2:25–3:05pm
Diagnosing and Treating Thyroid Disorders
SPEAKER
John Tayek, MD

Presenter Disclosure Information
The following relationships exist related to this presentation:
► John Tayek, MD, serves on the speaking bureau for Takeda, Eisai, and Jansen.

Off-Label/Investigational Discussion
► In accordance with pmICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Common Thyroid Disorders for 2014
email: tayeks@gmail.com
• SubClinical Hypo and Hyperthyroidism
• Thyroid Storm, Myxedema Coma
• Thyroid Disease and Miscarriages

Learning Objectives
• 10% of women at the age of 80 have hypothyroidism
• Identify risk factors associated with hyperthyroidism and new onset atrial fibrillation, anxiety disorder, psychosis and osteoporosis.
• Measure both FT4 and TSH in hospitalized patients
• Identify long term risk of mildly elevated or reduced TSH concentration.

Case A: GOITER

GOITER
and
Shortness
of Breath
**Case 1: Progressive Weakness for 3 Months**

- 82 y/o male with normal CBC, Chemistry, ANA, B12, Folate, Heavy Metal, S-PEP, U-PEP, RPR, CXR, nerve condition: reduced amplitude; nerve biopsy: axonal degeneration; LP: CSF: no cell, elevated protein 254 mg/dl (15-45).
- Dx: CIDP: Chronic Inflammatory Demyelinating Polyneuropathy; 5 iv IGG Tx without help
- TSH 144, free T4 0.4; 3-months of Tx: TSH 33 mild improvement; 12 months Tx: TSH normal, patient walks

(Razavi M, Lancet 355:38, 2000)

**FATIGUE AND MUSCLE PAIN**

- Subclinical hypothyroidism can cause an elevation in the CPK (creatinephosphokinase), aldolase, muscle pain and fatigue.
- Muscle pain as caused by hypothyroidism is very rare but it does exist.
- Biopsy shows loss of fast twitch muscle fibers (type II). Only 10 cases have been identified in 16 years.
- Treatment is simple, treat with thyroid hormone even if the TSH is only slightly elevated (5-15).

**HYPOTHYROID MYOPATHY (<1%)**

<table>
<thead>
<tr>
<th>CASE</th>
<th>TSH(4-4.4)</th>
<th>CPK (30-200) / ALDOLASE (0-8.1)</th>
<th>NOTES:</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>10</td>
<td>300* / --</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>21</td>
<td>1138* / --</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>16</td>
<td>3000* / --</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>158</td>
<td>816* / 4.8</td>
<td>LDH 317* (nl 109-230)</td>
</tr>
<tr>
<td>M</td>
<td>--</td>
<td>484* / --</td>
<td>AUTOPSY: pituitary increased TSH</td>
</tr>
<tr>
<td>F</td>
<td>207</td>
<td>1536* / 6.1</td>
<td>CPK decreased to 62 at 6 weeks Tx</td>
</tr>
<tr>
<td>M</td>
<td>15</td>
<td>39 / 4.8</td>
<td>LDH 353* /380*</td>
</tr>
<tr>
<td>F</td>
<td>377</td>
<td>1125* / 5.4</td>
<td>CK decreased to 183 at 6 months Tx</td>
</tr>
<tr>
<td>F</td>
<td>107</td>
<td>382* / --</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>47</td>
<td>139 / 12.7*</td>
<td></td>
</tr>
</tbody>
</table>

average: 106±41 896±295 / 6.8±3.3 (mean±sem)

**INCIDENCE AND ETIOLOGY OF HYPOTHYROIDISM**

- Cretinism (1:4000 live births)
- Adults (1:500); Seeking Medical Care (1:100)
- Chronic Autoimmune Thyroiditis (Hashimoto’s Disease)
- Postpartum Thyroiditis (occurs in 1-6% of women postpartum @ 4-6months p birth; lasts 2-8 weeks)
- Drugs (131I, Amiodarone, iodine, PTU, Methimizole)
- Secondary Hypothyroidism (TSH can be normal)

**HYPOTHYROIDISM WITH AGE AND SEX**

<table>
<thead>
<tr>
<th>AGE</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>0.025%</td>
<td>0.025%</td>
</tr>
<tr>
<td>20-50</td>
<td>0.1 %</td>
<td>0.2 %</td>
</tr>
<tr>
<td>60-70</td>
<td>0.5 %</td>
<td>1.0 %</td>
</tr>
<tr>
<td>70-80</td>
<td>1.0 %</td>
<td>4.0 %</td>
</tr>
<tr>
<td>80-90</td>
<td>2.0 %</td>
<td>10.0 %</td>
</tr>
</tbody>
</table>

**When To Screen for Thyroid Disease**

- USPSTF: The USPSTF concludes the evidence is insufficient to recommend for or against routine screening for thyroid disease in adults.
- Thyroid Society: American Thyroid Association (ATA), which recommends thyroid screening in all adults beginning at age 35 years, and every 5 years thereafter.
- The ATA/AACE Clinical Practice Guidelines for Hypothyroidism in Adults recommend screening for hypothyroidism be considered in patients over the age of 60.
- The American Academy of Family Physicians (AAFP) recommends routine screening only in asymptomatic patients older than 60.
SITE OF HYPOTHYROIDISM

- 99% of hypothyroidism originates at the thyroid gland.
- 1% of the time the pituitary or hypothalamus is responsible for the hypothyroidism.
- Don’t forget about the secondary causes since they are usually associated with other pituitary diseases (tumor, autoimmune, etc).

