THYROID
FOR THE BOARDS
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Discussion Points

- Thyroid function tests
- Thyroid disorders
  - Hypothyroidism
  - Hyperthyroidism
  - Thyroiditis
  - Thyroid nodules & cancers
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• Thyroid function tests

• Thyroid disorders
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1) Which of the following conditions is NOT associated with and elevated TSH?

A. Primary hypothyroidism
B. Hypothalamic hypothyroidism
C. Treated Graves' hyperthyroidism
D. Thyroid hormone resistance
E. Recovery phase of sick euthyroidism
Hypothalamo-Pituitary-Thyroid Axis

Hypothalamus

Pituitary

Thyroid

TRH

TSH

T₄

T₃

25%

75%

(-)

(-)
THYROID HORMONE BINDING

• More than 99% of circulating thyroid hormones is bound to:
  – Thyroid Binding Globulin (TBG)
  – Thyroid Binding Prealbumin (Transthyretin)
  – Albumin

• ONLY FREE HORMONE IS ACTIVE
THYROID FUNCTION TESTS

- TSH
- Total T$_4$
- Total T$_3$
- T$_4$U or T$_3$RU (estimates of binding)
- FTI (free thyroxine index)
- Free T$_4$
- Free T$_3$
OTHER DIAGNOSTIC TESTS

- Thyroid microsomal antibodies (TPO)
- TSH-receptor antibodies (Stimulating – Blocking)
- Thyroglobulin - Thyroglobulin antibodies
- TSH-R mRNA
- Urinary iodide
- Fine needle aspiration
- RAI uptake
- Thyroid scan (Radioiodine, pertechnetate or other isotopes)
- Thyroid ultrasound
- Other more expensive imaging tests
BINDING PROBLEMS

Factors which alter binding or binding capacity result in alterations in total $T_4$ and usually total $T_3$. 
2) What condition is associated with high total T4 and normal free T4 index:

A. A patient with Graves hyperthyroidism
B. A patient with Familial Dysalbuminemic Hyperthyroxiinemia
C. A patient with chronic active hepatitis
D. A patient with thyroid hormone resistance
E. An amiodarone-treated patient
TBG EXCESS

- Pregnancy
- Drugs - estrogen, tamoxifene, raloxifene, opiates, phenothiazines
- Liver disease (active)
- Acute intermittent porphyria
- Hereditary
TBG DEFICIENCY

- Hypoproteinemia
- Nephrotic syndrome
- Liver disease (chronic)
- Glucocorticoids (large doses)
- Androgens
- Acromegaly
- Hereditary
THYROID FUNCTION TESTS
A WORD OF CAUTION

Thyroid function tests are readily interpretable in ambulatory individuals but are often not helpful or confusing in the hospitalized sick patient.
3) Which panel is most consistent with Non-thyroidal illness?

A. High TSH, Low T4, Normal T3

B. Low TSH, High T4, High T3

C. Low TSH, Low T4, High T3

D. Low TSH, Normal T4, Low T3

E. Low TSH, Normal T4, Normal T3

- Early hypothyroidism
- Overt hyperthyroidism
- T3 Toxicosis
- Subclinical hyperthyroidism
THE BEST TEST - TSH

- Subclinical hypothyroidism (mildly high TSH and normal T4)
- Overt hypothyroidism $>10 \, \mu U/ml$
- Subclinical hyperthyroidism (low TSH and normal T4 and T3)
- Overt hyperthyroidism $<0.1 \, \mu U/ml$
TSH PITFALLS

- May be *elevated* (4.5-10 μU/ml) *in elderly*
- May be *low in acute illness*, pregnancy, drugs (e.g. Dopamine, glucocorticoids)
- May be *elevated* in "sick euthyroid" recovery phase
- May be *normal or low in hypoth-pit. hypothyroidism*
- Miscellaneous: - assay errors
  - thyroid hormone resistance
Euthyroid Sick Syndrome
or
Non-Thyroidal Illness
EUTHYROID SICK SYNDROME-LAB

- TSH: N or ↓ (↑ in recovery phase)
- T₃: ↓
- T₄: N or ↓
- FT₄ / FTI: N, ↓
- rT₃: ↑
EUTHYROID SICK SYNDROME - CLINICAL

• Clinical judgment
• Changes in TFT's may reflect severity of illness
• Treatment does not help and might harm
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CAUSES OF HYPOTHYROIDISM

1. Primary (thyroid)

2. Secondary to pituitary or hypothalamic disease
PRIMARY HYPOTHYROIDISM (I)

- Gland destruction
  - Autoimmune (Hashimoto's)
  - Idiopathic atrophy
  - Surgery
  - Irradiation
  - Replacement
PRIMARY HYPOTHYROIDISM (II)

- **Agenesis**
- **Inhibition of synthesis and release of thyroid hormone**
  - Iodine deficiency
  - Excess iodide in susceptible individuals
  - Ingestion/administration of goitrogens
  - Antithyroid drugs
  - Lithium
  - Inherited enzyme defects
- **Transient**
  - After surgery or therapeutic radioactive iodine
  - Postpartum
  - In the course of thyroiditis
4) 69-year-old woman; 20 year history of fatigue and obesity; on Armour Thyroid (thyroid extract) 3 grains daily. She remains tired and obese. *Lab results:* low-normal $T_4$; high-normal $T_3$, suppressed TSH.

Which one of the following options is NOT RECOMMENDED?

