN?

Tarek Bisat, M.D.
Pediatric Endocrinology Center
Beverly Knight Olson Children's Hospital , Navicent Health
Mercer University School of Medicine



Normal H-P-Thyroid **axis**

Total or Free thyroid hormone?

- T_4 & T_3 are bound to thyroid binding globulin (TBG) and other serum proteins
- Biologically active ***free*** T_4 & T_3 are < 1% of total serum T_4 & T_3
- Want to measure total T_4 ? You also need to measure T_3 Resin uptake (T_3RU) for indirect assessment of free hormone

Simpler and more relevant:

- For thyroid function assessment: Measure ***free*** T_4 & TSH
- Measure ***free*** T_3? Only for suspicion of hyperthyroidism

Practical Use of Thyroid tests

- When suspecting hypothyroidism
- When suspecting hyperthyroidism
- Incidentally noted goiter or thyroid nodule
- Abnormal neonatal thyroid screening test

Why assess thyroid function?
Suspect ***hypothyroidism***

Suspect hypothyroidism

- Slow height growth
- Fatigue & somnolence
- Constipation
- Rapid weight gain
- Delayed puberty
- Menstrual irregularity
- Goiter
- Family history

12y girl with slow height growth & no puberty

- TSH = 75 uU/ml (ref: 0.5-4.5)
- Free T_4 = 0.6 ng% (ref: 0.8-1.6)

High TSH, low free T_4: ➔ Primary hypothyroidism

Next : Measure anti-thyroid ab ➔ Elevated ➔ Autoimmune thyroiditis

Primary hypothyroidism

- **Autoimmune thyroiditis: Most common etiology**
  - Anti-TPO and/or anti-thyroglobulin ab are elevated
  - Thyroid US: Abnormal (heterogeneous) echotexture
- Iodine deficiency : Unlikely. Ruled out by measuring urine iodine
- Medications: e.g. methimazole, excess iodine

16y girl with rapid weight gain

- TSH = 8 uU/ml (ref: 0.5-4.5)
- Free T_4 = 1.0 ng% (ref: 0.8-1.6)

Mildly elevated TSH (< 10) with normal free T_4 Is this pattern clinically significant? It depends…

Mildly elevated TSH, with normal free T_4: Clinical significance

- TSH = 5-10, **anti-thyroid ab negative**.
  - Frequent in obesity , but *not the cause of obesity*
  - Frequent in Down syndrome
  - It may remain unchanged or become normal. ➔ Observe / repeat. Consider treatment if TSH > 10
- TSH = 5-10, **anti-thyroid ab positive** ➔ Autoimmune thyroiditis
  - It is likely to progress ➔ May elect to treat

5y boy with slow height growth

- TSH = 1.2 uU/ml (ref: 0.5-4.5)
- Free T_4 = 0.6 ng% (ref: 0.8-1.6)

Normal TSH, low free T_4 ➔ TSH is "abnormally normal" *vs.* low free T_4

When free T_4 is low with non-elevated TSH

Common – *and does not usually require treatment* - in:

- Sick patients: PICU patients, anorexia, cachexia, severe depression
- Medications: Anti-epileptics (*Dilantin, Trileptal, Tegretol), g*lucocorticoids

Central hypothyroidism (TSH deficiency)?

- Suspect pituitary disorder in context of slow height growth, CNS abnormality
- Assess other hypothalamic-pituitary functions *before* treatment

Why assess thyroid function?
Suspect ***hyperthyroidism***

Suspect hyperthyroidism

- Weight loss
- Palpitations, tachycardia
- Insomnia
- Goiter
- ADHD and academic deterioration in a child
- Heat intolerance, excessive sweating
- Irregular menses
- Prominent eyes

16y boy with weight loss and bulging eyes:

- TSH = 0.006 uU/ml (ref: 0.5-4.5)
- Free T_4 = 3.4 ng% (ref: 0.8-1.6). Free T_3 = 9 pg/ml (re: 2.8-4.4)

Very low TSH, high free T_3 /T_4 ➔ Hyperthyroidism

*Next: M*easure thyroid stimulating Ig (TSI) ➔ Elevated ➔ Graves d.

Radio-iodine thyroid uptake: Homogeneously high (u*nnecessary test)*

16y girl with weight loss:

- TSH = 0..006 uU/ml (ref: 0.5-4.5)
- Free T_4 = 2 ng% (ref: 0.8-1.6). Free T_3 = 5.5 pg/ml (re: 2.8-4.4)

Very low TSH, high free T_3/ T_4 ➔ Hyperthyroidism

*Next: M*easure thyroid stimulating Ig (TSI) ➔ Low ➔ NOT Graves d.

Next: Order radio-iodine thyroid uptake

When high free T_4 & very low TSH are NOT due to Graves d.

