

Treatment of Graves Disease in Children and Adolescents

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Disclosures

- None

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Objectives

1. Describe signs, symptoms and diagnostic criteria for Grave's disease.
2. Discuss current treatment options for Grave's disease.
3. Explain the current treatment guidelines for Grave's disease.

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Case Study

- AS is a 16 year old female referred by PCP for abnormal thyroid labs
- She had weight loss, chest pain, shortness of breath with exercising for last 6 months
- She had an echo done by cardiology for chest pain that was normal, she was scheduled for a stress test
- She saw pulmonary for shortness of breath

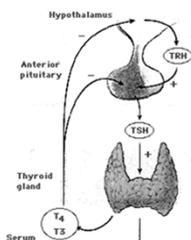
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Case study

- She went back to PCP and they noted enlarged thyroid
- She had thyroid labs done that showed
 - TSH <0.01 (0.4-4.5)
 - Free T4 9.4 (0.84-1.80)
- Referred to endocrinology

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Thyroid Feedback System



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DIAGNOSTIC EVALUATION

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Common Causes of Thyrotoxicosis

- Graves' Disease (up to 80% in children)
- Infectious Thyroiditis
- Chronic lymphocytic thyroiditis (Hashimotos)
- Toxic nodule
- Iatrogenic T4 ingestion

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Diagnostic criteria for Graves'

- Presence of clinic signs and symptoms of hyperthyroidism
- Laboratory findings consistent with hyperthyroidism
- Presence of TRab or thyroid stimulating immunoglobulin
- May also have findings of Hashimoto's, thyroid nodule, goiter

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Laboratory Confirmation

- TSH and free T4
- TSH should be completely suppressed
- Free T4 should be significantly elevated
 - If Free T4 normal, then may be need to check T3 (T3 may be elevated in early Graves')

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Autoimmune Markers for Graves'

- TSH-R antibody
 - Test for all antibodies
 - Quicker Turn around time
 - High sensitivity and specificity
- Thyroid stimulating immunoglobulin
 - Very specific and sensitive
 - Longer turn around time

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Autoimmune Markers

- Thyroid Peroxidase Antibody
- Thyroglobulin antibody
- Both may be present

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Other clinic findings

- Goiter
- Exophthalmos

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TREATMENT OPTIONS

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Treatment Options

- Antithyroid medications
- Radioactive Iodine
- Surgery

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Antithyroid medications

- Methimazole (MMI)
- Propylthiouracil (PTU)
- MMI is widely used because of liver toxicity concerns with PTU
- Inhibit oxidation and organic binding of thyroid iodide – decrease thyroid hormone synthesis

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Methimazole

- Half life 12-16 hours
- Dosing regimens is based on local flavor
- Adults recommended dosing is 5-40mg once daily depending on the level of free T4

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Methimazole

- Dosing may be divided multiple times a day for children that are very hyperthyroid

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Other side effects

- Hepatotoxicity
 - Need to monitor LFT's intermittently

- Minor side effects
 - Rash, pruritus, arthralgia

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Beta Blockade

- Recommended in all patients with symptomatic thyrotoxicosis

- Patients had less symptoms at 4-6 weeks with MMI and beta blockade combined

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Beta Blockade

- Propranolol
 - Given 3-4 times daily
 - May block T4 to T3 conversion at high doses

- Atenolol
 - Given 1-2 times daily
 - Increase compliance

- Metoprolol

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Remission rates with ATM

- Adults 30-50% depending on what study was used
- Children and Adolescents
 - Best 50-60%, remission may increase with duration of treatment
 - Usual most studies 20-30%

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Medication Treatment Duration

- 12-24 months for most cases
- Patients that are not euthyroid by 6 months should be considered for permanent treatment
- Stable patients may consider longer treatment, but remission rates do not usually improve after 4 years of treatment

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Predictors of outcomes

- No true long term predictors
- Large goiters, exophthalmia, younger age, high titers of TRab associated with poor remission rates
- Persistent Hyperthyroidism after short term medication treatment (4-6 months)
- TSub at end of medication treatment

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Side effects of medication treatment

- Low but real incidence of agranulocytosis and aplastic anemia 0.17%-2.8%
- Agranulocytosis <3/10,000 patient years
- Most occur with high doses and within 3 month of treatment initiation
- If patient has sore throat or fever, should stop medication and check WBC

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I-131 Thyroid Ablation

- Permanent treatment
 - They will become permanently hypothyroid
 - Even though thyroid is ablated, antibodies can still be present
- Family concerns about radiation exposure

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RAI Treatment

- Patients can go direct to treatment at time of diagnosis
- Should have beta blockade to control heart rate before and after treatment
- If significant symptoms or delay in treatment, can be treated with MMI prior to ablation, needs to be off for a short period of time prior to treatment. Can restart MMI after if needed

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RAI Treatment

- It may take 2-3 months for the patient to become hypothyroid
- Goal is hypothyroidism
- Should not leave any partially radiated thyroid tissue

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Risk of thyroid cancer

- Rates of thyroid cancer in children receiving RAI are extremely low
- To determine if any theoretical increased risk occurs, more than 10,000 patients would need to be included in 1 study
- Multiple studies did not show increase risk

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Considerations for RAI by age

- <5 years
 - Should be avoided
- 5-10 years
 - Should be considered if dose of I-131 <10mCi
- >10 years
 - Recommended

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Considerations for females

- RAI or Surgery
 - Antibodies may still be present
- Risk of passing antibodies with pregnancy

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Surgical Thyroidectomy

- Permanent Treatment for thyroid
- Risk of hypoparathyroidism
- Risk of vocal cord paralysis
- Scarring

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Surgical Thyroidectomy

- Should be performed by a surgeon with high thyroid surgery volume
- If surgeon does not have expertise, risk of complications are two fold
- Only removed the thyroid, antibodies can still be present

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Risks and Benefits of each treatment

- Decision making on treatment requires a honest and open discussion with family

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Ophthalmologic Complications

- Exophthalmos more common in adults than children
- Mild cases treat with eye drops
- Severe or progressive cases can be treated with steroid
- Worse cases may need surgery to reposition the eye

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Take home message

- Anti-Thyroid Medication
 - Anti-thyroid medication is the first line treatment for most children in the US
 - Small be real risk of side effects for MMI needs to be monitored for
 - Treatment is recommended for 12-24 months to assess for remission, (remission rates are low in most studies)

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Take home message

- RAI
 - Should be considered for children age 10 years and up
 - May be considered for children age 5-10 years with a smaller thyroid size and lower I-131 dose
 - Children under 5 are not recommended
 - Risk of thyroid cancer after RAI is exceeding low

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Take home message

- Thyroidectomy
 - Should be performed by a highly skilled high volume surgeon

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Case study

- Labs ordered by endo
 - TSH <0.01
 - Free T4 10
 - TSI >140
 - TPO 385
 - TG 184
 - CBC WNL
 - LFT's WNL

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Case Study

- Medications
 - Started on methimazole 20mg po TID
 - Started on atenolol 100mg po qhs
- She became euthyroid at by three months is is being maintained on methimazole 5mg po daily

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Questions

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