Update on Thyroid Disorders

Linda Rogers, PhD, DABCC, FACB
Objectives

1. Define hypothyroidism and hyperthyroidism and describe the common clinical presentations and the general laboratory diagnosis of each

2. Understand and describe the differences in the reference ranges of key thyroid tests in pediatric patients and pregnant women

3. Describe Grave’s Disease and the utilization of the thyroid stimulating antibodies (TSI) assay in its diagnosis and management.
Agenda

1. Overview of the thyroid endocrine system
2. Hypothyroidism: clinical presentation and the general laboratory diagnosis
3. Hyperthyroidism: clinical presentation and the general laboratory diagnosis
4. Grave’s Disease and the utilization of the thyroid stimulating antibodies (TSI) assay in its diagnosis and management
5. Thyroid disorders and pregnancy
6. Pediatric reference ranges
7. Clinical case studies
Epidemiology of Thyroid Dysfunction: United States

Affects 27 million Americans

80% are female

Most common endocrine disorder

More common than diabetes

http://www.suite101.com/content/how-many-americans-suffer-thyroid-disorders-a135894
Thyroid Dysfunction and Diagnosis

The right test... at the right time... facilitates correct diagnosis.
Thyroid Hormone Regulation

Thyroid Hormone Regulation

Hypothalamus

TRH

TSH receptor

Anterior pituitary

T3

T4

T3

T4

T3

T4

T3

T4

T3

T4

T3

T4

Thyroid Hormone Regulation
Thyroid Hormone Regulation

Lacuna

Thyrocyte
Thyroid Hormones are Essential

- Alters gene expression, protein production.
- Regulates metabolism – proteins, fats, carbohydrates.
- Essential for normal development of the fetus and newborn brain, and somatic tissue.
Laboratory Tests Aid Diagnosis

**Lab Tests**

- TSH
- Third generation TSH
- Free T₄
- Total T₄
- Free T₃
- Total T₃
- T₃ uptake
- Anti-thyroid peroxidase antibody
- Anti-thyroglobulin antibody
- Thyroglobulin
- Thyroxine-binding globulin
- TRAb
- TSI(TSAb)

Hypothyroidism
Hypothyroidism: Basics

**Primary Disease**
Disease of the thyroid gland

**Secondary and Tertiary Disease**
- Disease of the hypothalamus
- Disease of the pituitary

**Insufficient Thyroid Hormone**
- $T_4$ and/or $T_3$
Hypothyroidism: Risk Factors

- Age
- Female Gender
- Consistent Symptoms
- Family History
- Autoimmune Disease
# Classification of Hypothyroidism by Etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gland Injury</td>
<td>• Subacute/acute thyroiditis (subacute/acute, lymphocytic, autoimmune)</td>
</tr>
<tr>
<td></td>
<td>• Thyroid surgery or irradiation</td>
</tr>
<tr>
<td></td>
<td>• Thyroid cancer–related thyrotoxicosis</td>
</tr>
<tr>
<td>Drugs</td>
<td>• Drugs (amiodarone, stavudine, thalidomide)</td>
</tr>
<tr>
<td></td>
<td>• Iodine-induced hyperthyroidism</td>
</tr>
<tr>
<td>Congenital</td>
<td>• Thyroid dysgenesis</td>
</tr>
<tr>
<td></td>
<td>• Thyroid dysmorphogenesis</td>
</tr>
<tr>
<td>Other Diseases</td>
<td>• hCG-mediated thyrotoxicosis</td>
</tr>
<tr>
<td></td>
<td>• TSH-mediated thyrotoxicosis</td>
</tr>
<tr>
<td></td>
<td>• Hemochromatosis</td>
</tr>
<tr>
<td></td>
<td>• Tumors</td>
</tr>
<tr>
<td></td>
<td>• Sarcoidosis</td>
</tr>
</tbody>
</table>

Hypothyroidism

Nonspecific Symptoms

- Fatigue
- Muscle weakness
- Impaired memory
- Impaired learning
- Weight gain
- Alterations in appetite
- Cold intolerance
- Dry skin
- Sexual disturbances
- Menstrual disturbance
- Impaired fertility
- Mental disturbances (depression)
- Sleep disturbances (sleepiness)
- Constipation
- Hair loss
Impact of Hypothyroidism

Myxedema Coma
- Life threatening, mortality rates 25% to 75%.
- Extreme hypothermia (24°C to 32.2°C).
- Complication of long term hypothyroidism, rare.

