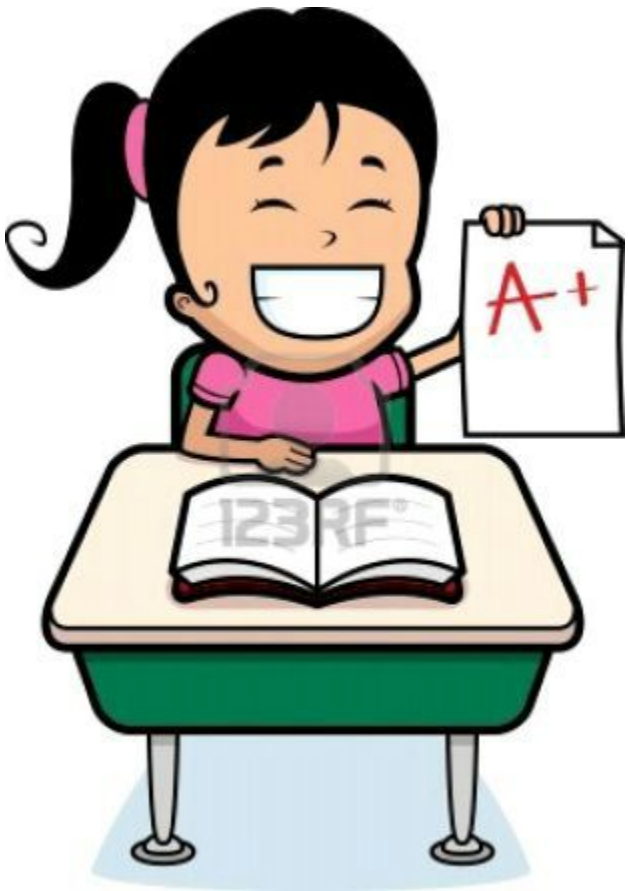
Midterm Revision



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1. Hypo,Hyperthyroidism

Hyperthyroidism (thyrotoxicosis)

Excess circulating T_3 and T_4 → induce a hypermetabolic state and clinical syndrome known as **thyrotoxicosis.** Causing **1-Increase metabolic rate 2-Increase in sympathetic activity.**

Aetiology

The three commonest causes of thyrotoxicosis are as follows:

- Graves' diseas
- Functioning adenoma
- Toxic nodular goiter: one or more nodules in a multinodular goiter → develop hypersecretory activity.

Graves disease (Graves thyroiditis)

- Affects young women,present with the clinical features of thyrotoxicosis and mild goiter.
- **Proptosis (protrusion of the eyes) , pretibial myxoedema, audible bruit.**
- 'organ- specific' autoimmune disease; autoantibodies bind to the TSH receptor on thyroid epithelial cells and mimic the stimulatory action of TSH.

Histologically

- Hyperplastic→ Increase of the number of cells lining the follicles
- A reduction in the amount of stored colloid, Scalloped colloid appearance.

Clinical features of thyrotoxicosis

- Eye changes (, lid lag, lid retraction)
- Hair loss, weight loss
- Anxiety, tremor, diarrhea, warm moist hands
- Cardiac manifestations (tachycardia, palpitations, atrial fibrillation)
- Pretibial myxoedema (accumulation of mucopolysaccharides in the skin) and exopht
- Menorrhagia, osteoporosis
- Proximal myopathy
- Proptosis (protrusion of the eyes) or pretibial myxoedema. (only seen in graves)
- hypercalcemia,hyperglycemia,hypo-cholesterolemia.

Hypothyroidism

- Insufficient circulating T_4 and T_3 → hypometabolic state resulting → clinical syndrome known as (hypothyroidism).
- If hypothyroidism occurs during infancy, →**Cretinism**, in which mental and physical development is impaired→Mental retardation,Short stature,coarse facial features,protruding tongue,umbilical hernia.
- If hypothyroidism occurs in older children or adults→ condition known as **Myxedema**, in which skin appears edematous and doughty due to the accumulation of mucopolysaccharides in the dermis.

Aetiology

- Commonest cause in adults is **Hashimoto's thyroiditis.**
- **Radiotherapy or surgery or are drug induced.**

Hashimoto's thyroiditis

- Autoimmune disease.
- Antibodies directed against thyroglobulin or peroxidase.
- HLA- B8 /HLA-DR5

Clinical presentation

1- **With goiter**, due to atrophy and fibrosis of the gland.
2- **With hypothyroidism**
3- **With thyrotoxicosis→** in the early stages of the disease.

Histologically:

- Infiltrated by lymphocytes and plasma cells.
- There are **lymphoid aggregates**, often with germinal centers.
- The thyroid epithelial cells become eosinophilic and granular, termed **oncocytes(Hurthle Cells)** .

Gross: In advanced cases, the gland is shrunken and fibrotic.

Clinical features of hypothyroidism

- Myxoedematous face
- Loss of the outer third of the eyebrows
- Dry hair, Hoarse voice
- Slowed physical and mental activity, lethargy, weight gain
- Psychosis, Cold intolerance
- Constipation, muscle weakness, carpal tunnel syndrome, menstrual irregularities.

Goiter

Enlargement of the thyroid gland.

