Diseases of the thyroid gland
third lecture
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Increased thyroid hormone = thyrotoxicosis

*Thyrotoxicosis means: increased thyroid hormone, regardless of the cause of the increase.

*Hyperthyroidism is the most common cause of thyrotoxicosis and it means there is actual increase in thyroid hormone production from the thyroid gland.

NOTE: 1. actual increase excludes relative increase in cases of thyroiditis where there is destruction of the gland causing increased release (not production) of thyroid hormones... so there is a relative net increase in T3 & T4. Here we have thyrotoxicosis but no hyperthyroidism.
A. Thyrotoxicosis Associated with hyperthyroidism (Thyroid hyperfunction):

1. **Primary**
   a. Diffuse toxic hyperplasia (Graves disease)
   b. Hyperfunctioning (Toxic) multinodular goitre.
   c. Hyperfunctioning (toxic) adenoma

2. **Secondary** -- TSH-secreting pituitary adenoma (rare)
B. Thyrotoxicosis not associated with hyperthyroidism: less common

- Excessive release of pre-formed hormones in thyroiditis (just increased release with no increased overall production)
Clinical manifestations of thyrotoxicosis

• Thyroid hormones increase basal metabolic rate, increase appetite, increase breakdown of fat and glucose
• Also increase heart rate, cause hypertension
• Increase body temperature

• SO if these hormones are increased you expect to see a wide range of symptoms.
Clinical manifestations of thyrotoxicosis

a. Constitutional symptoms: warm flushed skin, heat intolerance and excessive sweating, weight loss despite increased appetite.

b. Malabsorption, and diarrhoea (because of increased intestinal motility)

c. Tachycardia and elderly patients may develop heart failure due to aggravation of pre-existing heart disease
d. Nervousness, tremor, and irritability.
e. A wide, staring gaze and lid lag because of sympathetic overstimulation of the levator palpebrae superioris.
f. 50% develop proximal muscle weakness (thyroid myopathy).
Lab tests

- The measurement of serum TSH is the most useful single screening test for hyperthyroidism, because TSH levels are decreased even at the earliest stages, when the disease may still be subclinical.
Once the diagnosis of thyrotoxicosis has been confirmed, measurement of radioactive iodine uptake by the thyroid gland is valuable in determining the etiology. For example, such scans may show:

a. Diffusely increased (whole-gland) uptake in Graves disease,

b. Increased uptake in a solitary nodule in toxic adenoma

c. Or decreased uptake in thyroiditis.
II. HYPOTHYROIDISM

This disorder may be divided into
a. primary and
b. secondary categories
- depending on whether it arises from
  - an intrinsic abnormality in the thyroid
  - or from hypothalamic or pituitary disease
1. Primary hypothyroidism
   - can be caused by
a. congenital,
b. autoimmune, or
C. iatrogenic causes
1. *genetic defect perturb thyroid development (thyroid dysgenesis)* or the synthesis of thyroid hormone (dyshormonogenetic goiter) are rare overall.

2. *Endemic deficiency of dietary iodine* is typically *manifested* by hypothyroidism early in childhood and has been also called congenital.

- It is a common cause of hypothyroidism in infants and children worldwide.
3. **Autoimmune thyroid disease** is a common cause of **hypothyroidism** in regions of the world where iodine is supplemented in dietary salt products.

- The vast majority of cases of autoimmune hypothyroidism are due to **Hashimoto thyroiditis**

4. **Iatrogenic hypothyroidism** can be caused by either surgical or radiation-induced ablation of thyroid parenchyma, or as an unintended adverse effect of certain drugs
• The clinical manifestations of hypothyroidism include cretinism and myxedema

1. Cretinism
   - A. *Endemic cretinism is caused by iodine deficiency is now much less frequent because of the* supplementation of salt with iodine.
   - B. By contrast, enzyme defects that interfere with thyroid hormone synthesis are a cause of *sporadic cretinism*
• Clinical features of cretinism include
  a. impaired development of the skeletal system and
  b. central nervous system,
• severe mental retardation, short stature, coarse facial features, a protruding tongue, and umbilical hernia
2. Myxedema
- Hypothyroidism in older children and adults
- The initial symptoms include generalized fatigue, apathy, and mental sluggishness,
- Decreased sympathetic activity results in constipation and decreased sweating.
- The skin is cool and pale because of decreased blood flow,
III. Thyroiditis
1. Chronic Lymphocytic (Hashimoto) Thyroiditis

