Thyroid disorders

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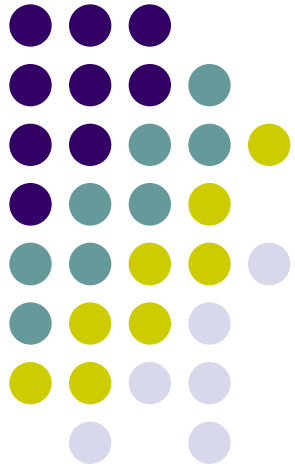


Objectives

* How to evaluate a patient with thyroid disease?

* Hypothyroidism and Hyperthyroidism: causes, pathogenesis, diagnosis and treatment.

* Other thyroid disorders.

Patients with thyroid disease

- Thyroid enlargement (goiter): diffuse or nodular
- Symptoms of hypothyroidism
- Symptoms of hyperthyroidism
- Complications of a specific form of hyperthyroidism-Graves' disease-which may present with:

- Striking prominence of the eyes (exophthalmos)
- Thickening of the skin over the lower leg (thyroid dermopathy)

History

- Exposure to ionizing radiation
- Iodide ingestion:
  - Kelp
  - Iodide-containing cough preparation
  - IV Iodide-containing contrast media
- Lithium carbonate
- Residence in an area of low dietary iodide

History

- Family history
- Thyroid disease
- Immunologic disorders:
    * Diabetes
    * Rheumatoid disease
    * Pernicious anemia
    * Alopecia
    * Vitiligo
    * Myasthenia gravis
    * MEN 2A

Physical examination

- Observe the neck, especially as the patient swallows
- Examine from the front, rotating the gland slightly with one thumb while palpating the other lobe with the other thumb
- Examine from behind, using three fingers and the same technique
- Determine the size of the thyroid lobes, consistency, presence of nodules

HYPOTHYROIDISM

Causes

- Primary:

1. Hashimoto's thyroiditis:
   - With goiter
   - "Idiopathic" thyroid atrophy, presumably end-stage autoimmune thyroid disease, following either Hashimoto's thyroiditis or Graves' disease
   - Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies
2. Radioactive iodine therapy for Graves' disease
3. Subtotal thyroidectomy for Graves' disease or nodular goiter
4. Excessive iodine intake (kelp, radiocontrast dyes)
5. Subacute thyroiditis
6. Iodide deficiency
7. Other goitrogens such as lithium, amiodarone, antithyroid drug therapy
8. Inborn errors of thyroid hormone synthesis

Causes

- Secondary

- Hypopituitarism due to:
  a- Pituitary adenoma
  b- pituitary ablative therapy
  c- pituitary destruction

- Tertiary

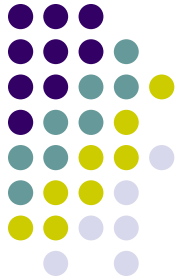
- Hypothalamic dysfunction (rare)

- Peripheral resistance of the action of thyroid hormone

Pathogenesis

- Thyroid hormone deficiency affects every tissue in the body, so that the symptoms are multiple
- Accumulation of glycosaminoglycans-mostly hyaluronic acid- in interstitial tissues
- Increase capillary permeability to albumin
- Interstitial edema (skin, heart muscle, striated muscle)

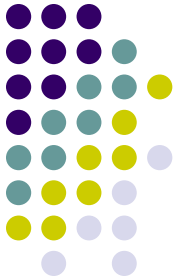
Clinical presentations and findings



- Adults

- Common feature: easy fatigability, coldness, weight gain, constipation, menstrual irregularities, and muscle cramps.
- Physical findings: cool rough dry skin, puffy face and hands, hoarse husky voice, and slow reflexes, yellowish skin discoloration.
- <u>Cardiovascular:</u>
- Bradycardia
- Decreased cardiac output
- Low voltage ECG
- Cardiomegaly
- Pericardial effusion
- <u>Pulmonary function</u>
- Shallow and slow respiration
- Respiratory failure

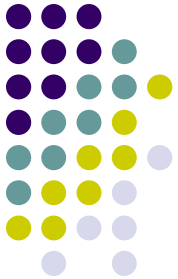
Clinical presentations and findings



- Adults (cont')

- GI:
- Chronic constipation
- Ileus
- Renal function:
- Impaired GFR
- Water intoxication
- Anemia:
- Impaired hemoglobin synthesis
- Iron deficiency
- Folate deficiency
- Pernicious anemia, with B12 deficient megaloblastic anemia

Clinical presentations and findings



- Adults (cont')