Cardiovascular Disease/Dysfunction
- Hypercholesterolemia.
- Impaired cardiac function (diastolic and systolic).
  - Increased systemic vascular resistance.
  - Decreased cardiac output.
Evaluating Hypothyroidism


Comprehensive Physical Exam

Serology: TSH, Total and Free $T_3$ and $T_4$

Imaging


Unrestricted © Siemens Healthcare Diagnostics Inc. 2015 All rights reserved.
“A TSH assay should always be used as the primary test to establish the diagnosis of primary hypothyroidism. The most valuable test is a sensitive measurement of TSH level.”

Primary Hypothyroidism: Overt Disease

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>High</td>
</tr>
<tr>
<td>Free T₄</td>
<td>Low</td>
</tr>
<tr>
<td>Free T₃</td>
<td>Low/normal</td>
</tr>
<tr>
<td>TgAbs</td>
<td>May be present</td>
</tr>
<tr>
<td>Anti-TPO</td>
<td>May be present</td>
</tr>
</tbody>
</table>

**Structural abnormalities**
- Thyroid scan
- Ultrasound

Primary Hypothyroidism: Subclinical Disease

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>High</td>
</tr>
<tr>
<td>Free T₄</td>
<td>Normal</td>
</tr>
<tr>
<td>Free T₃</td>
<td>Normal</td>
</tr>
<tr>
<td>TgAbs</td>
<td>May be present</td>
</tr>
<tr>
<td>Anti-TPO</td>
<td>May be present</td>
</tr>
</tbody>
</table>

Progresses to overt disease in 3% to 20% of cases

General Serology for Hypothyroidism

<table>
<thead>
<tr>
<th></th>
<th>TSH</th>
<th>FT4</th>
<th>FT3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Subclinical hypothyroid</td>
<td>↑</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

DS2

Should FT4 & FT3 have the #s as subscripts? Same question throughout.

Dina Salzer, 3/7/2016
Hypothyroidism: Monitoring Treatment

**TSH and Free T₄**
- Every 6-8 weeks until normalized
- Every 3–6 months
- Annually

Hyperthyroidism
“The sensitive TSH assay is the single best screening test for hyperthyroidism and in most outpatient clinical situations, the serum TSH is the most sensitive test for detecting mild (subclinical) thyroid hormone excess or deficiency.”

## Hyperthyroidism: Many Nonspecific Symptoms

<table>
<thead>
<tr>
<th>Hyperthyroidism - Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervousness and irritability</td>
</tr>
<tr>
<td>Palpitations and tachycardia</td>
</tr>
<tr>
<td>Heat intolerance or increased sweating</td>
</tr>
<tr>
<td>Tremor</td>
</tr>
<tr>
<td>Weight loss or gain</td>
</tr>
<tr>
<td>Alterations in appetite</td>
</tr>
<tr>
<td>Frequent bowel movements or diarrhea</td>
</tr>
<tr>
<td>Dependent lower-extremity edema</td>
</tr>
<tr>
<td>Sudden paralysis</td>
</tr>
<tr>
<td>Exertional intolerance and dyspnea</td>
</tr>
<tr>
<td>Menstrual disturbance (decreased flow)</td>
</tr>
<tr>
<td>Impaired fertility</td>
</tr>
<tr>
<td>Mental disturbances</td>
</tr>
<tr>
<td>Sleep disturbances (including insomnia)</td>
</tr>
<tr>
<td>Changes in vision, photophobia, eye irritation, diplopia, or exophthalmos</td>
</tr>
<tr>
<td>Fatigue and muscle weakness</td>
</tr>
<tr>
<td>Thyroid enlargement</td>
</tr>
<tr>
<td>Pretibial myxedema</td>
</tr>
</tbody>
</table>

Hyperthyroidism: Risk Factors

Evaluating Hypothyroidism

Comprehensive Physical Exam

Serology: TSH, Total and Free T₃ and T₄

General Serology for Hyperthyroidism

A Diagnostic Algorithm: Hyperthyroidism

1. **TSH**
   - Normal: No further testing
   - Low: Free T₄ or Total T₄

2. **Free T₄ or Total T₄**
   - Normal or Decreased: Free T₃ or Total T₃
     - Normal: Retest in 2–4 mos
     - Increased: T₃ thyrotoxicosis
   - Increased: Test for autoimmune disease
     - TRAb
     - TSI
     - Anti-TPO Ab

