

# Pediatric Thyroid Disorders: Is that a lump in your throat?

Christopher Blunden, MD FAAP

Section of Pediatric Endocrinology – Ochsner Health Center for Children  
15<sup>th</sup> Annual Update in Pediatrics CME Conference  
July 20, 2019



# Disclosures

- None

# Career Path



# Objectives

## Disorders of Thyroid Gland Development and Hormone Synthesis

- Recognize manifestations of abnormal embryologic development of the thyroid gland
- Identify potential pitfalls in the production of thyroid hormone
- Explain the role of thyroid hormone in maintaining normal metabolism

## Congenital Thyroid Disease

- Interpret thyroid function testing results from newborn screening labs
- Recognize the clinical features of congenital hypothyroidism and neonatal Graves' disease
- Identify the most common etiologies of congenital hypothyroidism
- Understand the natural history and clinical impact of untreated congenital hypothyroidism
- Plan the appropriate diagnostic evaluation and treatment for infants with congenital hypothyroidism and neonatal Graves' disease.

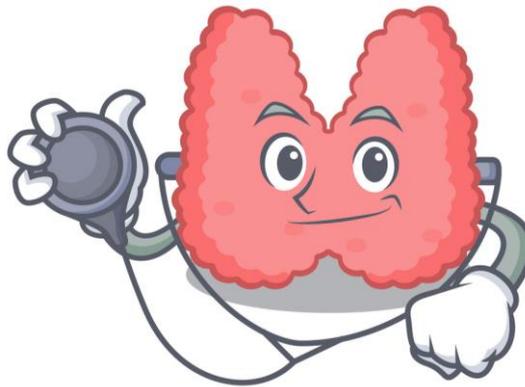
## Autoimmune Thyroid Disease

- Recognize the clinical features associated with autoimmune hypo and hyperthyroidism
- Identify the causes of autoimmune hypo and hyperthyroidism
- Plan the appropriate diagnostic evaluation of autoimmune hypo and hyperthyroidism
- Understand the management options for autoimmune hypo and hyperthyroidism

## Non-Autoimmune Thyroid Disease, Thyroid Nodules and Thyroid Cancer

- Recognize other acquired causes of abnormal thyroid function
- Plan the appropriate evaluation of thyroid nodules
- Describe two types of thyroid cancer and the prognosis for each

# Disorders of Gland Development and Thyroid Hormone Synthesis



# Thyroid Gland Development

- Descends from foramen cecum early in 1<sup>st</sup> trimester
- Failure of migration leads to lingual thyroid
  - Monitor for obstruction
- Failure of thyroglossal duct to involute leads to thyroglossal duct cyst
  - Diagnosis: Ultrasound
  - Risk of infection and malignancy → Surgical removal recommended
    - ⊙ Coordinate with Endocrinology and ENT



# Thyroid Hormone Synthesis



TPN  $\neq$  I<sup>-</sup>



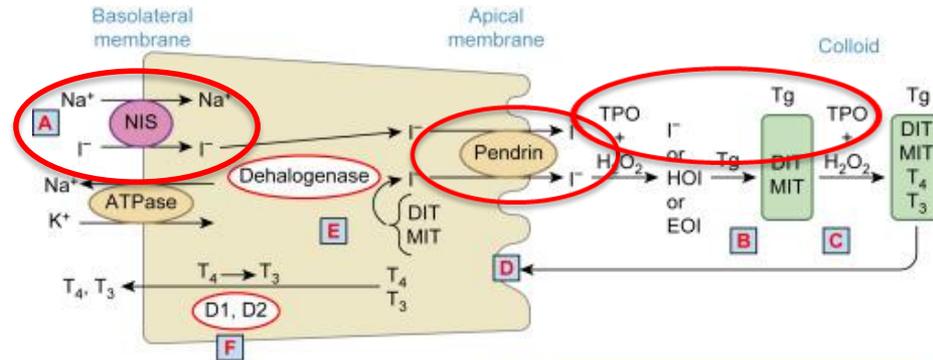
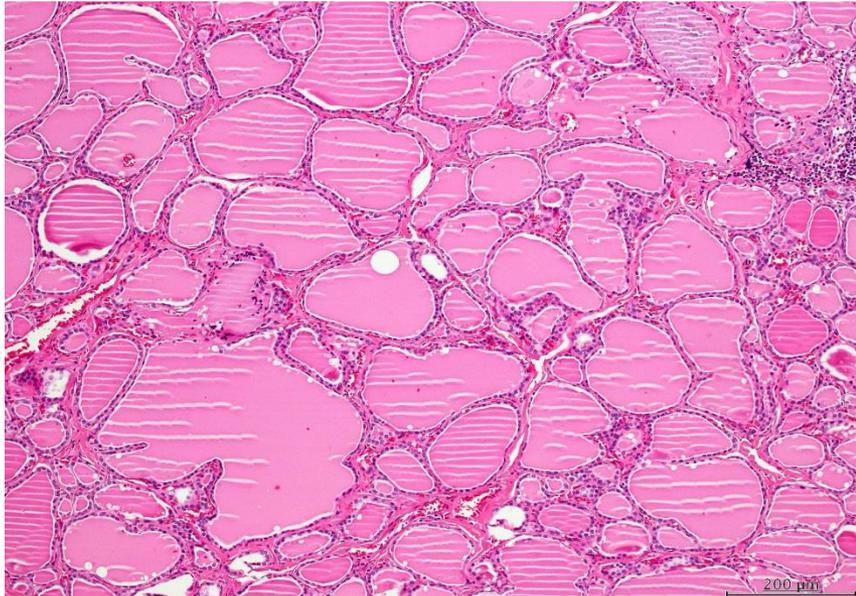
+



