Discussion Points

• Thyroid function tests

• Thyroid disorders
  – Hypothyroidism
  – Hyperthyroidism
  – Thyroiditis
  – Thyroid nodules & cancers
Discussion Points

• Thyroid function tests

• Thyroid disorders
  – Hypothyroidism
  – Hyperthyroidism
  – Thyroiditis
  – Thyroid nodules & cancers
1) Which of the following conditions is not associated with an 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 → TRH → Pituitary

Pituitary → TSH → Thyroid

Thyroid → T₃ → 75% → T₄

25% → 25%
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 $T_4$
- $T_4U$ or $T_3RU$ (estimates of binding)
- FTI (free thyroxine index)
- Free $T_4$
- Total $T_3$
- Free $T_3$
OTHER LAB TESTS

• **Thyroid microsomal antibodies (TPO)**
  - Proof of autoimmune thyroid disease

• **TSH-receptor antibodies (Stimulating – Blocking)**
  - Supports the diagnosis of Graves’ disease
  - Titer important in follow up during pregnancy

• **Thyroglobulin**
  - Crucial marker for follow up of differentiated thyroid carcinoma
  - Beware of thyroglobulin antibody interference

• **Fine needle aspiration**
  - Best test for triage of thyroid nodules
IMAGING TESTS

- **RAI uptake (¹²³I or ¹³¹I)**
  - Helpful for differentiating thyroid autonomy from thyroiditis

- **Thyroid scan (Radioiodine, pertechnetate or other isotopes)**
  - Helps delineate function and anatomy
  - Not indicated in work-up of nodules except in the presence of hyperthyroidism

- **Thyroid ultrasound**
  - Best imaging modality for thyroid gland anatomy
  - FNA guidance

- **Other more expensive imaging tests**
  - Usually not needed
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 chronic active hepatitis
C. A patient with thyroid hormone resistance
D. 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, even 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
THE BEST TEST - TSH

- Subclinical hypothyroidism (mildly high TSH and normal T4)
- Overt hypothyroidism >10 μU/ml
- Subclinical hyperthyroidism (low TSH and normal T4 and T3)
- Overt hyperthyroidism <0.1 μU/ml
TSH PITFALLS

• May be *slightly elevated* in euthyroid *elderly persons*

• May be *low* in acute illness, early 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
  • TSH secreting pituitary adenoma
Euthyroid Sick Syndrome
or
Non-Thyroidal Illness
EUTHYROID SICK SYNDROME-LAB

\[ T_4 \quad - \quad \text{N or } \downarrow \]
\[ FT_4 / FTI \quad - \quad \text{N, } \downarrow \]
\[ T_3 \quad - \quad \downarrow \]
\[ rT_3 \quad - \quad \uparrow \]
\[ TSH \quad - \quad \text{N or } \downarrow \ (\uparrow \text{ in recovery phase}) \]
EUTHYROID SICK SYNDROME - CLINICAL

• Use clinical judgment

• Magnitude of abnormality in TFT's may reflect severity of illness

• Treatment with thyroid hormones does not help and might harm
Discussion Points

• Thyroid function tests

• Thyroid disorders
  – Hypothyroidism
  – Hyperthyroidism
  – Thyroiditis
  – Thyroid nodules & cancers
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 partial surgery or therapeutic radioactive iodine
  - Postpartum
  - In the course of thyroiditis
4) Which patient would you treat with levothyroxine?

A. A patient with Wilson’s syndrome
B. Asymptomatic; TSH 6; T4 normal; T3 low normal
C. Asymptomatic; TSH 2; T4 normal; high TPO antibodies
D. Asymptomatic; TSH 6; T4 low; T3 normal
E. Tired; gaining weight; TSH 2; T4 normal; T3 low
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)
THYROXINE 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 LEAST ACCURATE:

A. SSKI should be administered before anti-thyroid drugs

B. Surgery, infections, and childbirth may precipitate thyroid storm in a patient with Graves' disease

C. Antithyroid drugs such as propylthiouracil should be given in higher and more frequent doses

D. $\beta$-blocking drugs are indicated in thyroid storm

E. Thyroid storm is associated with a rapid increase in thyroid hormone levels
Discussion Points

- **Thyroid function tests**
- **Thyroid disorders**
  - Hypothyroidism
  - Hyperthyroidism
  - Thyroiditis
  - Thyroid nodules & cancers
CAUSES OF HYPERTHYROIDISM (I)

A. Primary Thyroid Overproduction*

1) Graves’ disease
2) Toxic multinodular goiter
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)

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

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

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
  – Glucocorticoids
  – Removal of hormones
TREATMENT OF THYROID STORM

- β - blockers
- Sedation / seclusion
- Anti-thyroid drugs (high doses)
- Cold iodine (inorganic or organic)
- Glucocorticoids
- 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)
Discussion Points

- Thyroid function tests
- Thyroid disorders
  - Hypothyroidism
  - Hyperthyroidism
  - Thyroiditis
  - Thyroid nodules & cancers
6) The best next step in the 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
THYROID NODULES

- Malignant vs. benign
- Single vs. multiple
- Age
- Local symptoms
- Adenopathy
- Childhood head & neck irradiation
- Personal history of malignancy
- Family history - MEN II; MTC; Cowden’s syndrome
THYROID NODULES - DIAGNOSIS

- **Fine needle aspiration**
  - By palpation or Ultrasound guided
  - Need experienced cytologist
- **Ultrasound**
- **Radioisotope scan**
  - Limited value (except when Low TSH)
- **Calcitonin - Controversial**
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 \textbf{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 (conservative vs. total)
• Radioiodine ablation
• TSH suppression by levothyroxine
• Monitor
  – Serum thyroglobulin
  – Neck ultrasonography
  – Radioiodine scans
    • Off levothyroxine
    • Recombinant human TSH
THANK YOU