- Neuromuscular system:
- Severe muscle cramps
- Paresthesias
- Muscle weakness
- Carpal tunnel syndrome
- CNS:
- Chronic fatigue
- Lethargy
- Decreased concentration
- Anovulatory cycles and infertility
- Menorrhagia
- Depression
- Agitation

Diagnosis

- Low serum FT4
- Elevated serum TSH
- Thyroid antibodies
- TRH stimulation test

Complications

- 1- Myxedema coma
  - The end stage of untreated hypothyroidism
  - Progressive weakness, stupor, hypothermia, hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, and death.
  - Associate illnesses and precipitating factors: pneumonia, MI, cerebral thrombosis, GI bleeding, ileus, excessive fluid administration, and administration of sedatives and narcotics.
  - Three main issues: CO2 retention and hypoxia, fluid and electrolyte imbalance, and hypothermia.
- 2- Myxedema and heart disease
- 3- Hypothyroidism and neuropsychiatric disease

Treatment

- A- Hypothyroidism

- Levothyroxine (T4).
- Follow serum Free T4 and TSH
- Take dose in AM
- Do blood test fasting before taking the daily dose
- Adults: 1.7 ug/kg/d, but lower in elderly (1.6 ug/kg/d)
- For TSH suppression (nodular goiters or cancer): 2.2 ug/kg/d
- Increase dose of T4 in malabsorptive states or concurrent administration of aluminum preparations, cholestyramine, calcium, or iron compounds
- Increase dose of T4 in pregnancy and lactation
- The t1/2 of levothyroxine is 7 days

Treatment

- B- Myxedema coma

- Acute medical emergency
- Monitor blood gases
- Patient may need intubation and mechanical ventilation
- Treat associated medical problems
- Avoid excessive hydration
- Asses adrenal function and treat if needed
- In pituitary myxedema, glucocorticoid replacement is essential
- IV levothyroxine: loading 300-400 ug, daily maintenance 50 ug
- Be cautious in patients with coronary artery disease
- Active rewarming of the body in contraindicated

Recommendations for the treatment of myxedema coma

• hypothyroidism	large initial intravenous dose of 300-500 µg T4; if no response within 48 hours, add T3
• hypocortisolemia	intravenous hydrocortisone 200-400 mg daily
• hypoventilation	don’t delay intubation and mechanical ventilation too long
• hypothermia	blankets, no active rewarming
• hyponatremia	mild fluid restriction
• hypotension	cautious volume expansion with crystalloid or whole blood
• hypoglycemia	glucose administration
• precipitating event	identification and elimination by specific treatment (liberal use of antibiotics)

Treatment

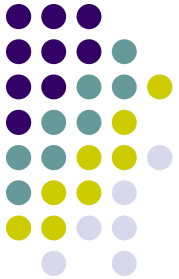
- C- Myxedema with heart disease

- Start treatment slowly in long standing hypothyroidism and in elderly patients particularly those with known cardiovascular disease
- 25 ug/d x 2 weeks, increase by 25 ug every 2 weeks until a daily dose of 100-125 ug is reached

Treatment

- Toxic effects of levothyroxine therapy

- No allergy has been reported to pure levothyroxine
- If FT4 and TSH are followed and T4 dose is adjusted, no side effects are reported
- If FT4 is higher than normal: hyperthyroidism symptoms may occur:
- Cardiac symptoms
- Osteopenia and osteoporosis

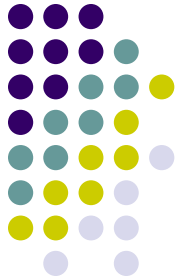


HYPERTHYROIDISM & THYROTOXICOSIS

Definitions

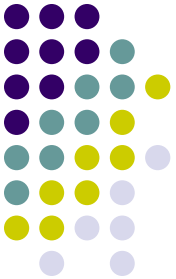
- Thyrotoxicosis: is the clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormone
- Hyperthyroidism: is the hyperactivity of the thyroid gland

Conditions associated with thyrotoxicosis



- Diffuse toxic goiter (Graves' disease)
- Toxic adenoma (Plummer's disease)
- Toxic multinodular goiter
- Subacute thyroiditis
- Hyperthyroid phase of Hashimoto's thyroiditis
- Thyrotoxicosis factitia
- Rare: ovarian struma, metastatic thyroid carcinoma (follicular), hydatiform mole, TSH secreting pituitary tumor, pituitary resistance to T3 and T4

Diffuse Toxic Goiter (Graves' disease)



- Most common form of thyrotoxicosis
- Females > Males
- Features:
  - Thyrotoxicosis
  - Goiter
  - Orbitopathy (exophthalmos)
  - Dermopathy (pretibial myxedema)

Etiology

- Autoimmune disease of unknown cause
- There is a strong familial predisposition
- Peak incidence in the 20- to 40- year age group

Pathogenesis

Local viral infection → inflammatory reaction leading to the production of IFN-g and other cytokines by non-thyroid-specific infiltrating immune cells

↓

will induce the expression of HLA class II molecules on the surface of thyroid follicular cells.