=

↑↑

I<sup>-</sup>



KEY	
METABOLIC STEP	INHIBITOR
A Iodine transport	ClO <sub>4</sub> <sup>-</sup> , SCN
B Iodination	PTU, MMI
C Coupling	PTU, MMI
D Colloid Resorption	Colchicine, Li <sup>+</sup> , I <sup>-</sup>
E Deiodination of DIT + MIT	Dinitrotyrosine
F Deiodination of T <sub>4</sub>	PTU

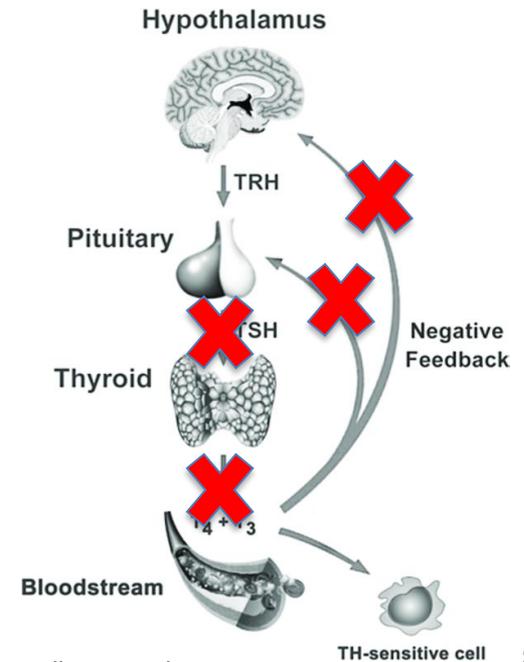
# Thyroid-CNS Axis

- Production of thyroid hormone is dependent on CNS signals from the hypothalamus (TRH) and pituitary (TSH) and negative feedback
- TSH deficiency = secondary hypothyroidism = central hypothyroidism



Antiepileptics

- Resistance to thyroid hormone (RTH)



# Thyroid Hormone in Circulation and Cellular Targets

- Binds Thyroid Binding Globulin (TBG) and albumin
  - May be low in liver disease (synthesis problem) or kidney disease (protein wasting problem)
  - Inherited TBG deficiency X-linked
  - Low total hormone, but normal amount of free hormone
    - ⦿ No clinical consequence!



FT4 often a better test than T4

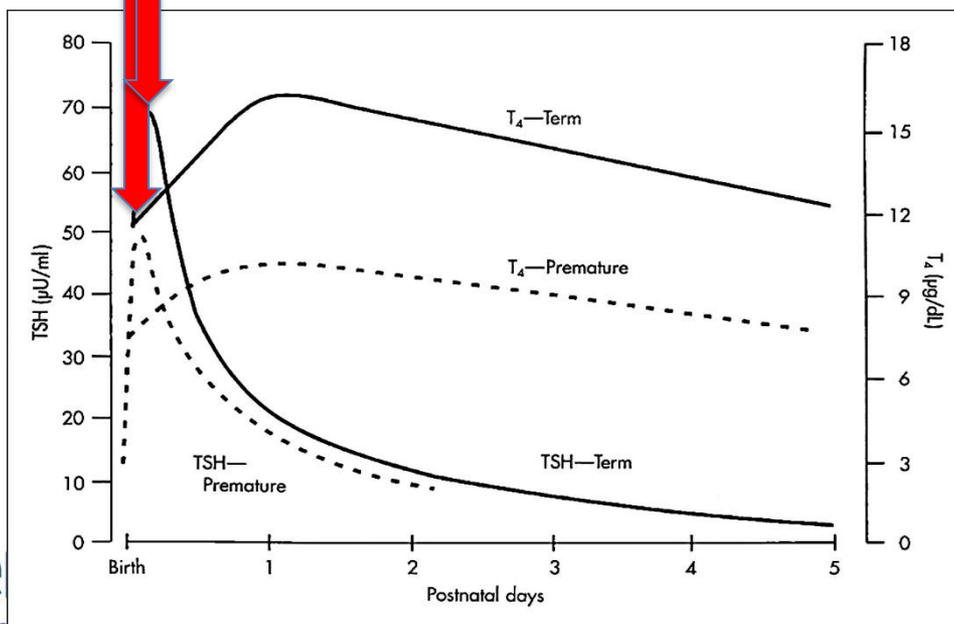
- Free hormone binds nuclear receptor in target cells all over the body

