Using Evidence Based Guidelines
Managing Hypothyroidism In Women

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No Disclosure

• I have no financial interest or other conflict of interest in relation to this program or presentation.

Objectives

• Brief review of the thyroid and thyroid hormones.
• Describe clinical presentation of women with hypothyroidism.
• Discuss screening for hypothyroidism and diagnostic workup.
• Discuss evidence based treatment and management of hypothyroidism.
Thyroid Gland

- Thyroid hormones made from Iodine
  - Thyroxine (T4)
  - Triiodothyronine (T3)
  - Mostly made in liver
- Many targets in human body

Hypothyroidism

- Common endocrine disorder
- The thyroid gland is unable to produce sufficient amounts of thyroid hormone.
- Risk of developing increases with age, during pregnancy, postpartum and menopause.
Causes

• Primary: ~95%
  • Iodine deficiency
  • Hashimoto’s Thyroiditis
  • Atrophic hypothroidism

• Secondary: ~5%
  • Radiation therapy to neck area
  • Radioactive iodine treatment
  • Use of certain medications
  • Thyroid surgery
  • Pregnancy
  • Pituitary gland disorder or thyroid problems at birth
  • Disorder of hypothalamus

Risk Factors

• Race
  • White or Asian
• Female
• Age >60

• Autoimmune Disorders
  • Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, vitiligo, pernicious anemia

• Turner syndrome or Down Syndrome

• Usage of certain meds (Lithium, Amiodarone)

Clinical Presentation

• Cardiac
  • Bradycardia
  • Hypotension

• Neurologic
  • Slow mentation
  • Slow, low pitched, slurred speech
  • Hyporeflexia
  • Delayed achilles reflex time
  • Depression
  • Carpel tunnel

• Reproductive
  • Menorrhagia
  • Repeat miscarriages
  • Infertility

• Dermatologic
  • Cool, dry, coarse hair
  • Brittle nails, yellow discoloration

• Hypothermia
  • Thin, coarse hair
  • Low, hoarse voice
  • Non-pitting generalized edema

Garber, J. et al. (2012) Endocrin Pract 21, 1161-1170
Differential Diagnosis

- Depression
- Non-thyroidal illness
- Thyrotropin-secreting pituitary adenomas
- Resistance to TSH

Screening & Workup

- Screening
- Health History Assessment
- Diagnostic Work-up

Screening Recommendations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Screening Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Thyroid Association</td>
<td>Women and men initial screening at age 35 and every 5 years thereafter</td>
</tr>
<tr>
<td>American Association of Clinical Endocrinology</td>
<td>Older patient especially women</td>
</tr>
<tr>
<td>American Academy of Family Physicians</td>
<td>Patients ≥ 60 years of age</td>
</tr>
<tr>
<td>American College of Physicians</td>
<td>Women ≥ 50 years of age with an incidental finding suggestive of symptomatic thyroid disease</td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force</td>
<td>Insufficient evidence for or against screening</td>
</tr>
</tbody>
</table>
Screening Recommendations for Pregnancy

<table>
<thead>
<tr>
<th>Organization</th>
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</tr>
</thead>
<tbody>
<tr>
<td>American Thyroid Association (2011)</td>
<td>Insufficient evidence to recommend for or against universal TSH screening in the first trimester. Consider screening in women who are high-risk</td>
</tr>
<tr>
<td>Endocrine Society Guideline (2012)</td>
<td>Divided Some recommend universal screening by 9 week gestation. Some recommend screening on high-risk basis</td>
</tr>
<tr>
<td>ACOG</td>
<td>Recommend against screening</td>
</tr>
</tbody>
</table>

Diagnosing Hypothyroidism Can Be Challenging

Health History Assessment

- Complaints of symptoms consistent with hypothyroidism
- Family history
- Other endocrine disorders
- Other autoimmune diseases
- Previous radiation to the neck
- Thyroid surgery
- Medications linked to hypothyroidism
- Physical exam finding of a goiter
Thyroid Stimulating Hormone (TSH)

- Serum TSH is the primary screening test for:
  - Thyroid dysfunction
  - Evaluation of thyroid hormone replacement in patients with primary hypothyroidism

- When is TSH not a sensitive indicator of thyroid function?

What Is a Normal Serum TSH Value?

- Reference population: 0.4 to 4 mIU/L[^1]
- Elderly population (older than 70 y): 5.9 to 7.5 mIU/L[^2]
- During pregnancy[^3]
  - First trimester: less than 2.5; range of 0.1 to 2.5 mIU/L
  - Second trimester: 0.2 to 3.0 mIU/L
  - Third trimester: 0.3 to 3.0 mIU/L


Thyroid Labs for Evaluating Suspected Hypothyroidism

- Thyroid Stimulating Hormone (TSH)
  - If abnormal repeat-level can be falsely elevated
  - Corticosteroids, Aspirin, and X-rays using iodine dye
- Free Thyroxine (Free T4)
  - If TSH is elevated

**Free Thyroxine (T4)**
- Evaluate serum T4 if TSH is elevated
- Evaluate serum T4 if Pituitary disease is suspected
- Elevated TSH and normal T4 is subclinical
- Use to elevate post thyroidectomy, ablation, anti-thyroid drug treatment.

