



Midterm Review (Lectures 1&2)

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Endocrine Block

(Hypo/Hyper)Thyroidism and Hashimoto's Thyroiditis

- The Thyroid gland is formed of 2 large lobes connected by isthmus, it's regulated by Hypothalamus-Pituitary-Thyroid axis.
- **Hypothyroidism:**
 - Caused by any structural or functional damage, leading to dropped levels of secreted hormones. Can be primary (Thyroidal disease) or Secondary (e.g. TSH deficiency)
 - Incidence is 0.1%, Affect women ten folds more than men.

Primary causes include:

1. Developmental (Acquired mutations, e.g. **PAX8**, **FOXE1**, **TSH** receptor mutations).
2. Surgery and Radioiodine therapy (Postablative)
3. Iodine deficiency (Most common cause of congenital hypothyroidism).
4. Autoimmune (e.g. Hashimoto's Thyroiditis) Most common cause of hypothyroidism in iodine-rich countries.
5. Congenital defects (e.g. **Dyshormonogenetic goiter**) less common cause of congenital hypothyroidism.

Manifestations differ according to the age affected:

- **Cretinism**: Due to congenital hypothyroidism, patients come with severe mental retardation and short stature.
- **Myxedema**: slowing of physical and mental activity, mental sluggishness and overweight.

- **Thyrotoxicosis:** Hypermetabolic state caused by elevated circulating levels of free T3 and T4.

Causes	Explanation	Examples
Associated with Hyperthyroidism	More common, hyperfunction of the thyroid gland.	Graves's disease/Adenoma/Multinodular goiter/Pituitary adenoma
Not Associated with Hyperthyroidism	Any other cause leads to high levels of the thyroid hormones.	Thyroiditis / Struma ovarii / Exogenous hormonal intake

- **Graves' disease:** Autoimmune disorder characterized by presence of Immunoglobulins against TSH-Receptor that mimic the action of TSH.
- Other antibodies against Peroxisome and Thyroglobulin may also be a finding.
- **Thyroiditis:** Inflammation of the thyroid gland.

Can be:

- Painful with Acute illness (Infectious, Subacute granulomatous thyroiditis*).

Thought to be caused infectiously (Coxsackie, Mumps viruses) More common in women (40-50)

- Painless with little inflammation (Subacute lymphocytic and fibrous Thyroiditis).
- **Hashimoto's Thyroiditis:** Gradual thyroid failure by autoimmune destruction of the thyroid gland (Against many thyroidal autoantigens e.g. Peroxidase enzyme and Thyroglobulin).
 - Patients come with diffusely symmetrically enlarged gland with Lymphocytic infiltration (**Struma Lymphomatosa**).
 - Female predominance of 10:1 to 20:1. Age 45-65.

- **Morphology:**
 1. Gross features: Diffusely enlarged gland with pale, yellow-tan and firm cut-surface.
 2. Microscopic features: extensive infiltration of the parenchyma by a mononuclear inflammatory infiltrate containing small lymphocytes, plasma cells, and well-developed germinal centers.
- Presence of what is called (**Hürthle cells**) with eosinophilic granular cytoplasm containing numerous mitochondria.

Thyroid nodules and Neoplasms

- Thyroid Neoplasm could be **Follicular-Adenoma** (Benign) or **Carcinoma** (Malignant). Benign neoplasms are more common than malignant.
- The major subtypes of thyroid carcinoma are:
 - Papillary carcinoma (> 85% of cases)
 - Follicular carcinoma
 - Medullary carcinoma
 - Anaplastic carcinoma
- Follicular Adenoma and all subtypes of thyroid carcinoma arise from follicular cells EXCEPT Medullary carcinoma from parafollicular (c-cells).
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- Benign neoplasms outnumber thyroid carcinomas by a ratio of nearly 10:1.
 - Solitary nodules, in younger male patient → neoplastic
 - Nodules that highly **uptake** radioactive iodine (**hot nodules**) → benign
- Careful evaluation of the integrity of the capsule is critical in distinguishing follicular adenomas from follicular carcinomas, which demonstrate **capsular and/or vascular invasion**.
 - Follicular adenomas: encapsulated mass lesion.
 - Follicular carcinomas: invasion of capsule or blood vessels.
- Follicular adenomas are the most common benign neoplasms, while papillary carcinoma is the most common malignancy.
- Extremely rare that thyroid neoplasms increase the production of thyroid hormones (generally are nonfunctional)

Carcinomas

- Genetics:

Follicular → RAS	Medullary → MEN-2, RET
Papillary → RET, NTRK1 or BRAF	Anaplastic → P53

1. Papillary Thyroid Carcinoma:

- The major risk factor is exposure to ionizing radiation.
- Between the ages of 25 and 50
- The first manifestation may be a mass in a cervical lymph node
- Have an excellent prognosis
- Papillary carcinomas are recognized based on nuclear features
- Morphology: Papillary structures, Orphan Annie nuclei and Psammoma bodies.

