

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

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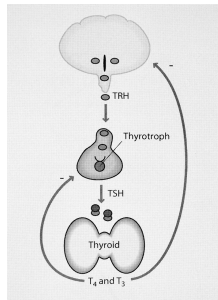
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Normal H-P-Thyroid axis

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**Total or Free thyroid hormone?**

- T<sub>4</sub> & T<sub>3</sub> are bound to thyroid binding globulin (TBG) and other serum proteins
- Biologically active **free** T<sub>4</sub> & T<sub>3</sub> are < 1% of total serum T<sub>4</sub> & T<sub>3</sub>
- Want to measure total T<sub>4</sub> ? You also need to measure T<sub>3</sub> Resin uptake (T<sub>3</sub>RU) for indirect assessment of free hormone

**Simpler and more relevant:**

- For thyroid function assessment: Measure **free** T<sub>4</sub> & TSH
- Measure **free** T<sub>3</sub>? Only for suspicion of hyperthyroidism

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**Practical Use of Thyroid tests**

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

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Why assess thyroid function?  
Suspect *hypothyroidism*

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Suspect hypothyroidism

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

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12y girl with slow height growth & no puberty

- TSH = 75 uU/ml (ref: 0.5-4.5)
- Free T<sub>4</sub> = 0.6 ng% (ref: 0.8-1.6)

High TSH, low free T<sub>4</sub>: → Primary hypothyroidism

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

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### 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

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16y girl with rapid weight gain

- TSH = 8 uU/ml (ref: 0.5-4.5)
- Free T<sub>4</sub> = 1.0 ng% (ref: 0.8-1.6)

Mildly elevated TSH (< 10) with normal free T<sub>4</sub> is this pattern clinically significant? It depends...

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Mildly elevated TSH, with normal free T<sub>4</sub>:  
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

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5y boy with slow height growth

- TSH = 1.2 uU/ml (ref: 0.5-4.5)
- Free T<sub>4</sub> = 0.6 ng% (ref: 0.8-1.6)

Normal TSH, low free T<sub>4</sub> → TSH is "abnormally normal" vs. low free T<sub>4</sub>

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When free T<sub>4</sub> 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*), glucocorticoids

Central hypothyroidism (TSH deficiency)?

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

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Why assess thyroid function?  
Suspect *hyperthyroidism*

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Suspect hyperthyroidism

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

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16y boy with weight loss and bulging eyes:

- TSH = 0.006 uU/ml (ref: 0.5-4.5)
- Free T<sub>4</sub> = 3.4 ng% (ref: 0.8-1.6). Free T<sub>3</sub> = 9 pg/ml (re: 2.8-4.4)

Very low TSH, high free T<sub>3</sub>/T<sub>4</sub> → Hyperthyroidism  
Next: Measure thyroid stimulating Ig (TSI) → Elevated → Graves d.  
Radio-iodine thyroid uptake: Homogeneously high (*unnecessary test*)

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16y girl with weight loss:

- TSH = 0.006 uU/ml (ref: 0.5-4.5)
- Free T<sub>4</sub> = 2 ng% (ref: 0.8-1.6). Free T<sub>3</sub> = 5.5 pg/ml (re: 2.8-4.4)

Very low TSH, high free T<sub>3</sub>/T<sub>4</sub> → Hyperthyroidism

Next: Measure thyroid stimulating Ig (TSI) → Low → NOT Graves d.

Next: Order radio-iodine thyroid uptake

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When high free T<sub>4</sub> & 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

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Large thyroid and/or thyroid nodule

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Common scenarios

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

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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

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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

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### Newborn Thyroid Screening

Screening test **alert**: Abnormal TSH &/or total T<sub>4</sub>

Next: Measure TSH, free T<sub>4</sub>

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### Baby #1

- TSH = 75 uU/ml (ref: 0.7-11)
- Free T<sub>4</sub> = 0.5 ng% (ref: 0.9-2.2)

High TSH, low free T<sub>4</sub> → Primary hypothyroidism

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### Congenital Primary hypothyroidism

**Permanent:**

- Most common: Dysgenesis of the thyroid gland (Absent, small and/or ectopic)
- Infrequent: Thyroid hormone defect (*a.k.a* *dysmorphogenesis*)
- 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

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**Baby #2**

- TSH = 8.5 uU/ml. Normal free T<sub>4</sub> = 1.2 ng%  
TSH standard lab reference = 0.5-4.5. TSH reference 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

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**Baby #3**

- TSH = 2 uU/ml (ref: 0.7-11)
  - Free T<sub>4</sub> = 0.5 ng% (ref: 0.9-2.2)
- Normal TSH, low free T<sub>4</sub> → TSH is "abnormally normal" vs. low free T<sub>4</sub>

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Newborn with "normal" TSH and low free T<sub>4</sub>

- **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

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**Baby #4**

- TSH = 0.01 uU/ml (ref: 0.7-11)
- Free T<sub>4</sub> = 3.4 ng% (ref: 0.9-2.2)

Low TSH, High free T<sub>4</sub> → Neonatal hyperthyroidism

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**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

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**Babies #5, #6**

- **Baby #5** neonatal screen: Normal TSH, *low total T<sub>4</sub>* = 3.5 mcg% (ref: 5.4-17)
- Confirmatory test: Normal TSH, *normal free T<sub>4</sub>*

- **Baby #6** neonatal screen: Normal TSH, *high total T<sub>4</sub>* = 24 mcg%
- Confirmatory test: Normal TSH, *normal free T<sub>4</sub>*

Incongruent *total vs. free T<sub>4</sub>* → Thyroid binding problem

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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

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Practical Use of Thyroid Tests  
Key points

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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

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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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