**Total T3 or Free T3**
- Total T3 includes bound and unbound
- Free T3 not bound to protein
- Not useful in diagnosing hypothyroidism because levels are often normal due to hyperstimulation of the remaining functioning thyroid tissue by elevated TSH
- T3 can be decreased due to other causes which prevents conversion of T4 to T3.
  - Garber, J. et al. (2012) *Endocrin Pract* 21, 1161-1170

**Thyroid Antibody Test**
- Thyroid Peroxidase (TPO)
- Thyroglobulin
- Aide in the diagnoses of Hashimoto’s Thyroiditis
- Aide in the diagnosis of Autoimmune Thyroid disease
- Consider evaluating when patient has a goiter or subclinical hypothyroidism.
- If positive and TSH and Free T4 are normal monitor TSH annually.
  - Garber, J. et al. (2012) *Endocrin Pract* 21, 1161-1170
Diagnostic Studies

Radioactive Iodine Uptake
- Elevated (High RAIU) with hyperthyroidism
- Decreased (Low RAIU) with hypothyroidism

Thyroid Ultrasound
- Palpable thyroid nodule(s)
- Evaluation of a goiter

Treatment
- Primary hypothyroidism with TSH level > 10 mIU/L
  - General agreement to treat
- TSH level 4.5 – 10 mIU/L
  - No general consensus to which patient will benefit from treatment
- TSH levels between 2.5 and 4.5 mIU/L
  - Some data to support treating patients with subclinical hypothyroidism with ischemic heart disease.
  - Data to support treating those age 40-70 resulted in decreased risk of cardiac events.
  - Data to support treating during pregnancy.

Levothyroxine (LT4)
- Monotherapy is the current standard of treatment
- Levothyroxine is the standard drug used for the treatment of hypothyroidism
- General dose for hypothyroidism approximately 1.6mcg/kg
- Dosing depends on:
  - Age
  - Body mass index
  - Co-morbid conditions such as cardiac disease

Garber, J. et al. (2012) Endocrin Pract 21, 1161-1170
Initiation of Medication in Hypothyroidism

- Young adults with overt hypothyroidism should begin treatment with FULL replacement dose.
- Patients 50-60 years old without evidence of coronary heart disease begin L-thyroxine dose at 50 mcg daily.
- Re-evaluate TSH 4 – 8 weeks after starting therapy.

<table>
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<tr>
<th>Population</th>
<th>Dosing</th>
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<tr>
<td>Non-pregnant</td>
<td>1.6 mcg/kg/day</td>
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<tr>
<td>Older patients with cardiac disease</td>
<td>25-50 mcg daily starting dose; increase by 25 mcg every 3-4 weeks until full replacement dose reached</td>
</tr>
<tr>
<td>Subclinical hypothyroidism TSH &lt; 10</td>
<td>50 mcg daily; increase by 25 mcg every 6 weeks until TSH 3.5-5.5; TSH &gt; 10 – 1.6 mcg/kg/day</td>
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Patient Education

- L-thyroxine should be taken with water consistently
  - 60 minutes before a meal ideally
  - 3 or more hours after a meal
  - At bedtime
  - The goal is to take it at the same time daily

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Patient Education

- Do not take with food or coffee results in decreased absorption
- Important to notify providers of all new medications, changes in dosages and over the counter medications, vitamins and herbals.
- Notify provider of changes in the pill
  - color or size with prescription refills.
  - Changes from brand to generic

Consideration if Patient is Requiring Higher Dose of Levothyroxine

- Evaluate for Helicobacter Pylori
- Gastritis
- Celiac Disease
  - When placed on a gluten free diet, less Levothyroxine is required.

Different Formulations of LT4

- Different LT4 preparations (brand or generic) may be associated with varying TSH values<sup>a</sup>
  - Reassess the TSH level to identify if fluctuations occur among the various preparations designated as interchangeable by the FDA
- According to US FDA absorptive data, there is a difference of up to 12.5% among the various preparations<sup>b</sup>
- Inform patients to notify their healthcare provider if they see changes in pill size, shape, or color
  - This may occur if they are ordering their medication from a different pharmacy or a mail order pharmacy


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Alternative Preparations for the Treatment of Hypothyroidism

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Effect of Biotin on Thyroid Function Tests

- Patients take biotin supplements to improve hair, skin, and nails
- Interferes with immunoassays that measure thyroid hormone with a biotinylated antibody
- Results: falsely high T4 and T3 results and falsely low TSH levels
- Patient education point:
  - Disclose all current medications and supplements
  - Do not take biotin supplements 2 days before laboratory tests<sup>c</sup>

<sup>c</sup> References cited in the slide.
**Risk of Overprescribing Levothyroxine**

- Hyperthyroidism
- Atrial fibrillation
- Osteoporosis
- Angina
- Cardiac Tachydysrhythmias

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Risk of Inadequate Levothyroxine

- Atherosclerotic heart disease
- Congestive Heart Failure
- Dyslipidemia
- Infertility
- Cognitive Impairment
- Myxedema Coma


Treatment Prior to Pregnancy

- LT4 should be considered in women of childbearing age with serum TSH levels between 2.5 mIU/L and the upper limit of normal for lab’s reference range if in 1st trimester or planning pregnancy soon.
- Pre-conception education and stabilize LT4 dose
- Check thyroid function tests as soon as pregnancy confirmed.

- McNeil & Stanford, 2015
LT4 Treatment in Pregnant Women

- Increased dosage required in majority of women
- Average dose increase about 30%
- Increase usually required before 1st OB visit (7-8 weeks).
  - Example: Take 2 additional doses of medication/week
- Monitor TSH during pregnancy

Garber, J. et al. (2012) Endocrin Pract, 21, 1161-1170

Circumstances for Endocrine Consult

- Difficulty maintaining euthyroid state
- During pregnancy
- Planning to become pregnant with history of hypothyroidism
- Cardiac disease
- Presence of nodule or other structural thyroid changes
- Presence of other endocrine abnormalities such as pituitary and adrenal disorders

ICD-10 Codes

- E03.9 Hypothyroidism, unspecified
- E06.3 Autoimmune thyroiditis
- E89.0 Postprocedural hypothyroidism
Questions?

• Thank you!!