# Congenital Thyroid Disease



# Newborn Screening for Congenital Hypothyroidism

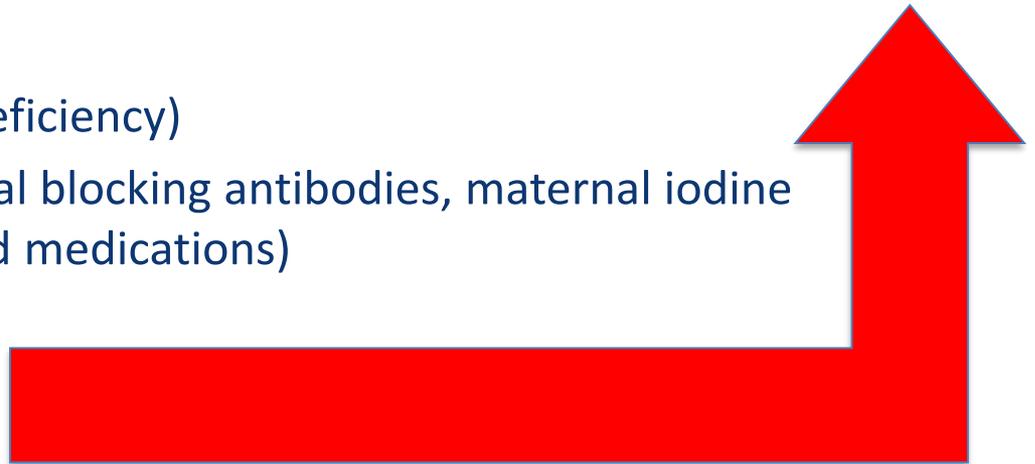
- Stress of birth + cold exposure → TSH surge
  - TSH peak within 30-60 minutes after birth, with rise in T3 and T4 in the 1<sup>st</sup> 24 hrs
- Earlier draw → higher likelihood of false positive result
- Prematurity → higher likelihood of false negative result



# Congenital Hypothyroidism – Prevalence and Etiology

- Approximately 1/2000 infants in the US
- Causes
  - Thyroid dysgenesis (agenesis, ectopy, hypoplasia)
  - Dyshormonogenesis
  - Central hypothyroidism (TSH deficiency)
  - Transient (prematurity, maternal blocking antibodies, maternal iodine deficiency, maternal antithyroid medications)
- Most common cause??

75-85%



# Congenital Hypothyroidism - Symptoms

Prevalence of individual symptoms of hypothyroidism at the time of diagnosis. (modified from: Alm et al. *Brit Med J* 289:1171-175, 1984 [13].)

Features listed in questionnaire	Group 1 (n = 215) Initial T4 ≤ 30 nmol/L % with feature	Group 2 (n = 232) Initial T4 > 30 nmol/L % with feature
Prolonged Jaundice	59	33**
Feeding Difficulty	35	16**
Lethargy	34	14**
Umbilical Hernia	32	18*
Macroglossia	25	12*
Constipation	18	10
Cold or mottled skin	18	10
Hypothermia	3	3
No symptoms	16	33**
Other clinical features reported:		
Abnormal cry	7	6
Edema	5	3
Hypothyroid appearance	6	2
Hypotonia	3	3

# Congenital Hypothyroidism - Treatment

- After repeating the lab to confirm an abnormal TSH consider...
  - 1. Immediacy of need
    - ⊙ Milder TSH elevations with normal T4 may be trended for a short time
    - ⊙ Significantly elevated TSH and/or low T4 likely indicates permanent disease and greater risk of neurodevelopmental harm with delayed onset of treatment
  - 2. Potential barriers
    - ⊙ Family reliable? Resource barriers for travel to frequent labs and appointments?
    - ⊙ Have system in place to ensure no loss to follow-up?
  - 3. Who will counsel family about diagnosis, prognosis, and treatment?
  - 4. Starting dose
    - ⊙ Levothyroxine 10-15 mcg/kg/day for severe hypothyroidism, 5-10 mcg/kg/day for more mild cases
    - ⊙ Repeat TSH and T4 in 2 weeks with the goal of normalizing T4 by 2 weeks and TSH by 4 weeks

# Levothyroxine

- Brand names - Synthroid, Tiroshint, Levoxyl
- T4
  - Converted to T3 by deiodinase enzymes in vivo
- Half-life 4-6 days
  - May double dose next day if missed to maintain steady state
- Pregnancy/OCPs → TBG increase → 50% higher dose needs

Armour?



