



# Thyroid Disease in Children

Friends, Romans,  
countrymen, lend me  
your goiters

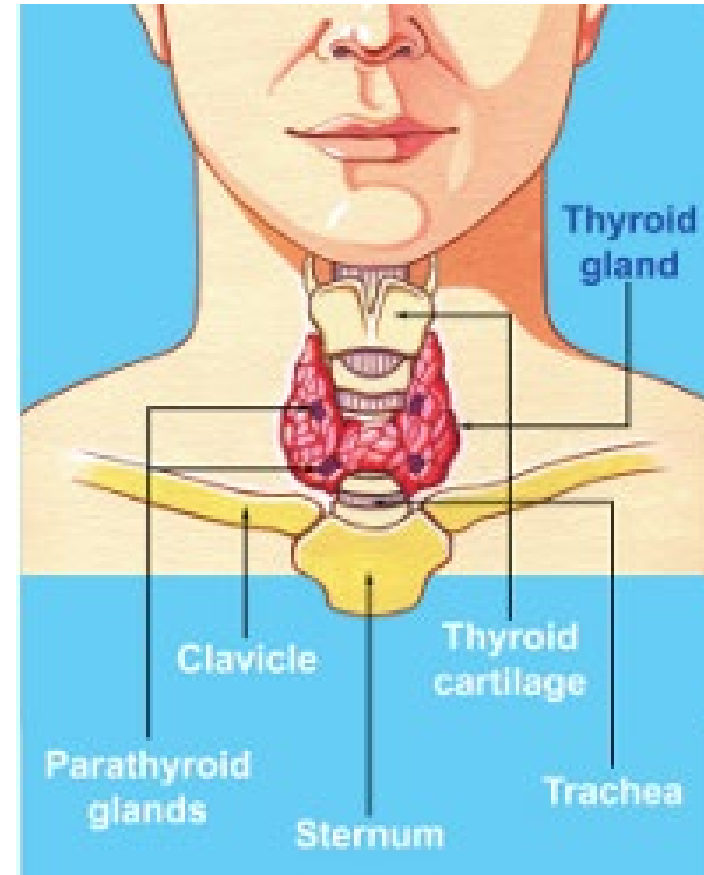
Kimberly Martin, M.D.  
Pediatric Endocrinology Update  
Akron Children's Hospital  
January 31, 2020