A. Continue current regimen
B. Discontinue the medication and recheck TSH in 6 weeks
C. Switch to a brand-name L-T4 preparation at a dose of 1.6 $\mu$g/kg body weight
D. Obtain a more detailed history and examine her neck
E. Consult your neighborhood endocrinologist
TIPS IN THYROID REPLACEMENT THERAPY (I)

- Might need to use name brand L-T₄ only
- Average adult dose 1.6 μg/kg (higher in pediatrics)
- Full doses in young from outset
- Aim for normalization of TSH
- Wait minimum 6 weeks for TSH recheck
TIPS IN THYROID REPLACEMENT THERAPY (II)

• Caution in elderly and/or cardiac patients
  – L-T₄ 0.025 mg daily to start
  – Work up slowly (± 2-4 week intervals)

• In secondary hypothyroidism
  – Replace cortisol first
  – Use T₄/T₃ as guides (TSH of no value)
THYROIDRE replacement: Drug interference

Absorption
1. Soybean (infant formula; soy milk)
2. Cholestyramine
3. Sucralfate (polyaluminum hydroxide)
4. Antacids (aluminum hydroxide; calcium carbonate)
5. Proton-pump inhibitors
6. Iron
7. Others

Metabolism
1. Anticonvulsants (phenytoin; phenobarbital; carbamazepine)
2. Rifampin
5) Which statement about thyroid storm is most accurate:

A. “Cold” iodine should be administered before antithyroid drugs

B. The presence of precipitating factors is associated with better survival

C. Antithyroid drugs such as propylthiouracil should be given in lower doses

D. Propranolol should not be used because of risk of heart failure

E. Thyroid storm is associated with a sudden increase in thyroid hormone levels
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CAUSES OF HYPERTHYROIDISM (I)

A. Primary Thyroid Overproduction*

1) Graves’ disease
2) Toxic multinodular
3) Toxic adenoma
4) Follicular thyroid carcinoma (metastatic)
5) HCG-mediated
   - Trophoblastic disease
   - Hyperemesis gravidarum
   - TSH receptor abnormality
6) Fetal / neonatal
7) TSH-mediated
   - Pituitary adenoma
   - Pituitary thyroid hormone resistance
8) Iodide excess (Jod Basedow)
9) Amiodarone induced

* RAIU elevated or high normal
CAUSES OF HYPERTHYROIDISM (II)

B. Thyroid Damage**
1) Subacute (painful) thyroiditis
2) Painless & post-partum thyroiditis
3) Amiodarone associated thyroiditis

C. Non-thyroidal Disease**
1) Thyrotoxicosis factitia
2) Accidental exposure (laced hamburgers)
3) Struma ovarii (v. rare)

** RAIU - low
TREATMENT OF HYPERTHYROIDISM

- Symptomatic
  - $\beta$-blockers

- Therapeutic
  - Anti-thyroid drugs
  - Radioiodine
  - Surgery
TREATMENT OF THYROID STORM

- β-blockers
- Sedation / seclusion
- Anti-thyroid drugs (high doses)
- Cold iodine (inorganic or organic)
- Stress steroids
- Bile acid sequestrants
- Treat underlying illness
Spectrum of Autoimmune Thyroid Disease

Graves’
Hashimoto’s

Thyroid
Eyes
Skin
Clinical manifestations at a particular time depend upon:

1. Morphologic state of thyroid gland
2. Mixture of circulating antibodies against:
   - Thyroid
     - Anti-TPO
     - Tg antibodies
     - Thyroid damaging
     - TRAB (stimulating; blocking; binding)
     - Growth promoting
   - Eye (orbit)
   - Skin (connective tissue)
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6) The most cost-effective work-up for a patient with a palpable thyroid nodule is:

A. Ultrasound of the neck
B. MRI neck and chest
C. 24-hr. RAI uptake and scan
D. Fine needle aspiration biopsy
THYROID NODULES

- Malignant vs. benign
- Single vs. multiple
- Age
- Local symptoms
- Adenopathy
- Childhood head & neck irradiation
- Personal history of malignancy
- Family history – FMTC; MEN-2
- Family history – Familial non-MTC
THYROID NODULES - DIAGNOSIS

- Fine needle aspiration
  - Most cost effective
  - Palpation or Ultrasound guided
  - Need experienced cytologist
- Ultrasound
- Radioisotope scan
  - Limited value (except when Low TSH)
- Calcitonin
THYROID NODULES - TREATMENT

• Observation for low risk nodules
• L-thyroxine suppression - Controversial
• Surgery – cancer, suspicious, rapidly growing, symptomatic, etc…
• RAI is not an option unless the nodule is toxic
• RAI has been used for symptomatic non-toxic MNG
7) Factors that would increase the suspicion of malignancy in a thyroid nodule include all the following **EXCEPT**:

A. Female gender  
B. Family history of thyroid cancer  
C. History of neck or chest irradiation  
D. Young age  
E. Rapidly expanding size
THYROID CANCER - PATHOLOGY

1) Primary
   • Papillary
   • Follicular
   • Mixed
   • Medullary (sporadic, familial, MEN II)
   • Anaplastic
   • Hürthle cell

2) Metastasis

3) Lymphoma (Large B-cell or MALT)
8) Management of papillary thyroid carcinoma includes all of the following except:

A. Surgery - usually total thyroidectomy
B. $^{131}$I ablation
C. TSH suppression with levothyroxine
D. Surveillance with serial thyroglobulin, chest x-ray and neck and body scans
E. Molecular analysis of the $RET$ proto-oncogene in the patient and, if positive, in her parents and children
TREATMENT OF THYROID CARCINOMA

- **Surgery** - *(total vs. more conservative)*
- **RAI ablation** - *(for intermediate or high-risk patients)*
- **TSH suppression by levothyroxine**
- **Monitor**
  - Serum thyroglobulin
  - Neck ultrasonography
  - Radiiodine scans
    - Off T<sub>4</sub>
    - Recombinant human TSH
THANK YOU