- Hashimoto thyroiditis is the most common cause of hypothyroidism in areas of the world where iodine levels are sufficient.
- It is characterized by gradual thyroid failure secondary to autoimmune destruction of the thyroid gland.
- It is most prevalent between 45 and 65 years of age and is more common in women.
- Although it is primarily a disease of old women, it can occur at any age, including childhood.
MORPHOLOGY

- The thyroid usually is diffusely and symmetrically enlarged.
- Microscopic examination reveals
  a. widespread infiltration of the parenchyma by a mononuclear inflammatory infiltrate containing small lymphocytes, plasma cells, and well-developed germinal centers
b. The thyroid follicles are
   1. atrophic and are
   2. lined by epithelial cells distinguished by the presence of abundant eosinophilic, granular cytoplasm, termed Hürthle, or oxyphil, cells.
Hashimoto thyroiditis
Clinical manifestation

• *Painless enlargement of the thyroid, usually associated with some degree of hypothyroidism.*
- The enlargement of the gland usually is *symmetric and diffuse*,
- In the usual clinical course, hypothyroidism develops gradually
- In some cases, however, it may be preceded by transient thyrotoxicosis caused by disruption of thyroid follicles,
- with secondary release of thyroid hormones called Hashitoxicosis and during this phase, free T4 and T3 concentrations are elevated, TSH is diminished, and radioactive iodine uptake is decreased.

- As hypothyroidism supervenes, T4 and T3 levels progressively fall, accompanied by a compensatory increase in TSH.
a. Patients with Hashimoto thyroiditis often have *other autoimmune diseases*

b. Are *at increased risk for the development of B-cell non-Hodgkin Lymphomas* which typically arise within the thyroid gland.

c. The relationship between Hashimoto disease and thyroid epithelial cancers remains controversial, with some morphologic and molecular studies suggesting a predisposition to papillary carcinomas.
2. Subacute Granulomatous (de Quervain) Thyroiditis

- Is much less common than Hashimoto disease.
- Is most common between 30 and 50 years of age
- Occurs more frequently in women than in men.
- Is believed to be caused by a viral infection, and not by an autoimmune process.
- A majority of patients have a history of an upper-respiratory infection shortly before the onset of thyroiditis
- The process spontaneously remits.
• MORPHOLOGY
- The gland is has an intact capsule.
- Histologic examination reveals disruption of thyroid follicles, extravasation of colloid, and infiltrating neutrophils, which are replaced over time by lymphocytes, plasma cells, and macrophages.
- The extravasated colloid provokes an exuberant granulomatous reaction with giant cells, some containing fragments of colloid.
De-Quervain thyroiditis-granuloma
Clinical Features

- The onset often is acute.
- It is characterized by *neck pain (particularly with swallowing)*, fever, malaise, and variable enlargement of the thyroid.
- Transient Thyrotoxicosis may occur, as a result of disruption of thyroid follicles and release of excessive thyroid hormone.
- The leukocyte count and erythrocyte sedimentation rates are increased.
- With progression of the gland destruction, a transient hypothyroid phase may ensue.
- The condition typically is **self-limited**, with most patients returning to a euthyroid state within 6 to 8 weeks.
3. Subacute Lymphocytic Thyroiditis

- Also is known as *silent or painless thyroiditis*;

- *In a subset of patients, the onset follows pregnancy* (postpartum thyroiditis)

- *This disease is* most likely autoimmune in etiology, as circulating antithyroid antibodies are found in a majority of patients.
- The patients present with a painless neck mass or features of thyroid hormone excess.
- The initial phase of thyrotoxicosis is followed by return to a euthyroid state within a few months.
- In a minority of affected individuals, the condition eventually progresses to hypothyroidism.
4. Riedel thyroiditis

- Is characterized by extensive fibrosis involving the thyroid and contiguous neck structures.
- Clinical evaluation demonstrates a hard and fixed thyroid mass, simulating a thyroid neoplasm.
- It may be associated with idiopathic fibrosis in other sites in the body, such as the retroperitoneum.
Riedel thyroiditis