Absorption altered by soy, calcium, iron, PPIs

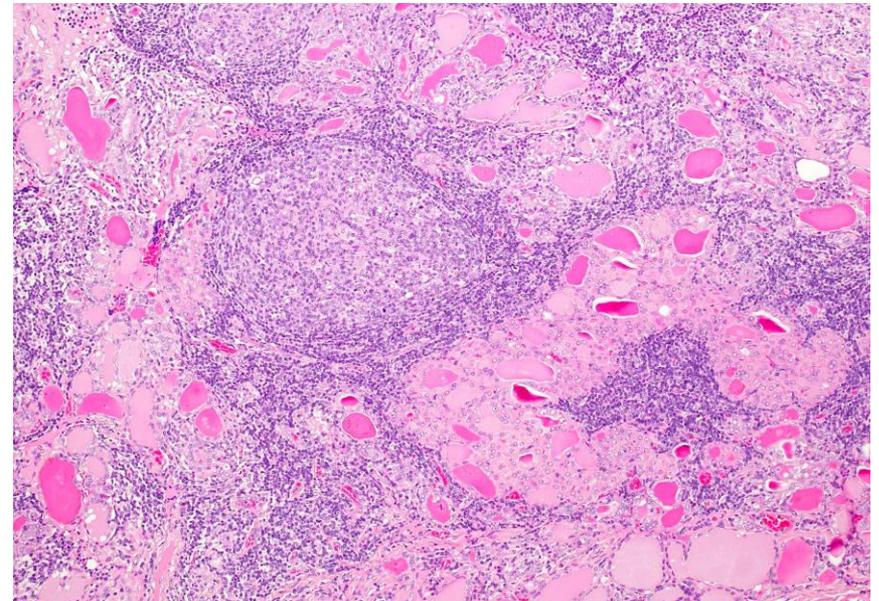
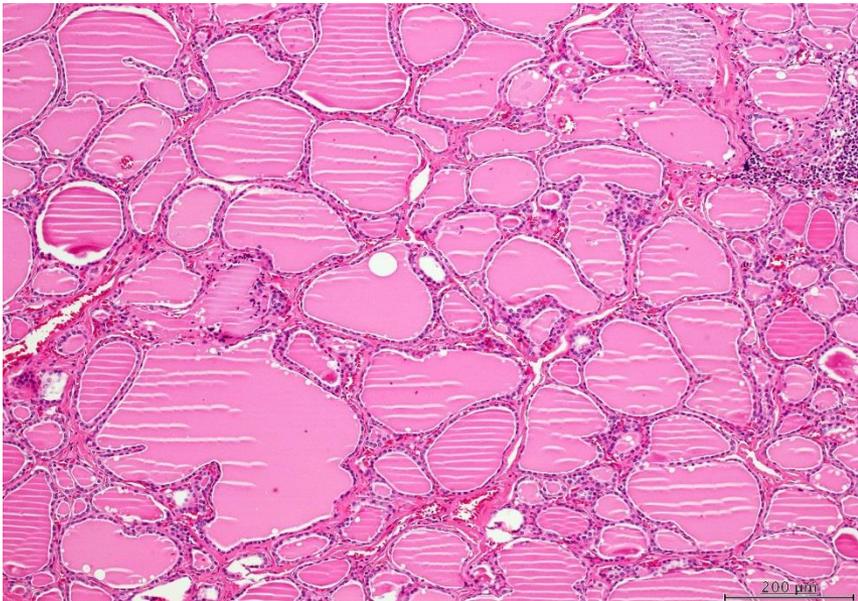
- If necessary, space out from thyroid hormone



# Neonatal Graves' Disease

- 1-5% of infants born to mothers with Graves'
  - Higher antibody titer in 3<sup>rd</sup> trimester = higher risk
  - May have concurrent blocking antibodies causing transient hypothyroidism
- Symptoms
  - Low birth weight or prematurity
  - Frontal bossing and triangular facies
  - Goiter
  - Warm skin
  - Irritability
  - Tachycardia
- Resolves spontaneously in 1-2 months once maternal antibodies are cleared

# Autoimmune Thyroid Disease



# Case

- A 13 year-old previously healthy female presents for a WCC with the complaint of light periods (menarche at 11) and fatigue. As you review her family history you notice that her paternal aunt has RA. Vitals show a pulse of 60, T 97.4, and BP 92/57. You notice a mildly prominent thyroid with a cobblestone texture on physical exam and decide to draw thyroid function tests.

# Case

- A 13 year-old previously healthy female presents for a WCC with the complaint of light periods (menarche at 11) and fatigue. As you review her family history you notice that her paternal aunt has RA. Vitals show a pulse of 60, T 97.4, and BP 92/57. You notice a mildly prominent thyroid with a cobblestone texture on physical exam and decide to draw thyroid function tests.
- TFTs reveal a TSH of 12.2 uIU/mL (0.5-4) and a FT4 of 1.0 (1.0-2.9). Subsequent testing confirms elevated TPO antibody titers.

