THYROID DISEASE IN CHILDREN

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Neither I nor any immediate family members have any financial interests that may be construed as a conflict of interest with this presentation.
LEARNING OBJECTIVES
At the end of this lecture, participants will be able to:

1. Recognize and evaluate the following conditions in children:
   - congenital hypothyroidism
   - acquired hypothyroidism
   - hyperthyroidism
   - thyroid nodules

2. Initiate treatment for congenital hypothyroidism

3. Treat acquired hypothyroidism
Lingual Thyroid

Courtesy of Dr. Dennis Brenner
Ectopic Thyroid
SIGNS OF CONGENITAL HYPOTHYROIDISM
PERCENT WITH SIGN AT 5 WEEKS

- 31% prolonged jaundice
- 23% umbilical hernia
- 21% constipation
- 21% macroglossia
- 19% feeding problems
- 16% hypotonia
- 16% hoarse cry
- 13% large posterior fontanelle
- 10% dry skin
- 5% hypothermia
- 2% goiter
- 40% delayed bone age
Congenital hypothyroidism occurs in 1:4000 infants.
Congenital hypothyroidism with goiter due to maternal PTU.
MANAGEMENT OF CONGENITAL HYPOTHYROIDISM

- Documentation
  - Free T4, TSH
- Thyroid scan, ultrasound (optional)
- Treatment (normal size full term)
  - start L-thyroxin at 10-15mcg/Kg daily
  - Monitor TSH every 2-3 months during first 2 years of life.
SYMPTOMS OF ACQUIRED HYPOTHYROIDISM

- Weakness
- Lethargy
- Decreased appetite
- Cold intolerance
- Constipation
- Weight gain
SIGNS OF ACQUIRED HYPOTHYROIDISM

- Goiter
- Growth failure
- Delayed dentition
- Delayed or precocious puberty
- Galactorrhea
- Carotenemia
- Pale dry skin
Girl with TSH of 366.51
Acquired hypothyroidism

Treated hypothyroidism
All forms of thyroid disease are more common in children with Down syndrome.
EVALUATION OF ACQUIRED HYPOTHYROIDISM

• Documentation
  – TSH
  – Free T4
  – Microsomal antibodies
TREATMENT OF ACQUIRED HYPOTHYROIDISM

- L-thyroxine
  - start with a low dose
  - 0.025 or 0.05 mg daily
- Monitor TSH level every 4 - 6 weeks
- Increase L-thyroxine by 0.0125 mg increments until TSH is normal.
- Monitor TSH every 6 months
SICK EUTHYROID SYNDROME

T4  T3  rT3  TSH

Sick euthyroid  Low  Low  High  Low or Normal

Hypothyroidism  Low  Low  Low  High
CAUSES OF HYPERTHYROIDISM

• Excess production of T4
  – Graves’ disease
  – toxic adenoma
  – pituitary resistance to T4
  – McCune-Albright syndrome
  – TSH receptor mutations
  – TSH producing pituitary tumor

• Excess release of T4
  – Subacute thyroiditis
  – Hashimoto’s toxic thyroiditis
  – iodine induced hyperthyroidism
SIGNS AND SYMPTOMS OF GRAVES’ DISEASE IN ADOLESCENTS

- 98% goiter
- 82% tachycardia
- 82% nervousness
- 80% increased pulse pressure
- 65% proptosis
- 60% increased appetite
- 52% tremor
- 50% weight loss
- 30% heat intolerance
Graves’ disease
EVALUATION OF HYPERTHYROIDISM

• Documentation
  – Free T4, TSH
• Determine etiology
  – thyroid stimulating immunoglobulins
  – radioactive iodide uptake scan
TREATMENT OF GRAVES’ DISEASE

• Antithyroid medications
  – PTU 5-10 mg/Kg divided t.i.d.
    • Not recommended due to liver toxicity
  – Methimazole 0.5-1 mg/Kg daily
• $^{131}$I radioactive ablation
• Thyroidectomy
SIDE EFFECTS OF ANTITHYROID DRUGS

- Rash
- Nausea
- Headache
- Puritus
- Lupus

- Arthritis
- Alopecia
- Hepatic toxicity
- Agranulocytosis
It is possible to make an antibody that is directed against the antigen binding site of another antibody (i.e., the antigen binding site is the epitope). This type of antibody is called an anti-idiotype antibody. In this case, the antigen binding site of the anti-idiotype antibody can be similar in structure to the original antigen (they both recognize the same antibody.)
STIMULATING AUTO-ANTIBODIES (Graves’ disease)

- Pituitary gland
- TSH
- TSH receptor
- Auto-antibody to receptor
- Stimulates hormone synthesis
- Thyroid cell

Negative feedback control

Regulated production of thyroid hormones

Unregulated overproduction of thyroid hormones
Neonatal Graves’ Disease
SIGNS AND SYMPTOMS OF NEONATAL GRAVES’ DISEASE

- Premature birth
- Low birth weight
- Goiter
- Restlessness and irritability
- Fever, flushing
- Tachycardia, cardiomegally, heart failure
- Lid retraction, proptosis, periorbital edema
- Poor weight gain, or weight loss
- Increased gastrointestinal motility, frequent stooling
Neonatal Graves’ disease
TREATMENT OF NEONATAL GRAVES’ DISEASE