Akron Children's Hospital

# Anatomy

- Over Trachea
- Two Lobes connected together by an isthmus
- 15 to 20 g





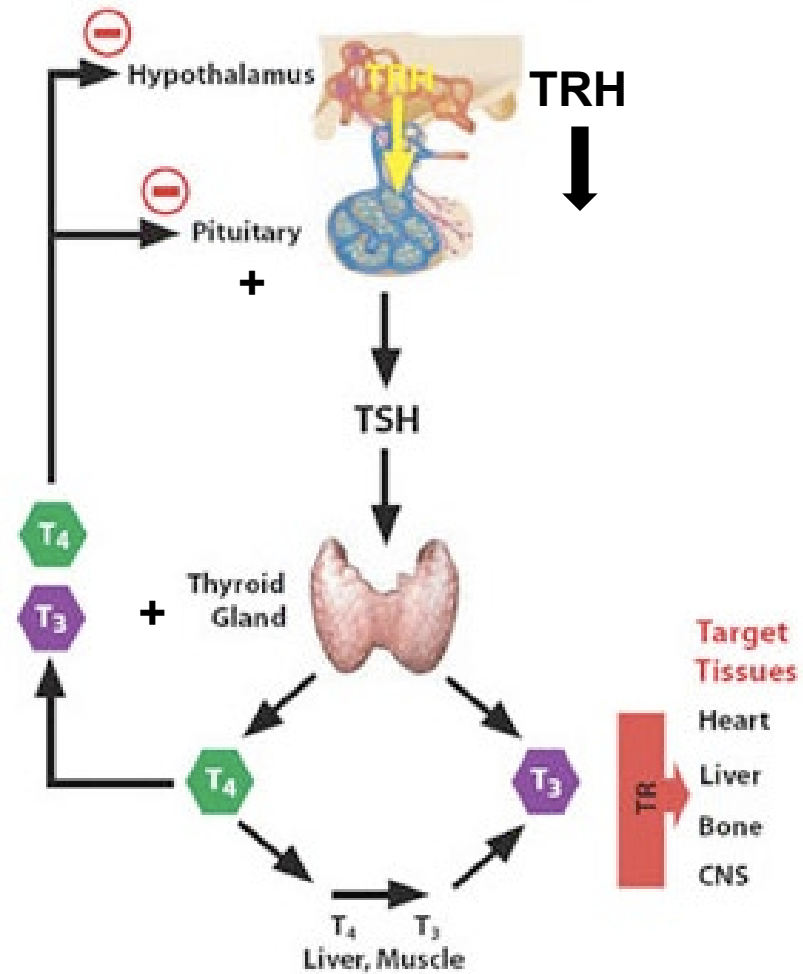
# Thyroid Hormone

- Thyroid gland normally secretes mainly T4
- 70 % of T3 derived from T4 in peripheral tissues
- Both T4 and T3 are in bound form (TBG, prealbumin and albumin)
- Only 0.025% of T4 and 0.35% of T3 are free
- **Free T4 (not total T4) and total T3 (not free T3) concentration best correlates with thyroid status**



# Thyroid Regulation

## Hypothalamic-Pituitary-Thyroid Axis



# Effects of thyroid hormones

- Fetal brain & skeletal maturation
- Increase in basal metabolic rate
- Inotropic & chronotropic effects on heart
- Increases sensitivity to catecholamines
- Stimulates gut motility
- Increase bone turnover
- Increase in serum glucose, decrease in serum cholesterol
- Play role in thermal regulation



# Case 1

- Full term, healthy newborn
- Mild neonatal jaundice – no phototherapy needed
- Gaining weight, eating well
- Newborn Screen
  - TSH: 46 mcu/ml (<34)
  - T4: 9 mcg/dl (>8)



# Congenital Hypothyroidism

- Congenital
  - Primary Hypothyroidism
    - Thyroid agenesis/ectopic
    - Dyshormonogenesis
  - Secondary Hypothyroidism
    - Hypopituitarism
      - Isolated
      - Multiple Hormone Deficiency



# Permanent Congenital Hypothyroidism

- Incidence
  - 1:2000-4000
  - Slightly higher in female infants
  - Higher in Asian babies
  - Lower in African American infants
- Primarily sporadic in occurrence
- Overt symptoms not present at birth
- Profound effects on brain development

**The earlier and more aggressive one is  
with treatment the better**





# Transient Congenital Hypothyroidism

Causes of transient hypothyroidism:

- Iodine deficiency
- Iodine exposure
  - Maternal Amiodarone exposure
  - Iodine antiseptic (maternal/fetal)
- Maternal blocking antibodies:
  - TSH receptor blocking Abs
- Maternal anti-thyroid drugs



# Congenital Hypothyroidism: Treatment

- Confirm all abnormal newborn screens with laboratory TSH and free T4
  - Borderline results (TSH  $<50$ , normal free T4) requires repeat testing in 1 week
  - Can keep testing weekly if TSH borderline and free T4 is normal until 21 days of life
- If repeat labs significantly abnormal (TSH  $>50$ , low free T4, TSH not normal near 21 days of life) need to start Synthroid

Call and ask to talk to Endocrinologist on call for further guidance



Akron Children's Hospital

# Congenital Hypothyroidism: Treatment: Pearls

- **NEVER** prescribe liquid Synthroid
- Use brand name Synthroid in infants



# Case 2

- 10 yo female no pmhx
  - History:
    - Slowing of growth for height
    - Weight gain family can't explain
    - Constipation
    - More tired than usual
  - Exam:
    - Thyroid gland feels enlarged



# Acquired Hypothyroidism

- Symptoms:
  - Fatigue
  - Depression
  - Modest Weight Gain
  - Stalled growth for height
  - Cold Intolerance
  - Dry skin
  - Constipation
  - General Aches/Pains
  - Brittle Hair
  - Menstrual irregularities