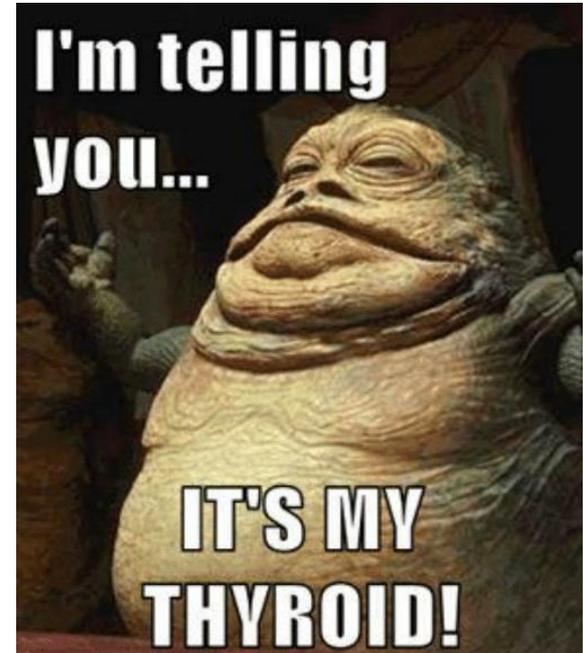
# Hashimoto's Disease/Chronic Lymphocytic Thyroiditis/Autoimmune Hypothyroidism

- Most common cause of acquired hypothyroidism in the United States
- Increased risk in some genetic and autoimmune conditions:
  - ⊙ Down syndrome\*\*\*
  - ⊙ Turner syndrome
  - ⊙ Type 1 Diabetes

# Other Hypothyroidism Symptoms...

- Poor linear growth
- Goiter
- Dry Skin
- Brittle or thin hair
- Constipation
- Depressed appetite
- Depressed mood
- Fluid retention with mild weight gain
- Delayed/precocious puberty\*\*\*
- Mild End: None
  - “Subclinical hypothyroidism”
- Extreme End: Myxedema coma, pituitary hyperplasia

Symptoms may be preceded by “Hashitoxicosis” - hyperthyroidism from rapid release of colloid stores upon autoimmune attack





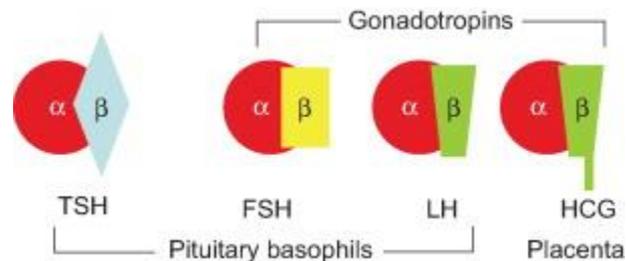
# Who Wants To Be An Endocrinologist?!?

♦ \$500,000 ♦

- What is the syndrome called in which severe primary hypothyroidism induces precocious puberty?
  - Von Wyk-Grumbach syndrome

\$1,000,000

- What is the pathophysiologic mechanism by which this occurs?