• Acutely may require beta-blocker, prednisone and Lugol’s solution.
• Methimazole 0.5 – 1mg/Kg daily
  – Goal is to completely suppress the thyroid gland
• Must give L-thyroxin
  – Usually start 25mcg daily
    • Adjust to keep free T4 and TSH in normal range
• Treat for 6 months
  – Maternal antibodies will be cleared by that time
  – Stop Methimazole and L-thyroxin at same time.
SUBACUTE THYROIDITIS

- Physical exam
  - painful swelling of the thyroid
  - signs of hyperthyroidism
- Laboratory evaluation
  - high T4, low TSH, high ESR, absent TSI
  - decreased radioactive iodide uptake scan
- Treatment
  - beta blockers
  - ASA, glucocorticoids
Thyroid nodule
## THYROID NODULES IN CHILDREN

<table>
<thead>
<tr>
<th>Carcinoma</th>
<th>Adenoma</th>
<th>Author</th>
<th>Year</th>
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<tbody>
<tr>
<td>35%</td>
<td>52%</td>
<td>Hayles</td>
<td>1956</td>
</tr>
<tr>
<td>20%</td>
<td>25%</td>
<td>Adams</td>
<td>1968</td>
</tr>
<tr>
<td>40%</td>
<td>24%</td>
<td>Kirkland</td>
<td>1973</td>
</tr>
<tr>
<td>17%</td>
<td>58%</td>
<td>Scott</td>
<td>1976</td>
</tr>
</tbody>
</table>
M.E.N. SYNDROMES

• M.E.N. 1
  – parathyroid, pituitary, and pancreatic adenomas
• M.E.N. 2a
  – medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma
• M.E.N. 2b
  – medullary thyroid carcinoma, pheochromocytoma, mucosal neuromas, intestinal neuromal dysplasia, marfanoid habitus
• Familial medullary thyroid carcinoma
M.E.N. 2

- **M.E.N. 2a**
  - Due to mutations in the extra-cellular region of the RET receptor.
  - Usually autosomal dominate inheritance.
  - Recommend thyroidectomy at age 3 years.

- **M.E.N. 2b**
  - Due to mutations in the intra-cellular region of the RET receptor.
  - Usually sporadic mutations.
  - Earlier development of medullary thyroid carcinoma.
  - Thyroidectomy done as soon as diagnosis made.
MEN 2b
# EXPECTED BLOOD TEST RESULTS IN PEDIATRIC THYROID DISEASE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Free T4</th>
<th>TSH</th>
<th>Antibodies</th>
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<tbody>
<tr>
<td>Congenital hypothyroidism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>athyrotic</td>
<td>low</td>
<td>high</td>
<td></td>
</tr>
<tr>
<td>nonathyrotic</td>
<td>normal / low</td>
<td>high</td>
<td></td>
</tr>
<tr>
<td>Acquired hypothyroidism</td>
<td>normal / low</td>
<td>high</td>
<td>microsomal</td>
</tr>
<tr>
<td>Euthyroid sick syndrome</td>
<td>low</td>
<td>normal/ low</td>
<td>absent</td>
</tr>
<tr>
<td>Graves’ disease</td>
<td>high</td>
<td>low</td>
<td>T.S.I.</td>
</tr>
<tr>
<td>Subacute thyroiditis</td>
<td>high</td>
<td>low</td>
<td>absent</td>
</tr>
</tbody>
</table>
Question 1
A 16 y.o. girl complains of weight loss, nervousness and tenderness in her anterior neck. Which of the following will clearly differentiate Graves’ disease from subacute thyroiditis?

A  Free T4  
B  T3  
C  TSH  
D  radioactive iodide uptake scan
Question 2
Which of the following medications is **NOT** helpful in treating subacute thyroiditis?

A  PTU  
B  Propanolol  
C  Aspirin  
D  Prednisone
Question 3
A goiter (thyroid enlargement) is usually NOT present in which of the following?

A  Hashimoto’s thyroiditis
B  Congenital hypothyroidism
C  Graves’ disease
D  Subacute thyroiditis
Question 4
A 15 y.o. girl complains of constipation, tiredness and galactorrhea. On exam you note an enlarged firm thyroid gland. What is the most cost effective blood test to confirm your suspicion of hypothyroidism?

A  TSH
B  T4, TSH, microsomal antibodies
C  Free T4, TSH, prolactin
D  T4, T4RU, TSH, thyroglobulin antibodies
Question 5
A child’s father has M.E.N. 2. Which screening test should be performed?

A  Fasting calcitonin level
B  Calcitonin level after calcium infusion
C  24 hour urine for metanephrines
D  Genetic testing on both the father and child
Question 6
This boy has:
A) just broken a neighbor’s window with his baseball
B) just watched the movie “Halloween”
C) subacute thyroiditis
D) Graves’ eye disease
Question 7.
An adolescent female complains about her tall stature. On physical exam you notice some nodules on her lips and tongue. She has a history of severe constipation. No other family members have similar problems or findings.

What is your next step.
A. Obtain RET mutation analysis
B. Exam patient’s parents.
C. Obtain calcitonin and CEA levels
D. Obtain Ca++ and PTH levels.
Answers

1. D
2. A
3. B
4. A
5. D
6. D
7. A