Severe Complications of Hyperthyroidism

Thyroid storm

- Confusion, psychosis, spasticity, convulsions coma
- Hyperthermia
- Nausea, vomiting, diarrhea
- Irregular pulse, tachycardia, hypertension followed by hypotension, cardiac collapse, heart failure
- Fatal without treatment, requires immediate therapy: 20% to 50% mortality even with treatment

Cardiovascular disease

- Decreased systemic vascular resistance
- Increased cardiac preload and output
- Systolic hypertension
- Congestive heart failure

Osteoporosis
Grave’s Disease

I've gotta cut back on the caffeine
Graves’ Disease

Diffuse Goiter
- Symmetrical
- Firm

Ophthalmopathy

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Jonathan Trobe, MD. CC-BY 3.00
Autoimmunity in Graves’ Disease

[Diagram showing the interaction between Anti-TSH Ab and TSH]
The TSH receptor

Stimulating epitope

Blocking epitope

Membra (lipid bilayer)

Thyocyte
TSH Autoantibodies

Thyroid stimulating antibody (TSAb) / Thyroid stimulating immunoglobulin (TSI)

Thyroid blocking antibody (TBAb) / Thyrotropin blocking inhibiting immunoglobulin (TBII)

Neutral antibody
Effect of Thyroid Stimulating Antibody
Effect of Thyroid Blocking Antibody
<table>
<thead>
<tr>
<th>Antibody type</th>
<th>Action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAb</td>
<td>Binds TSH receptor antibodies to either inhibit or stimulate</td>
<td>Hypothyroidism or Hyperthyroidism (depending on antibody type and possibly ratio)</td>
</tr>
<tr>
<td>TbAb</td>
<td>Blocks TSH binding, depresses T3/T4 production</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>TSAb</td>
<td>Blocks TSH binding, stimulates T3/T4 production</td>
<td>Hyperthyroidism</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assay type</th>
<th>Antibody type(s) detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAb</td>
<td>TBAb (blocking) and TSAb (stimulating)</td>
</tr>
<tr>
<td>Anti-TSHR</td>
<td>TBAb (blocking) and TSAb (stimulating)</td>
</tr>
<tr>
<td>TBII</td>
<td>TBAb (blocking) and TSAb (stimulating)</td>
</tr>
<tr>
<td>TSI</td>
<td>TSAb only stimulating</td>
</tr>
</tbody>
</table>
the text is in the tables and appears on a click - you'll see it in show mode - for the sake of animation, there is a white box over the text which fades to reveal text on a click.

Dina Salzer, 3/7/2016
# Overview of TSI Utility in Graves’ Disease

<table>
<thead>
<tr>
<th>Indication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of Graves’ Disease</td>
<td>• Differential diagnosis (vs. other hyperthyroid disease)</td>
</tr>
<tr>
<td>Ophthalmopathy</td>
<td>• Differential diagnosis in&lt;br&gt;  • unilateral orbitopathy&lt;br&gt;  • orbitopathy with euthyroid status&lt;br&gt;  • orbitopathy with hypothyroid status&lt;br&gt;  • Treatment guidance</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>• Useful in pregnant women with&lt;br&gt;  • current or past treatment&lt;br&gt;  • previous children with neonatal thyrotoxicosis&lt;br&gt;  • Fetal hyperthyroidism diagnosis</td>
</tr>
<tr>
<td>Neonatal hyperthyroidism</td>
<td>• Prediction and diagnosis</td>
</tr>
<tr>
<td>ATD treatment</td>
<td>• Helps predicts remission</td>
</tr>
</tbody>
</table>
Graves’ Disease Diagnosis

- Clinical signs and TSH, free T₄, and/or free T₃ results
- TSI(+) → Graves’ Disease
- TSI detected in 77.8%–100% of GD patients

<table>
<thead>
<tr>
<th></th>
<th>TSH</th>
<th>FT3</th>
<th>FT4</th>
<th>TSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonautoimmune hyperthyroidism</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>Neg</td>
</tr>
<tr>
<td>T₃ toxicosis</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>Neg / ↑</td>
</tr>
<tr>
<td>Graves’ Disease</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

Better Diagnostic Accuracy of TSI vs. TRAb

- 182 sera: 79 GD, 103 non-GD
- TSI assay demonstrated
  - 100% sensitivity
  - 100% specificity
  - 100% diagnostic accuracy
- TRAb assay: 96.9% diagnostic accuracy

Is it Graves’ Disease?