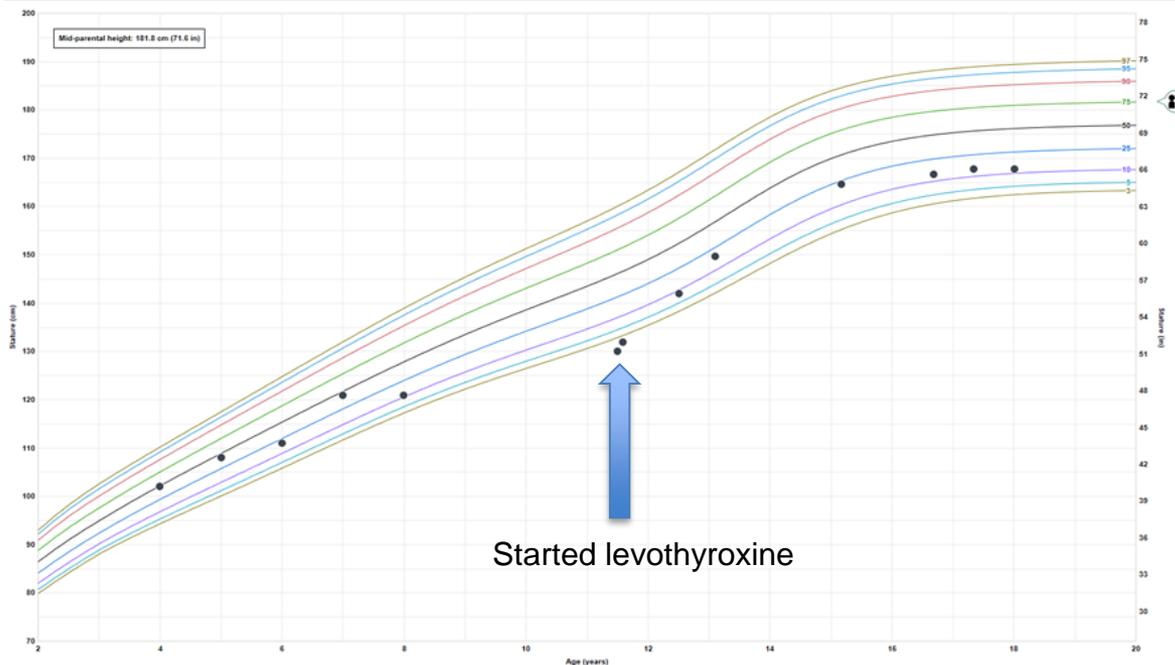


# Goiter



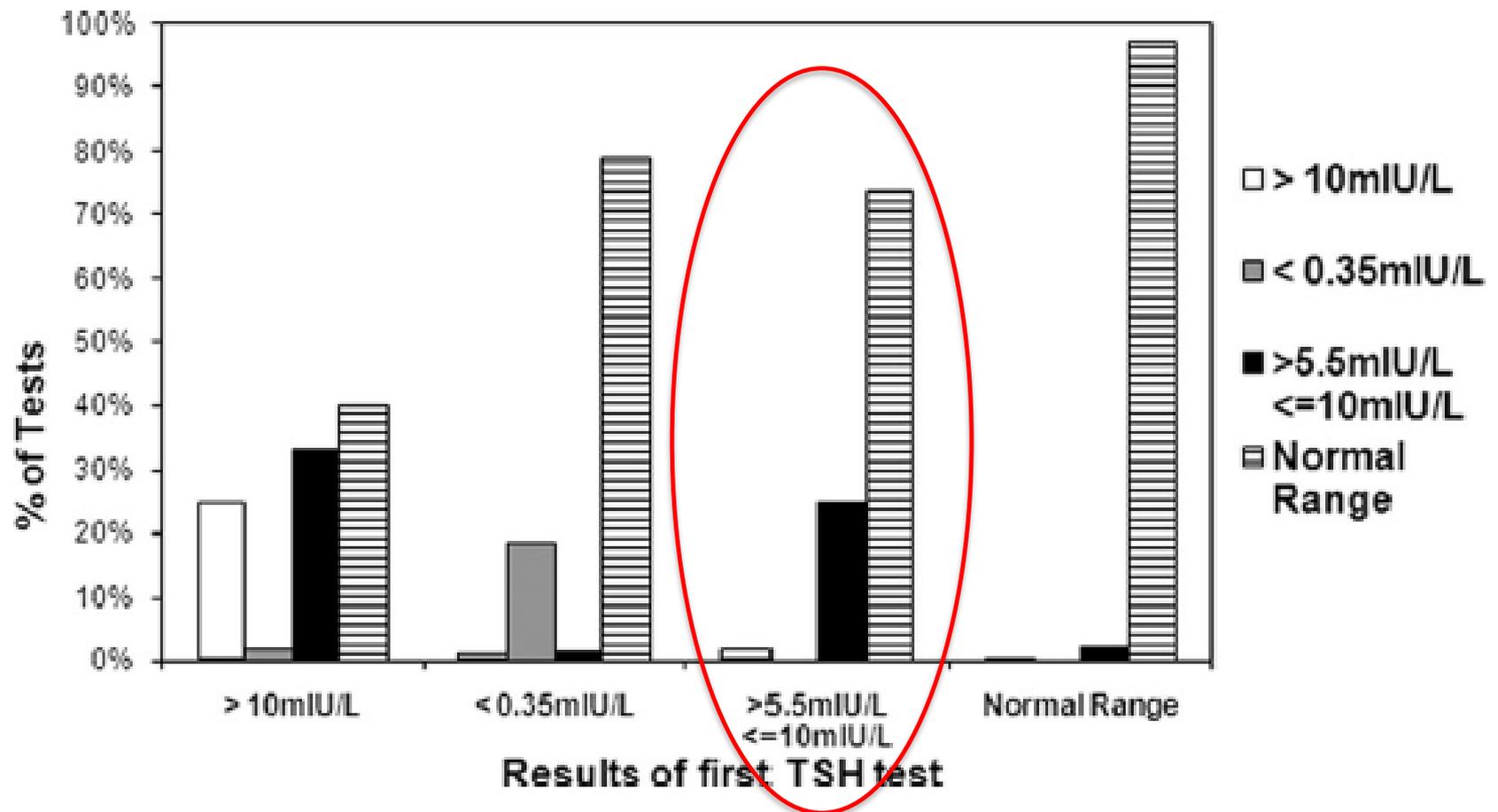
- Usually autoimmune-mediated
- Thorough lymph node exam and symptom assessment
- Work-up: TSH, free T4, thyroid autoantibodies
- Ultrasound may not be useful if goiter is uniform
- Symptoms of dysphagia or airway compromise → ENT

# Diagnosis and Treatment of Hypothyroidism – Case Example



T4			2.5
T4 EXT			
T4 FREE BY DIRECT ...	<0.4 *		
T4 FREE EQUILIBRIU...			
T4 FREE EXT			
TSH	>500.000		>500.000
TSH EXT			
CORTISOL 0 MIN LO ...			
CORTISOL 20 MIN LO...			
CRP			
THYROGLOBULIN AB			69.2
THYROID PEROXIDASE...			420.6

- Treatment: Levothyroxine 1.5-2 mcg/kg/day or more with younger age
  - Start lower dose and titrate up in severe cases
- Trend TSH +/- free T4 only for treatment decisions
  - 4-6 weeks after starting treatment and with dose changes
  - If the brain is happy...