There are two main causes:

1- Simple and multinodular goiter
2- Inflammation of the thyroid (thyroiditis)

Simple and multinodular goiter *(it wasn't mentioned in lecture but in handout)*

- Characterized by diffuse hypertrophy and hyperplasia of the thyroid gland, without the production of discrete nodularity.
- Nearly all longstanding simple goiters develop into multinodular goiters, where tracts of fibrosis separate hyperplastic areas, producing nodularity.
- IT arise from overstimulation of the thyroid tissue by excess TSH→ due to a deficiency of the thyroid hormones.
- The compensatory rise in the TSH levels usually renders the individual euthyroid, although hypothyroidism may occur Goiters can arise in four main settings:

1. **Endemic goiters due to iodine deficiency**
2. **Ingestion of certain foodstuffs**
3. **Rare inherited defects in thyroid hormone synthesis**
4. **Drug-induced goiters, e.g. amiodarone, lithium**

Thyroiditis (a rare cause of goiter).

There are four main forms of thyroiditis:

- Hashimoto's thyroiditis
- Subacute granulomatous (giant cell or de Quervain thyroiditis)
- Riedel's thyroiditis
- Acute bacterial thyroiditis

Subacute granulomatous thyroiditis

- Infiltrated by multinucleate giant cells admixed with other inflammatory cells→ granuloma.
- uncertain cause. (may be a viral infection,Coxsackie or mumps.)
- Patients usually present with an abrupt onset of thyroid swelling and tenderness on palpation and painful thyroid gland.
- There may be a fever.
- Initial **thyrotoxicosis** from gland destruction.
- The condition is self-limiting.

Riedel's thyroiditis

- Characterized by replacement of the thyroid by fibrous tissue, often with involvement of adjacent tissues.
- The aetiology is unknown.
- Patients present with an enlarged thyroid, which is hard and immobile on palpation thereby mimicking carcinoma.

Acute bacterial thyroiditis *(mentioned only in handout)*

- Acute inflammation of the thyroid can result from direct bacterial spread from adjacent tissues or by blood-borne spread.
- Patients present with thyroid **pain,tenderness and enlargement.** There may be *systemic features* of infection. The condition usually resolves with **antibiotic treatment.**

2.Thyroid Nodules & neoplasms

Solitary masses

A Palpable discrete swelling.**Majority:** localized, non-neoplastic conditions or benign neoplasms such as follicular adenomas.

*The **differential diagnosis** of solitary thyroid masses are as follows:*

- One dominant nodule in a multinodular goiter
- Thyroid cysts
- Asymmetrical enlargement due to non-neoplastic disease (e.g. Hashimoto's thyroiditis)
- Thyroid neoplasm

Thyroid neoplasms

- Most thyroid tumors are non-functioning → appear 'cold' → do not take up radioactive iodine.
- Minority are functioning → appearing 'warm/hot' possibly causing thyrotoxicosis.

Follicular adenomas (benign tumor)

- More Common than malignant.
- Mostly nodules uptaking radioactive iodine → Hot nodules.

Gross: -well-circumscribed encapsulated mass lesion.
-No invasion of capsule or blood vessel.

Histologically:

-Variety of appearances.
-Most commonly being a Microfollicular architecture comprising multiple closely follicles with little colloid.

Carcinoma

- Uncommon
- More common in females than males.

Papillary carcinoma (most common type)

- Rearrangements of the tyrosine kinase receptors RET or NTRK1 or activating point mutations in **BRAF**.
- More common in women young age 30-40.
- Cervical lymph node metastases.
- Indolent course(asymptomatic), the overall prognosis is excellent.

Gross: Papillary structures and unencapsulated,infiltrative and may be multifocal.

Histologically:

- Large hypochromatic nuclei termed "Orphan Annie" nuclei.
- Nuclear grooves.
- Eosinophilic cytoplasmic inclusions.
- Psammoma bodies (calcified glycoprotein bodies).

Follicular carcinoma

- Follicular carcinoma occurs in Female older age groups.
- More frequent in areas with **dietary iodine deficiency.**

Histologically - solitary encapsulated tumors
-consisting of closely packed small follicles, and

- **Note that: in follicular ADENOMA there was *no invasion of capsule* while in follicular CARCINOMA *there's capsular or vascular invasion*.**

(cannot distinguish by FNA)

- associated with mutation RAS and Pax8/PPAR γ gene.
- Can widely metastasize , most commonly involving the lung or bones.
- The prognosis for theses tumors is poorer than for papillary carcinomas.

Medullary carcinomas

- Derived from the C-cells within the thyroid→ Neuroendocrine tumors.
- Most secrete calcitonin.
- Rarely it → ***Secrete other hormones (e.g. ACTH, or 5-hydroxytryplamine).***
- These tumors may pursue an indolent or aggressive course.
- Most medullary carcinomas are **sporadic**, but around 20% are hereditary and occur as part of one of the MEN syndromes.
- Associated with RET oncogene.

Histologically:

- Consists of nests or sheets of tumor cells in a characteristic amyloid stroma.
- Granular chromatin and neurosecretory granules in cytoplasm.

Two stain for diagnosed:

1-Immunohistochemistry → calcitonin 2-Congo Red → amyloid.

Anaplastic carcinoma

- Anaplastic carcinoma more common in elderly individuals.
- Have a rapid growth rate, and metastasize widely.
- Inactivating point mutation in the p53 , The prognosis is very poor.

Histologically :

-The tumors are poorly differentiated
-Large, pleomorphic giant cells and atypical,