# Acquired Hypothyroidism

- Hashimoto's thyroiditis
  - most common thyroid problem (4% of population)
  - most common cause in iodine-replete areas
  - Associated with TPO antibodies (90%), less commonly Tg antibodies



# Acquired Hypothyroidism

- Other causes of acquired hypothyroidism:
  - ingestion of goitrogens
    - Amiodarone
    - Lithium
    - Tyrosine kinase inhibitors
  - iodine deficiency
  - post thyroidectomy
  - hypothalamic/pituitary disorders



# Non-Thyroidal Illness

- Sick Euthyroid
  - Abnormalities in thyroid function tests observed with systemic non thyroidal illness
  - Thyroid function should not be assessed in ill patients
    - low serum TSH followed by transient elevations in serum TSH concentrations (up to 20 mU/L) during recovery
    - Free T4 levels may be normal, increased, or decreased
  - No treatment



# Case 2 Cont...

- Labs:
  - TSH: 15 uIU/ml (0.35-5.50)
  - Free T4: 0.7 ng/dl (0.8-1.4)
- Repeat labs in 4-6 weeks
  - TSH: 23 uIU/ml (0.35-5.50)
  - Free T4: 0.8 ng/dl (0.8-1.4)
  - Thyroid peroxidase AB: 600 IU/ml (0-20)
  - Thyroglobulin Ab: 65 IU/ml (0-100)

Make a referral to Endocrinology



# Case 3

- 14 yo male with no pmhx
  - History
    - 30 lbs weight gain in last year
    - Decline in growth velocity for height
    - Started having body odor and pubic hair 12 yo
    - Fatigue and nausea for last few months
    - Daily headaches that he wakes with
  - Exam
    - Small for age and obese
    - No goiter
    - Tanner 2 pubic hair but small testicles
    - Mild ptosis and one pupil larger than other





# Case 3 Cont...

- CT Brain: **mass centered in the suprasellar region** with **multiple calcifications** near the sella
- MRI Brain: Brain: **Suprasellar retro-chiasmatic mass** measuring approximately 5.3 x 3.2 x 3.1 cm extending into the third ventricle consistent with **craniopharyngioma**. The optic chiasm lies ventral to the mass and is lifted superiorly. The anterior pituitary gland and stalk appear normal. The neurohypophyseal bright spot is not seen

## Labs:

Free T4: 0.7 ng/dl (0.9-1.6)

TSH: 5.60 uIU/ml (0.35-5.50)

Testosterone: <2.5 ng/dl

FSH: 0.9 mIU/mL

LH: 0.1 mIU/ml

**IGF-1: 69 ng/ml (79-506)**

**IGF-BP3: 2.1 mcg/dl (2.4-8.4)**

Cortisol: 8 mcg/dl

Prolactin: 16.4 ng/ml (2.1-17.7)

Someone needs to call  
and ask to talk to  
Endocrinologist on call  
for further guidance



# Central Hypothyroidism

- Causes:
  - Hypothalamic Pituitary masses
  - Developmental abnormalities: SOD
  - Infiltrative disorders affecting the pituitary or hypothalamus
    - hemochromatosis, lymphocytic hypophysitis, tuberculosis, syphilis, sarcoidosis, fungal infections, toxoplasmosis, and histiocytosis
  - Traumatic brain injury with injury to the pituitary stalk
  - Subarachnoid hemorrhage
  - Cranial radiation



# Acquired Hypothyroidism

- Treatment: T3 (Cytomel) vs T4 (levothyroxine)
  - Although T3 is the biologically active thyroid hormone, the majority of T3 is derived from deiodination of T4; thus, it is not necessary to use T3
  - Insufficient evidence to support the routine use of a combination of T4 and T3 therapy when looking at mood, quality of life, and psychometric performance
  - T3 short half life:
    - More variability of thyroid hormone levels
    - Requires more frequent dosing