- Thyroid radio-iodine uptake: ***High in nodule,*** low everywhere else ➔ Toxic nodule
  - To thyroid surgeon
- Thyroid radio-iodine uptake: ***Low*** ➔ Decreased function due to thyroiditis,
  - Release of pre-formed hormone
  - Etiology: Subacute (viral, idiopathic), autoimmune
  - Observe: Return to normal after few weeks or onset of hypothyroidism
- Exogenous intake: Based on history

Large thyroid and/or thyroid nodule

Common scenarios

- 14y girl, asymptomatic: Thyromegaly noted during routine physical
- 16y girl: Thyroid nodule incidentally noted by CT following concussion

Presenting problem: Goiter

- Is it dysfunctional: Hypo- or hyperthyroid?
  - Measure TSH
- Is it due to autoimmune thyroiditis?
  - Measure anti-thyroid ab titers
- Is it asymmetric? Suspect a nodule in it?
  - Thyroid US
- Is it tender: Suspect subacute thyroiditis
  - ESR

Presenting problem: Thyroid nodule

- Detected by physical exam or CT, MRI:
  - Thyroid US
- TSH very low
  - Confirm toxic nodule by radio-iodine uptake & send to surgeon
- TSH is normal, nodule < 10 mm
  - Observe and repeat US
- TSH is normal, nodule $\geq$ 10 mm
  - Fine needle aspiration to exclude malignancy

Newborn Thyroid Screening

Screening test ***alert***: Abnormal TSH &/or total T_4

Next: Measure TSH, free T_4

Baby #1

- TSH = 75 uU/ml (ref: 0.7-11)
- Free T_4 = 0.5 ng% (ref: 0.9-2.2)

High TSH, low free T_4 ➔ Primary hypothyroidism

Congenital Primary hypothyroidism

Permanent:

- Most common: Dysgenesis of the thyroid gland (Absent, small and/or ectopic)
- Infrequent: Thyroid hormone defect (*a.k.a dyshormonogenesis)*
- Imaging – US, Tc scan – not mandatory but may be informative

Transient:

- Maternal autoimmune thyroiditis: Placental transfer of anti-thyroid ab
- Maternal meds: PTU for Graves disease
- Excess use of iodine in extreme prematurity
- Undetermined

Baby #2

- TSH = 8.5 uU/ml. Normal free T_4 = 1.2 ng%
  TSH *standard lab reference* = 0.5-4.5. TSH r*eference up to age 2 mos* = 0.7-11

- Congenital hypothyroidism is unlikely. Repeat after age 2 months

- Use appropriate reference ranges to avoid unnecessary consults & treatment

Baby #3

- TSH = 2 uU/ml (ref: 0.7-11)
- Free T_4 = 0.5 ng% (ref: 0.9-2.2)

Normal TSH, low free T_4 ➔ TSH is "abnormally normal" *vs.* low free T_4

Newborn with "normal" TSH and low free T_4

- **Central Hypothyroidism (TSH deficiency)?**
  - Suspect congenital pituitary disorder in context of hypoglycemia, micropenis, CNS abnormality, cleft lip/palate, optic nerve hypoplasia
  - Assess other hypothalamic-pituitary functions ***before*** treatment. Pituitary MRI

  - **Prematurity, *a.k.a. hypothyroxinemia of prematurity***
  - Use post-conception age reference ranges
  - Treatment is often not indicated

Baby #4

- TSH = 0.01 uU/ml (ref: 0.7-11)
- Free T_4 = 3.4 ng% (ref: 0.9-2.2)

Low TSH, High free T_4 ➔ Neonatal hyperthyroidism

Neonatal hyperthyroidism

- Infrequent occurrence in offspring of mothers with currently or previously treated Graves' disease, or undiagnosed
- Maternal thyroid stimulating Ig detected in newborn
- Transient disorder but may need treatment

Babies #5, #6

- **Baby #5** neonatal screen: Normal TSH , ***low total T4*** = 3.5 mcg% (ref: 5.4-17)
- Confirmatory test: Normal TSH, ***normal free T4***

- **Baby #6** neonatal screen: Normal TSH, ***high total T4*** = 24 mcg%
- Confirmatory test: Normal TSH, ***normal free T4***

Incongruent ***total vs. free*** T_4 ➔ Thyroid binding problem

Thyroid binding problems

- Low total T_4, normal free T_4 ➔ Thyroid binding globulin **deficiency**
- High total T_4, normal free T_4 ➔ Thyroid binding globulin **excess**
- Confirm: measure serum TBG
- Clinically inconsequential TBG gene mutations

Practical Use of Thyroid Tests
Key points

Practical use of thyroid tests

- Use free T_4, *not total* T_4, with TSH to assess thyroid function
- TSH = 5-10 with negative anti-thyroid ab (e.g. obesity, DS) : Observe
- Mild thyroid test abnormality in newborn: Use age-appropriate reference ranges
- Child with high TSH, goiter, or family history: Measure anti-thyroid ab
- Graves disease is suspected: Measure thyroid stimulating Ig
- TBG deficiency or excess is suspected: Measure thyroid binding globulin

Practical use of thyroid tests

- Thyroid US:
  - Evaluation of gland size & echotexture, esp. if nodule is suspected
  - Evaluation of gland morphology in congenital hypothyroidism
- Thyroid radio-iodine uptake:
  - When hyperthyroidism is NOT due to Graves disease
- Hypothalamic-pituitary function work-up and MRI:
  - If central hypothyroidism is suspected

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