CASE 2

- UNSURE: Repeated the T4 level of 3.3 the day of consult: which was 1.1 * (Dangerously low)
- TSH 3.3
- Cortisol 3.4 (normal random cortisol for hospitalized patients is between 10 and 30 (without liver disease)
- ACTH stimulation test 3.4, 9.0 at 30 min and 10 at 60 min: confirming the diagnosis of secondary adrenal insufficiency
- Diagnosis Pan-Hypo Pituitarism (partial); AKA Mild Myxedema Coma

MYXEDEMA COMA

- This is Medical Emergency:
- She was tx with 100 of hydrocortisone and 200 mcg of oral L-thyroxine. Serum T4 increased to 4.4 the next day. Patient woke up the next day and was discharged on day 4.
- She had loss of menstrual period 30 years prior just after the birth of her child at age 35. She had no axillary or pubic hair.

Myxedema Coma
(3 of 11 had near normal TSH)

Inpatient Confused Female

- Always get at the minimum of T4, TSH and cortisol. Better yet, get:
  - T4
  - TSH
  - Cortisol
- (Do not forget my case of the lady with 3 3’s)
- T4 =3; TSH = 3 and Cortisol 3. This is Panhypopit until proven otherwise.
**MYXEDEMA COMA**

- This is a Clinical Diagnosis: overt hypothyroidism with progressive stupor and coma; look for triad: **hypothermia, hypotension and hypoventilation**
- Patients may also have seizures, hyponatremia, hypoglycemia, and respiratory acidosis.
- Give T4 (0.3 mg) by IV push into vein. **Do not give it piggy back; it is not soluble and will stick to the plastic tubing.** Also give hydrocortisone 50mg Q 8hrs; and T4 0.1 mg daily by IV push.

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**Top 6 Causes of Hyponatremia**

1) Diuretics
2) The Three Failures: CHF
3) Cirrhosis
4) Nephrosis
5) SIADH (Syndrome of Inappropriate ADH hormone)
6) Exercise-associated hyponatremia (EAH), 13% of Marathon Runners are hyponatremia at end of race.

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**Top 7 Causes of Hyponatremia**

- Diuretics
- The Three Failures: CHF
- Cirrhosis
- Nephrosis
- SIADH
- Exercise-associated hyponatremia
- Pan-hypopituitarism (usually women)

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**CASE 3 Continued:**

- **CORRECTED TFT VALUES**
  - cT3 = T3 x patients Tuptake/normal Tuptake
    
    \[
    \frac{200 \times 60/40}{40} = 300^* \text{ (normal 80 - 220)}
    \]
  - FT4 = Very elevated at 3.8* (normal 0.8-1.8)
  - TSH 4.2 (normal 0.4 to 4.4)
  - **Dx: TSH SECRETING PITUITARY TUMOR.**
  - Two of the 3 (FT4, cT3 and TSH) should be consistent to make the diagnosis.
  - She had 3 of 3 elevated consistent with Pit Tumor

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**THYROID STORM**

- Medical Emergency- treat in ER
- Clinical Diagnosis; look for signs of hyperthyroidism (a goiter is common)
- Fever (>38.5) and Tachycardia, (but the patients may have anorexia, nausea, vomiting, abdominal pain and CHF).
- Tx: Methimizol 30 mg @8 hrs po. ng or pr. Propranolol 40mg Q 6 hr, & hydrocortisone 50mg Q 8hrs; One hour after PTU give SSKI 5 gts Q6 hrs (iodine)
Atrial Fibrillation

- 6% of men and 3% of women over the age of 65 have Afib.
- 16% of men and 12% of women over age of 75 have Afib.
- While the most common cause is idiopathic, the second most common cause of thyroid disorder with approximately 75% due to hyperthyroidism and 25% due to hypothyroidism.
- Always check both TSH and FT4.

### Relative Risk of Developing Atrial Fibrillation in > 60-Year Old Individuals

<table>
<thead>
<tr>
<th>REL. RISK</th>
<th>TSH mU/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>1</td>
<td>0.1 - 0.4</td>
</tr>
<tr>
<td>2</td>
<td>0.4 - 5.0</td>
</tr>
<tr>
<td>3</td>
<td>&gt; 5.0</td>
</tr>
</tbody>
</table>

*Sawin NEJM 331:1249, 1994*

\[ \text{p} < 0.05 \]

68 y/o have a 13% risk of New Onset Afib over 8 years with a “Low-Normal” TSH

- New onset AFib occurred in 13% (105/1426) of patients with “normal” TSH
- The authors set at a odds ratio of 1 (TSH 2.2-4.0), OR was 1.3 for a TSH 1.05-2.2 (not significant)
- But: the Odds Ratio was 1.97 (p<0.05) if you have a “normal” TSH of 0.1 – 1.04 (Rotterdam Study, Heeringa J, 2008)