# Acquired Hypothyroidism

- Treatment: Levothyroxine
  - Daily med
  - Long half life – recheck TSH and free T4 in 4-6 weeks
  - Avoid taking with within 4 hours of Levothyroxine
    - Foods with soy
    - Iron
    - Calcium
    - Multivitamins
    - Antacids
    - Fiber

AGE	mcg/day	mcg/kg/day
0-6 months	25-50	8-10 mcg/kg/day
6-12 months	50-75	6-8 mcg/kg/day
1-5 years	75-100	5-6 mcg/kg/day
6-12 years	100-150	4-5 mcg/kg/day
>12 years	150-200	2-3 mcg/kg/day

# Hypothyroidism Pearls

- Obesity
  - TSH can be mildly elevated ( $<6-8$  mU/L) with normal free T4
  - Elevated TSH is a consequence, not a cause of the obesity
  - No treatment needed
- Thyroid antibodies
  - Pts with subclinical hypothyroidism (TSH 5-10) and thyroid antibodies
    - No treatment needed
    - Overt hypothyroidism occurs at a rate of approximately 5 percent per year
    - Recheck TSH and free T4 with symptoms of hypothyroidism or every 1-2 years





# Hypothyroidism Pearls

- Labs
  - Some labs will give adult reference ranges for thyroid labs
  - Only get TSH and free T4, never total T4
  - If labs on initial check are abnormal (TSH  $<30$ ) then recheck labs in 6 weeks and include antibodies: anti-thyroglobulin Ab and anti-thyroid peroxidase Ab

**If after 2<sup>nd</sup> check TSH is still high then refer to Endocrinology**



# Case 4

- 15 yo female with ADHD
  - History
    - Having trouble in school and ADHD meds not working
    - Weight loss
    - Fatigue
    - Diarrhea
  - Exam
    - Moving all over room
    - Tachycardic
    - Goiter
    - Exophthalmos



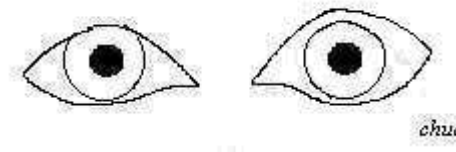
# Hyperthyroidism

- Symptoms
  - Jittery, shaky, nervous
  - Difficulty concentrating
  - Emotional lability
  - Insomnia
  - Rapid HR, palpitations, feeling Hot
  - Weight Loss
  - Diarrhea
  - Fatigue
  - Menses : lighter flow, shorter duration



# Hyperthyroidism

- Exam Findings
  - Eye findings (20%): exophthalmos, lid lag, stare
  - Goiter
  - Thyroid bruit or thrill
  - Tachycardia: Sinus Tachycardia, Atrial Fibrillation
  - Flow murmur
  - Systolic hypertension
  - Hyperreflexia
  - Tremors
  - Proximal muscle weakness



# Hyperthyroidism

- Concerning exam findings
  - Fever
  - Mental status changes: agitation, delirium, lethargy, confusion, seizure
  - Nausea/Vomiting
  - Abdominal pain
  - Unexplained jaundice
  - Signs of heart failure: edema, rales,
  - Atrial Fib
  - Tachycardia at rest >140

**Need to consider Thyroid Storm**





# Hyperthyroidism: Graves Disease

- Graves Disease
  - Hyperthyroidism occurs in about 1:5000 children and adolescents
  - 95% of hyperthyroidism due to Graves disease
  - Females > males
  - T-cell dependent autoimmune disease
    - stimulating antibodies to the thyrotropin receptor (TSI)
    - Can often see Ab seen in Hashimoto's thyroiditis



# Case 4 cont...

- Labs
  - TSH: 0.01 uIU/ml (0.35-5.50)
  - Free T4: 3.2 ng/dl (0.8-1.8)
- Repeat labs a few days later
  - TSH: 0.02 uIU/ml (0.35-5.50)
  - Free T4: 3.3 ng/dl (0.8-1.8)
  - Total T3: 248 (80-185 ng/dl)
  - TSI: 12.2 ( $\leq 1.3$ )
  - Thyroid peroxidase AB: 80 IU/ml (0-20)
  - Thyroglobulin Ab: 65 IU/ml (0-100)
  - CBC: normal
  - Comprehensive chemistry: normal LFTs