**FIG. 2.** Distribution of TSH results in the second test according to the category of the first TSH measurements in untreated patients (tests were performed between 2002 and 2006).

# Hyperthyroidism Illustrative Case

17 yo male presents to adolescent medicine with tremulousness, abdominal pain, dizziness and diaphoresis with standing.

Pulse 104

BP 130/84

Labs: TSH 0.051 (L), FT4 of 4.73 (H), +TRAb

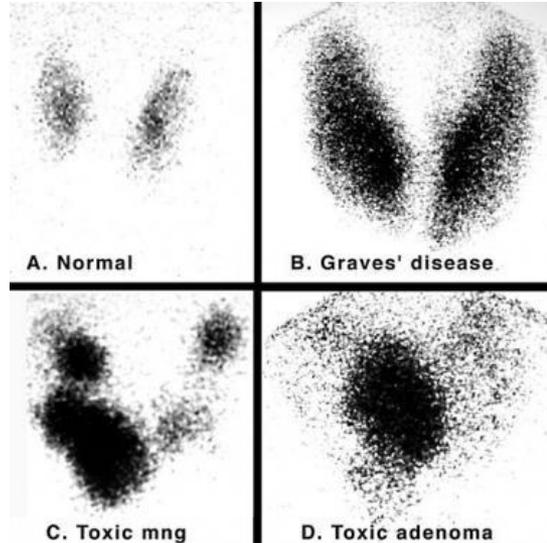
Prescribed atenolol, but did not pick-up prescription

No-show with Endocrinology

1 year later presents to ED and found to have fever, n/v, diarrhea, 10# weight loss over 1 week, 10% EF, admitted to PICU on ECMO

# Graves' Disease Symptoms

- Goiter
- Rapid growth
- Weight loss
- Tremors
- Hyperreflexia
- Palpitations
- Frequent loose stools
- Oily skin and hair
- Lack of concentration
- Ophthalmopathy
- Tongue fasciculations
  - <https://www.youtube.com/watch?v=xuwdvBXcr30>
- Extreme End: Thyroid storm
  - Fever, delirium, cardiac failure

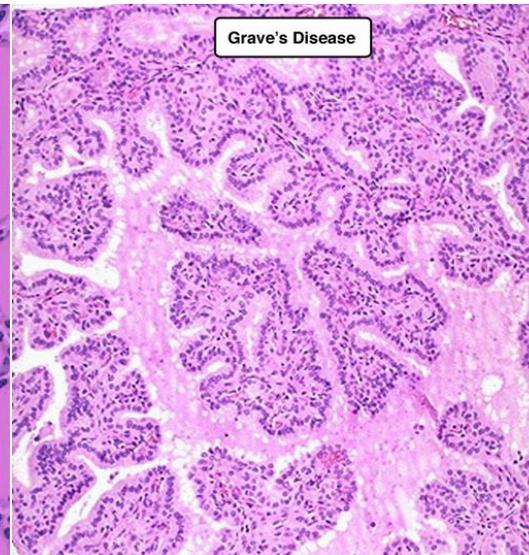
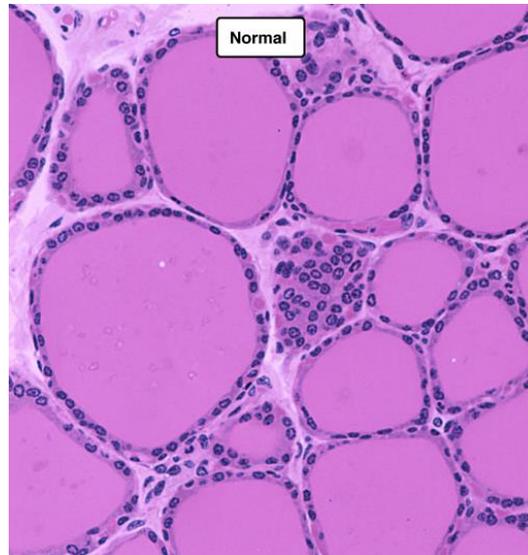


# Hyperthyroidism - Biochemical Diagnosis

T3 TOTAL	3.70	▲
T4	29.7	▲
T4 FREE		
T4 FREE BY DIRECT ...	>10.0 *	▲
TSH	<0.005	▼



THYROID STIM IMM		299 *	▲
TSH REC AB		29.35 *	▲



# Hyperthyroidism - Treatment

- Medical

- Usually initial treatment
- Methimazole ONLY
  - ⦿ Start around 0.5 mg/kg/day divided 1-3 times daily
  - 🐚 Risk of allergic reaction, agranulocytosis, hepatitis
- Propothiouricil (PTU)? → black box warning for hepatotoxicity
- Beta-blockers
  - ⦿ Atenolol vs propranolol
- High dose iodine (Lugol's)
- Steroids

- Surgical

- Ideally by high volume thyroid surgeon (>30/yr)
- Risks: recurrent laryngeal nerve damage, transient/permanent hypoparathyroidism