- (Keep TSH 2.0 to 4.0 in 60+ year old patients)

ETIOLOGY OF HYPERTHYROIDISM

- Graves Disease (most common)
- Early Hashimoto’s Thyroiditis (anti-TPO Diagnostic)
- Postpartum Thyroiditis (occurs in 1-6% of women postpartum @ 2-6months p birth; lasts 2-8 weeks)
- Subactue thyroiditis (post viral syndrome)
- Toxic Nodule(s)
- Thyroid CA; Pituitary Tumor; Trophoblastic tumor (HCG cross reacts with TSH receptor)

METHOD TO DIAGNOSIS SOURCE OF HYPERTHYROIDISM

- Graves Disease: 24hr ¹²³I uptake ≥40%, +TSI, proptosis >24mm, or pretibial plaquing (myxedema)
- Hashimoto’s Thyroiditis: ¹²³I uptake patchy; TPO + ABs
- Postpartum & Subacute Thyroiditis: ¹²³I uptake <5%
- Toxic Nodule(s): ¹²³I uptake only in nodule(s)

SICK EUTHYROID IN CRITICAL ILLNESS

- Diagnosis: very low T3, normal cT4 and normal TSH.
- No Need to treat “low T3 syndrome”.
- Beneficial Response to Conserve Energy.
- TSH increases during recovery but usually does not exceed 16 IU/ml.

- Only consider treating if patient has TSH >16 and has an increased PaCO2, decreased body temperature (hypothermia) or an altered mental status; Or a reduced “corrected T4” <3.0.
Long term Mortality Associated with Mildly Abnormal TSH (Subclinical Thyroid Disease)

- 6.2% have high TSH with nl fT4 and T3 or fT3
- 8.9% have low TSH with “

7-year follow-up: 12.1% vs 5.1 if TSH was mildly elevated (2-fold increase in morality; NNT=14).

- However if TSH was mildly depressed the mortality was increased from 5.1% to 21.7% or a 4-fold increase in mortality(NNT=6)
- My personal opinion is to Tx mildly depressed TSH levels (<1.0 if patients have symptoms) (Sgarbi 2008)

Thyroid Disorders in Women with Mild Iodine Deficiency

- TSH is increased in 7.2% of pregnant pts in Belgium
- TSH was decreased 3.6% (subclinical)
- TSH was in the hyperthyroid range in 0.5%

- Therefore: 11.3% of pregnant women have mild thyroid disease (Moreno-Reyes JCEM 2013)

TSH, anti-TPO and Pregnancy

- Treatment of a NORMAL TSH may reduce miscarriage rates n=984 if you have a + TPO titer (12%+ for TPO)
- Miscarriage rate for TPO+ untreated 13.8%
- Miscarriage rate for TPO+ treated was 3.5% (NNT= 10)
- Control group (TPO-) miscarriage rate was 2.4%

Progression of SubClinical Hypothyroidism

- 73 pts (>60yo) with SubclinicalHypo were followed for 1 yr. 17.8% progressed to overt hypothyroidism. 5.5% normalized, 76.7% unchanged.
  - TSH>10
  - + antithyroid abs
- 76 pts (>60y/o) with Subclinical Hypothyroidism 10 yr f/u. 40% developed overt hypothyroidism

Parfe et. al. Clin Endocrinol. 1991;31:77-83

Treating Hypothyroidism

- Most generic L-thyroxine have a variable rate of absorption.
- Follow TSH every year while on the same generic medication.
- Remember that L-thyroxine taken on an empty stomach will increase absorption by 20 to 30%
- Likewise, PPI therapy (raising stomach pH from 2 to 5) will reduce absorption by 20-30%

Summary (In Patient)

- When evaluating a patient with any alteration in the mental status, the TSH may not accuracy direct you towards the correct diagnosis.
- Pituitary disease and other illnesses can alter the accuracy of the meaning of a “Normal” TSH (Remember the rule of 2 out of 3).
- T3 is not useful in critical illness as it is frequently very low due to euthyroid sick syndrome.
- Get additional thyroid hormone measurements (and repeat them as needed) in someone who has an altered mental status.
Summary (Out-Patient)

- TSH accounts for approximately 95% in the accuracy of the outpatient diagnosis.
- Subclinical hypothyroidism should be treated in patients with TSH over 6; or if they have TPO+ AB since approximately 42-58% will progress to overt hypothyroidism.
- Treat all women with a history of miscarriage who are pregnant and are TPO+.
- Keep TSH between 2-4 to prevent new onset Afib.
- Worry about TSH less than 1.0 as it may contribute to new onset Afib in the elderly.

Learning Objectives

- 10% of women at the age of 80 have hypothyroidism
- Identify risk factors associated with hyperthyroidism and new onset atrial fibrillation, anxiety disorder, psychosis and osteoporosis.
- Measure both FT4 and TSH in hospitalized patients
- Identify long term risk of mildly elevated or reduced TSH concentration.

Questions

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