Make a referral to Endocrinology



# Hyperthyroidism

- Other causes
  - "Hashitoxicosis"
  - Synthroid ingestion
  - Iodine-induced hyperthyroidism
  - TSH-producing pituitary adenomas
  - Toxic adenoma and toxic multinodular goiter



# Hyperthyroidism:Treatment

- Antithyroid drugs
  - Methimazole
    - 0.25 and 1.0 mg/kg/day (given in once daily or in two divided doses)
  - Propylthiouracil
    - black box warning
- Beta Blockers
  - Used for tachycardia
  - Atenolol: cardio-selective



# Hyperthyroidism: Treatment

- Anti-thyroid Drugs:
  - Side effects:
    - Minor Side Effects: can stop for a few days and then resume treatment once sx gone
      - Papular or urticarial skin rashes
      - Arthralgias
      - Nausea
      - Abnormal taste sensation
    - Major Side effects: stop tx and go to surgery or RAI
      - Agranulocytosis
      - Hepatotoxicity
      - Steven-Johnson Syndrome
    - Adolescent females of reproductive age should be warned about the risks of birth defects with anti-thyroid drug use during pregnancy



# Hyperthyroidism:Treatment

- Radioactive Iodine
  - restricted to children > 10 years of age
  - Risks
    - Theoretical risk of thyroid cancer if <10 yo
    - May not work
    - Thyroid Storm
    - Local pain
- Surgery: Subtotal thyroidectomy
  - Risks:
    - Infection
    - Recurrent Laryngeal Nerve Damage
    - Transient/Permanent Hypoparathyroidism



# Case 5

- 3 day old 37 week, IUGR male
  - History
    - Continues to loose weight
    - Poor feeding but seems hungry
    - Irritable, doesn't want to sleep
    - Sweating a lot
    - Maternal Hx of Graves Disease s/p RAI on Synthroid during pregnancy with normal TFTs
  - Exam:
    - Tachycardic
    - Fussy
    - Goiter



# Neonatal Graves: Symptoms

- IUGR
- Premature birth
- Microcephaly
- Frontal bossing and triangular facies
- Warm, moist skin
- Irritability, hyperactivity, restlessness, and poor sleep
- Tachycardia with a bounding pulse, and sometimes cardiomegaly, cardiac arrhythmias, or heart failure
- Hyperphagia, but poor weight gain, and increased frequency of bowel movements
- Hepatosplenomegaly
- Diffuse goiter
- Stare and occasionally exophthalmos





# Neonatal Graves Disease

- Only occur with 5% of thyrotoxic mothers
- 20% mortality if untreated
- Evolves rapidly, evident by day 7 of life
- Associate with cranial synostosis and learning difficulties, if not treated



# Neonatal Graves: Evaluation

- Infants born to mothers with a history of Graves' disease
  - Labs: TSH, free T4, total T3
    - Right after delivery
    - 3-5 Days of Life
    - 10-14 Days of Life
  - Infants with biochemical evidence of hyperthyroidism (elevated fT4 and total T3, and low TSH) at any of these time points have neonatal Graves' disease and should be treated until the disease resolves



# Case 5 Cont...

- Labs:
  - TSH: 0.02 uiu/ml (0.8-6.9)
  - Free T4: 7.8 (2-4.9)
  - Total T3: 201 ng/dl (24-132)
- Call and ask to talk to Endocrinologist on call for further guidance



# Neonatal Graves

- Treatment
  - Methimazole or Iodine
  - Beta Blocker
- Monitoring
  - Weekly labs: TSH, free T4, T3
  - usually resolves spontaneously between 3-12 weeks of life but can persist for six months or even longer



# Thyroid Nodule

- Approximately 2 percent of children have palpable thyroid nodules
- ~25% of nodules in children are malignant (versus ~5% in adults)
- Exposures/genetic syndromes associated with thyroid cancer
  - Thyroid radiation (chest, neck, spine)
  - Multiple endocrine neoplasia type 2
  - Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome (PTEN hamartoma tumor syndromes)
  - Gardner syndrome
  - Carney complex type
  - Werner syndrome