- Radioactive Iodine Ablation

- Goal: Complete gland ablation with conversion to hypothyroid in 4-16 weeks
- Must be over age 5 and ideally able to swallow a pill

- Not “block and replace”

# Non-autoimmune Acquired Thyroid Disease, Thyroid Nodules, and Thyroid Cancer



# Other causes of thyroid disease (or not...)

- Neck/spine/chest radiation
- Status-post BMT
- Iodine load or deficiency
- Adenomas (pituitary or thyroid)
- McCune-Albright Syndrome
- Medications
  - Lithium, amiodarone
  - Exogenous thyroid hormone intake
  - Heparin
- Obesity



Recommend not checking TSH on routine obesity screening labs without other symptoms or family history of autoimmunity

Recommend repeating any TSH <10 uIU/mL with free T4 +/- antibody profile

- Non-thyroidal illness



Do not check TFTs within 1 month of illness

# Thyroid Nodules

## History

- Radiation exposure? Family history of thyroid carcinoma? Type? Symptoms of thyroid dysfunction?

## Exam

- Lymphadenopathy? Goiter?

## Labs

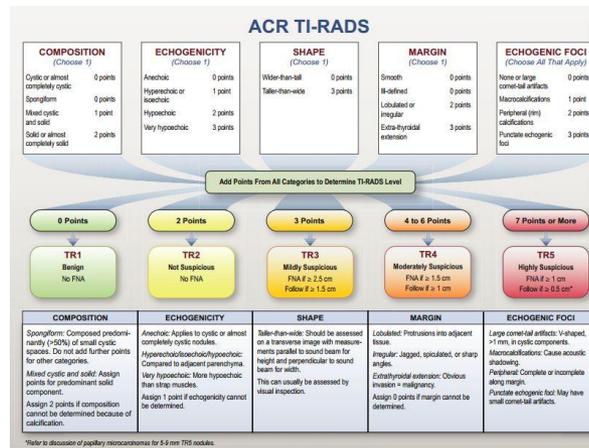
- TFTs and antibodies

## Imaging

- I-123 Uptake Scan
- Ultrasound TI-RADS →

## Biopsy

- Fine needle aspiration biopsy for Bethesda Score →



### Diagnostic category

- I. Nondiagnostic
- II. Benign
- III. AUS/FLUS
- IV. Suspicious for follicular neoplasm
- V. Suspicious for malignancy
- VI. Malignant

# Thyroid Malignancies

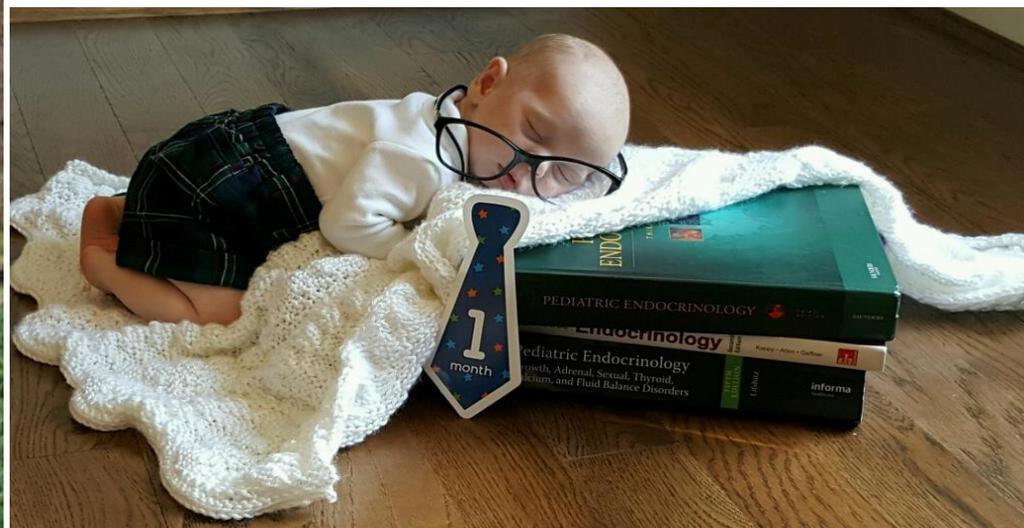
- Follicular and papillary thyroid cancer (DTC)
  - Excellent prognosis – 98% long term survival, even with recurrent disease
  - Surgery and I-131 as indicated
  - Thyroglobulin levels trended
- Medullary thyroid cancer
  - Calcitonin-producing C cell malignancy
  - Associated with MEN2A and MEN2B
    - ⊙ RET oncogene
    - ⊙ Thyroid cancer, pheochromocytoma, hyperparathyroidism in relatives?
  - Prophylactic thyroidectomy indicated in known carriers
  - 95% survival at 5 years, declines to 15% by 30 years



# Useful Clinic Resources

[Hormone.org](http://Hormone.org)

[Pediatric Endocrine Society Patient Education Materials](#)



Email: [ceb11@albion.edu](mailto:ceb11@albion.edu)

Cell: (313) 319-7668