- **TSH Low**
  - **Free T4 High**
    - **TSI Assay (+)**
      - Graves’ Disease
    - **TSI Assay (-)**
      - Non-Autoimmune Hyperthyroidism
        - **TRab Assay (+)**
          - Stimulating Ab (+)?
          - Blocking Ab (+)?:
            - Is it Graves’ Disease?
            - Further investigation necessary
        - Non-Autoimmune Hyperthyroidism (e.g. toxic multi-nodular goiter, toxic thyroid adenoma)
    - Autoimmune Hyperthyroidism? (Graves’ Disease)
Do you want me to recreate this chart? It looks okay but it is placed as an image so the font is wrong.
Dina Salzer, 3/7/2016
TSI: Time and Cost Advantages

Based on a study by McKee and Peyerl, the use of algorithms that incorporate TSI testing early in the primary care setting resulted in:

- 46% less time to diagnosis (5.3 weeks earlier)
- 47% annual payer cost savings ($698,892 or $760/person)
- Fewer misdiagnoses
- Faster referral from primary care physicians to endocrinologists
- Fewer specialist visits
- Increased patient productivity

Total Payer Costs of GD Diagnosis

$1,480,328

47% decrease = $698,892

$780,918

Average Time to Diagnosis

11.7 weeks

46% decrease

6.4 weeks

## Summary: Utility of TSI Testing in ATD, Radioiodine, and Surgical Treatments

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>TSI Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithyroid drugs</td>
<td></td>
</tr>
<tr>
<td>Prognostic during treatment</td>
<td>High</td>
</tr>
<tr>
<td>à relapse</td>
<td>Low</td>
</tr>
<tr>
<td>Low à remission</td>
<td></td>
</tr>
<tr>
<td>Therapy guidance in 3rd trimester</td>
<td>High</td>
</tr>
<tr>
<td>à continue ATD</td>
<td></td>
</tr>
<tr>
<td>Radioiodine Treatment</td>
<td></td>
</tr>
<tr>
<td>guidance for patients at high risk of worsening Graves' ophthalmopathy</td>
<td>High (pretreatment) à avoid radioiodine therapy</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Treatment guidance for anticipated pregnancy (with 4–6 months of treatment)</td>
<td>High (pretreatment) à surgery preferred over radioablation</td>
</tr>
</tbody>
</table>

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Dina Salzer, 3/7/2016
Pregnancy
Pregnancy and the Thyroid

- Pregnancy has a profound impact on the thyroid gland and thyroid function tests
- Serum TBG concentrations rise almost two-fold because estrogen increases TBG production
- To maintain adequate free thyroid hormone concentrations during this period, $T_4$ and $T_3$ production by the thyroid gland increase
- Total $T_4$ and $T_3$ concentrations rise during the first half of pregnancy, plateauing at approximately 20 weeks of gestation, at which time a new steady state is reached and the overall production rate of thyroid hormones returns to prepregnancy rates
- Considerable homology between the beta-subunits of hCG and TSH. As a result, hCG has weak thyroid-stimulating activity
<table>
<thead>
<tr>
<th>Physiologic change</th>
<th>Thyroid test change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid enlargement</td>
<td>Serum thyroglobulin</td>
</tr>
<tr>
<td>Iodine clearance</td>
<td>Hormone production in deficiency</td>
</tr>
</tbody>
</table>

Abalovich, et al., J Clin Endocrinol Metab. 2007;92(8 Suppl):S1-47.


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Dina Salzer, 3/7/2016
Hypothyroidism in Pregnancy

- Subclinical hypothyroidism has an estimated prevalence of 2-3%

- Overt hypothyroidism is seen in about 0.3-0.5% of pregnancies

- The most common cause of hypothyroidism is the autoimmune disorder known as Hashimoto’s thyroiditis

- Endemic iodine deficiency accounts for most hypothyroidism in pregnant women worldwide while chronic autoimmune thyroiditis is the most common cause of hypothyroidism in iodine sufficient parts of the world
Complications of Hypothyroidism in Pregnancy

Maternal complications:
- miscarriages
- anemia
- pre-eclampsia
- abruptio placenta
- postpartum hemorrhage

Neonatal complications:
- premature birth
- low birth weight
- increased neonatal respiratory distress
Hyperthyroidism in Pregnancy

- Hyperthyroidism occurs in about 0.2-0.4% of all pregnancies

- The most common cause of maternal hyperthyroidism during pregnancy is the autoimmune disorder Graves’ disease