# Thyroid Nodule

- Evaluation
  - Neck Ultrasound
  - Thyroid function tests: TSH, free T4, T3
  - Make a referral to Endocrinology if a nodule is identified on ultrasound
  - If ultrasound is done at a non Akron Children's Hospital center please make sure that the family brings ultrasound images to their Endocrine appointment

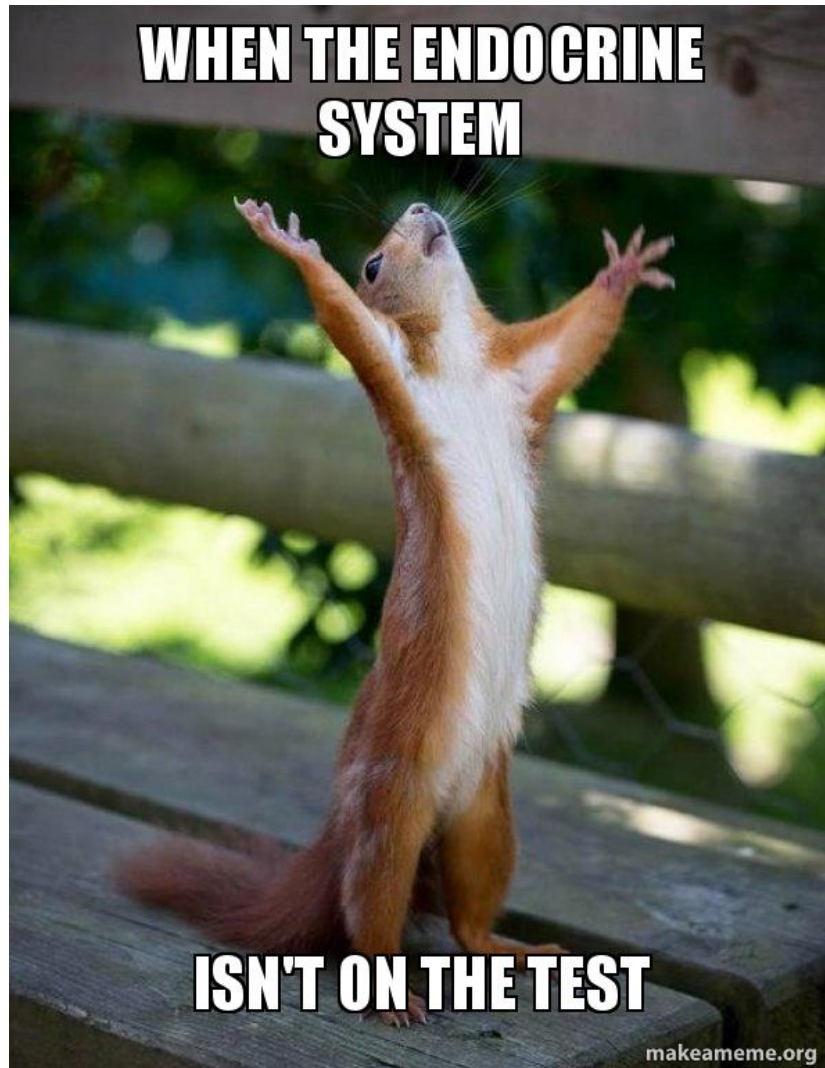


# Thyroid Endocrinology Referral

- What to send with referral
  - Please send me
    - all labs
    - pertinent imaging – if not done at Akron Children's Hospital please have family bring a disc with the actual images
    - last note
    - growth chart



# Questions?



Akron Children's Hospital



# About Akron Children's

- Ranked a Best Children's Hospital by *U.S. News & World Report*
- Magnet® Recognition for Nursing Excellence
- Largest independent pediatric provider in northern Ohio
  - 2 hospital campuses
  - 60+ locations offering primary care, specialty services and urgent care
  - 5,800 employees
- With more than 1 million patient visits each year, we've been leading the way to healthier futures for children and communities through expert medical care, prevention and wellness programs since 1890.



Akron Children's Hospital