↓

Subsequently, thyroid specific T-cells will recognize the antigen presented on the HLA class II molecules and will be activated

Pathogenesis

The activated thyroid-specific T-cells stimulate B cells to produce

↓

TSH receptor-stimulating antibodies

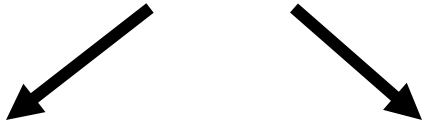
↓

hyperthyroidism

Diagnosis

- Elevated FT4
- Suppressed TSH

Eye signs



+ No further test

– Thyroid scan

Radioiodine uptake scan

- Elevated uptake:
  - Graves' disease
  - TMN
- Low uptake:
  - Spontaneous resolving hyperthyroidism
  - Subacute thyroiditis
  - Thyrotoxic phase of Hashimoto's thyroiditis
  - Iodine loaded patients
  - Patients on LT4 therapy
  - Struma ovarii

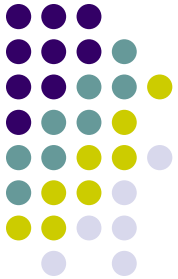
Diagnosis

- TSH-R Ab [stim]
- Free T3
- Atypical presentations:
  - Thyrotoxic periodic paralysis
  - Thyrocardiac disease
  - Apathetic hyperthyroidism
  - Familial dysalbuminemic hyperthyroxinemia

Complications

- Thyrotoxic crisis (thyroid storm)
- Predisposing conditions
- Clinical features:
  * Fever / Agitation
  * Altered mental status
  * Atrial fibrillation / Heart failure

Treatment of Graves' disease



- Antithyroid drug therapy
  - Propylthiouracil or methimazole
  - Spontaneous remission 20-40%
  - Relapse 50-60%
  - Duration of treatment 6 months – years
  - Reactions to antithyroid drugs

Treatment of Graves' disease

- Surgical treatment
- Subtotal thyroidectomy
- Preparation for surgery
- Complications:
  * hypothyroidism/ hypoparathyroidism
  * Recurrent laryngeal nerve injury

Treatment of Graves' disease

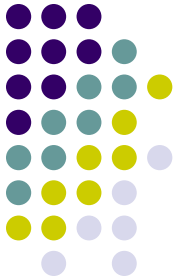
- Radioactive iodine therapy

- ^{131}I is most commonly used

- Dose:

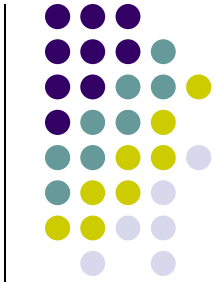
$$^{131}I_{(uci/g)} \times \text{thyroid weight} \times \frac{100}{\text{24-hr RAI uptake}}$$

Treatment of Graves' disease



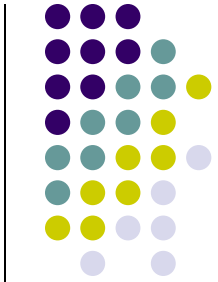
- β–blockers
- SSKI

Treatment of Graves' disease complications



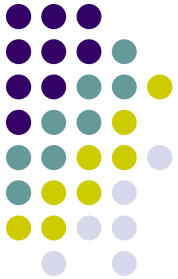
- Thyrotoxic crisis
- Orbitopathy
- Thyrotoxicosis and pregnancy

Treatment of other forms of thyrotoxicosis

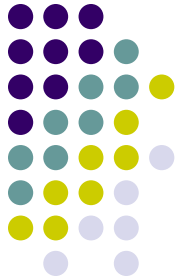


- Toxic adenoma
- TMN
- Amiodarone
- Subacute thyroiditis
- Thyrotoxicosis factitia
- Struma ovarii

Other thyroid disorders



- Nontoxic goiter
- Subacute thyroiditis (De Quervain’s)
- Chronic thyroiditis
- Acute thyroiditis
- Thyroid nodules
- Thyroid cancer



- **Thank you**