- Must be distinguished from gestational transient thyrotoxicosis, a self-limiting hyperthyroid state due to the thyroid stimulatory effects of beta-hCG

- Untreated hyperthyroidism is associated with an increased risk of severe pre-eclampsia and up to a four-fold increased risk of low birth weight deliveries
Pregnancy: Congenital Hyperthyroidism
TSAb is Predictive of Graves’ Disease vs Other Thyrotoxicoses

Excess hormone present at birth

Rare
  • 0.01% of pregnancies

Maternal TSAb levels
  • Higher levels, higher risk for poor outcomes

Fetal disease
  • Preterm delivery
  • Death
  • Growth restriction


## TSI Assay - Clinical Utility

<table>
<thead>
<tr>
<th>Indication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of Graves' Disease</td>
<td>Aids in differentiating GD from other forms of thyrotoxicosis</td>
</tr>
<tr>
<td>Ophthalmopathy</td>
<td>Useful for differential diagnosis of GD in patients with unilateral orbitopathy or orbitopathy with euthyroid or hypothyroid status</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Useful in women who are currently on antithyroid drug therapy, have had either radioactive iodine or surgery for thyrotoxicosis, or have had children with neonatal neonatal thyrotoxicosis</td>
</tr>
<tr>
<td>Neonatal Test</td>
<td>Neonate if mother's TRAb levels are high in third trimester</td>
</tr>
<tr>
<td>Therapy guidance/prognosis</td>
<td>Helps identify patients on ATD who are more likely to remit</td>
</tr>
</tbody>
</table>


[http://www.thyroid.org/what-is-a-goiter/](http://www.thyroid.org/what-is-a-goiter/)
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Dina Salzer, 3/7/2016
Summary: TSI Testing

- **Aids Diagnosis**: Patients diagnosed and treated sooner
- **Can be Automated**: Ready to use. Improved lab efficiency
- **Specific**: Detects ONLY stimulating Abs, the cause of GD (differs from TRAB)

Your Solution to Graves’ Disease Testing
Children are not small adults...

Thyroid function abnormalities are among the most common endocrine problems in children.

One of the most challenging aspects of establishing pediatric reference intervals is the availability of well-characterized healthy pediatric samples and sufficient blood volume to conduct studies across multiple assays.

Children’s thyroid hormone levels show a clear age dependency. Therefore age-specific reference intervals are critical for proper clinical interpretation of test results.

Repeated requests from our global customers over the years have been to establish Siemens system specific pediatric thyroid reference intervals.

We are pleased to announce the launch of Siemens Thyroid Pediatric Reference Intervals.
**Project Objective**

**Objective**
To design and run appropriate studies to establish pediatric reference intervals for thyroid hormones across all major Siemens platforms for infant, child and adolescent age groups

**Scope**
- Assays: 3rd Gen TSH, FT4, FT3, T₄, T₃
- IA Systems: ADVIA Centaur systems, IMMULITE 2000*, Dimension Vista, Dimension EXL (T4 extended to RxL, Xpand)
- Age Groups: Infants (1–23 mo), children(2–12 yr), adolescents (13–20 yr)
- IFU updates with claims after FDA 510K clearance

* data not yet available
Study Design:

- 8 collection sites used across the US to collect samples
- Samples were aliquoted and shipped frozen to one laboratory for testing
- Testing was conducted in batch, and run in singleton on the Siemens platforms listed previously
- Samples were tested with handling conditions recommended for each assay as per the IFU
- Sample size total per platform:
  - ADVIA Centaur: 391
  - Dimension Vista: 422
  - Dimension EXL: 408

Statistical Approach:

- For the 2-12 yr and 13-20 yr old age groups, the lower and upper reference limits were established as the 2.5th and 97.5th percentiles of the test result distribution
- For the infants, the lower and upper reference limits were estimated as the 2.5th and 97.5th percentiles of the distribution produced by the robust method
- For the child and adolescent subgroups, where >120 subject results were available, a non-parametric approach was used (CLSI guideline)
- For the infant subgroup where <120 subject results were available, a robust approach by Horn and Pesce were used
### ADVIA Centaur Pediatric Reference Intervals

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sample Size</th>
<th>TSH3-UL*</th>
<th>FT4</th>
<th>FT3</th>
<th>T4</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants (1-23 mo)</strong></td>
<td>72</td>
<td>0.87-6.15</td>
<td>0.94-1.44</td>
<td>12-19</td>
<td>3.28-5.19</td>
<td>5.1-8.0</td>
</tr>
<tr>
<td><strong>Children (2-12 yr)</strong></td>
<td>190</td>
<td>0.67-4.16</td>
<td>0.86-1.40</td>
<td>11-18</td>
<td>3.34-4.80</td>
<td>5.1-7.4</td>
</tr>
<tr>
<td><strong>Adolescents (13-20 yr)</strong></td>
<td>129</td>
<td>0.48-4.17</td>
<td>0.83-1.43</td>
<td>11-18</td>
<td>3.04-4.65</td>
<td>4.7-7.2</td>
</tr>
</tbody>
</table>

* The sample size for TSH3UL is the following: infants-94, children-198 and adolescents-150
Case 1

27-year-old female complaining of fatigue, weight gain, and weakness who is trying to get pregnant. Most recent pregnancy test was negative.

Is this individual at risk for thyroid dysfunction?

Should thyroid testing be performed?

What is the first test that should be run?

What other tests should be considered?
Case 1

Is this patient at risk for thyroid dysfunction?
Yes, her symptoms are consistent with hypothyroidism

Should thyroid testing be performed?
Yes

What is the first test that should be run?
A sensitive TSH test

What other tests should be considered?
Free $T_4$, total $T_4$, anti-TPO
Case 1

What is the likely diagnosis?

*Hypothyroidism*  
*(Hashimoto’s disease)*

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>High</td>
</tr>
<tr>
<td>Free $T_4$</td>
<td>Low</td>
</tr>
<tr>
<td>Free $T_3$</td>
<td>Normal</td>
</tr>
<tr>
<td>Anti-TPO</td>
<td>Present</td>
</tr>
</tbody>
</table>
Case 2

A 45-year-old female complains of nervousness, irritability, and palpitations and difficulty sleeping. She thinks that she might be entering menopause. Her thyroid gland is enlarged but no distinct nodules apparent.

Is this individual at risk for thyroid dysfunction?

Should thyroid testing be performed?

What is the first test that should be run?

What other tests should be considered?
Case 2

Is this patient at risk for thyroid dysfunction?

Yes, her symptoms are consistent with hyperthyroidism

Should thyroid testing be performed?

Yes

What is the first test that should be run?

A sensitive TSH test

What other tests should be considered?

Free $T_4$, Total $T_4$, TRAb, TSI, thyroid scan
Case 2

What is the likely diagnosis?

*Hyperthyroidism*  
*(Graves’ disease)*

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>Low</td>
</tr>
<tr>
<td>Free T₄</td>
<td>High</td>
</tr>
<tr>
<td>Free T₃</td>
<td>Normal</td>
</tr>
<tr>
<td>TSI</td>
<td>Present</td>
</tr>
</tbody>
</table>
A 31-year-old female, mother of one, with a history 3 miscarriages and difficulty getting pregnant is planning another pregnancy. She complains of weight gain and decreased heat tolerance.

Is this individual at risk for thyroid dysfunction?

Should thyroid testing be performed?

What is the first test that should be run?

What other tests should be considered?
Case 3

Is this patient at risk for thyroid dysfunction?
Yes, her symptoms are consistent with thyroid dysfunction

Should thyroid testing be performed?
Yes

What is the first test that should be run?
A sensitive TSH test

What other tests should be considered?
Free $T_4$, TRAb, TSI, TPO
Case 3

What is the likely diagnosis?

*Hyperthyroidism, T₃ (Early Graves Disease)*

<table>
<thead>
<tr>
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<tbody>
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<td>TSI</td>
<td>Present</td>
</tr>
</tbody>
</table>
Case 4

47-year-old male found a painless lump in his throat while shaving and has also noticed increased fatigue for the past few weeks. He has no other complaints and is a well controlled type 1 diabetic. On physical examination the lump is in the left lobe of the thyroid gland.

Is this individual at risk for thyroid dysfunction?

Should thyroid testing be performed?

What is the first test that should be run?

What other tests should be considered?
Case 4

Is this patient at risk for thyroid dysfunction?
Yes, he has a nodule and is complaining of fatigue

Should thyroid testing be performed?
Yes, the nodule will also require investigation

What is the first test that should be run?
A sensitive TSH test

What other tests should be considered?
Free T₄, fine needle aspiration and biopsy, radiological studies
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