2. Follicular Carcinomas:

- Between 40 and 60 years and More common in women (3:1)

3. Medullary Carcinomas:

- Neuroendocrine neoplasms derived from C cells.
- Measurement of Calcitonin plays an important role in the diagnosis and postoperative follow-up of patients.
- About 70% of tumors arise sporadically and the remainder occurs in the setting of MEN syndrome 2A or 2B
- Morphology: polygonal to spindle cells and Amyloid deposition. (Detected by Congo red stain)

4. Anaplastic Carcinomas

- Undifferentiated tumors of the thyroid follicular epithelium.
- Lethal (100%).
- Older age group > 65 year.
- Morphology: composed of highly anaplastic cells → giant cells, spindle cells and small cells.

MCQs

1-A 46-year-old woman complains of increasing fatigue and muscle weakness over the past 6 months. She reports an inability to concentrate at work and speaks with a husky voice. The patient denies drug or alcohol abuse. Physical examination reveals cold and clammy skin, coarse and brittle hair, boggy face with puffy eyelids, and peripheral edema. There is no evidence of goiter or exophthalmos. Laboratory studies show reduced serum levels of T3 and T4. Which of the following is the most likely underlying cause of these signs and symptoms?

- A. Amyloidosis of the thyroid
- B. Hypothyroidism
- C. Thyroid follicular adenoma
- D. Multinodular goiter

2-A patient presents with signs of hyperthyroidism (thyrotoxicosis). To investigate the matter, you measure the levels of T4 and TSH. If the patient has a benign thyroid adenoma ("toxic nodule"), you can expect the following results?

- A. T4 elevated, TSH reduced
- B. T4 reduced, TSH reduced
- C. T4 elevates, TSH elevated
- D. T4 reduced, TSH elevated

3-A patient presents with signs of hypothyroidism. To investigate the matter, you measure the levels of T4 and TSH. If the patient suffers from iodine deficiency, you can expect the following results?

- A. T4 reduced, TSH reduced
- B. T4 elevated, TSH reduced
- C. T4 elevates, TSH elevated
- D. T4 reduced, TSH elevated

4-The Exact cause of Hashimoto's thyroiditis is?

- A. therapeutic radiation
- B. thyroid resection
- C. hypopituitarism
- D. autoimmune destruction

5-In Grave's disease, enlargement of the thyroid gland is caused by?

- A. constitutive activation of the Gs-protein as a result of a somatic mutation
- B. an antibody that stimulates TSH receptors
- C. abnormally elevated TSH levels
- D. a transport defect for iodine in the membrane of the follicular cell

6-A 40-year-old woman complains of chronic constipation and anovulatory menstrual cycles for the last 8 months. Her vital signs are normal. Physical examination reveals peripheral edema and a firm, diffusely enlarged thyroid gland. Serum levels of T3 and T4 are abnormally low. A thyroid biopsy is shown in the image. What is the appropriate diagnosis?

- A. Graves' disease
- B. Hashimoto's thyroiditis
- C. Lymphadenoid thyroiditis
- D. Subacute (de Quervain) thyroiditis

7-A 43-year-old woman complains of low-grade fever and has a 3-day history of pain in her neck. Physical examinations reveals a slightly enlarged thyroid. A CBC is normal. A biopsy of the thyroid reveals granulomatous inflammation and the presence of giant cells. What is the appropriate diagnosis?

- A. Graves' disease
- B. Hashimoto's thyroiditis
- C. Lymphadenoid thyroiditis
- D. Subacute (de Quervain) thyroiditis

8-Patient has symptoms of hyperthyroidism. Which of the following best summarizes the clinical symptoms expected in this patient?

- A. Tremor, tachycardia, weight loss
- B. Hyperpigmentation, weakness, hypotension
- C. Nervousness, irritability, paresthesia, tetany
- D. Dry skin, hypogonadism, fatigability

9-Which one of the following is the most susceptible group to be affected by Hashimoto's Thyroiditis?

- A. 20 Years old, male
- B. 80 Years old, male
- C. 50 Years old, female
- D. 35 Years old, female

10-The appropriate reason behind the appearance of hypothyroid manifestations between the episodes of hyperthyroidism in some patients with Graves' disease is?

- A. Presence of immunoglobulins that are directed to antigens other than TSH receptor
- B. Coexistence of TSH-receptor stimulating and inhibiting autoantibodies
- C. Excessive levels of plasma TSI
- D. None of these

11-The most common type of thyroid carcinoma is?

- A. Papillary carcinoma
- B. Follicular carcinoma
- C. Medullary carcinoma
- D. Anaplastic carcinoma

12-Young male came to the hospital with solitary nodule of the thyroid .On examination with radioactive iodine, the nodule appear to be cold. What is the most likely diagnosis?

- A. Non neoplastic nodule
- B. Neoplastic nodule, malignant nodule
- C. Neoplastic benign nodule

13-The definitive diagnosis of thyroid adenoma by?

- A. Gross examination
- B. Careful histological examination
- C. Radiological examination

14-Ionising radiation is the major risk factor for papillary carcinoma?

- A. True
- B. False

15-A 35 years old female comes to the hospital with cervical lymph node enlargement, Microscopic examination shows finely deposit chromatin (Orphan Annie eye) and pseudoinclusion, what is the most likely diagnosis?

- A. Papillary carcinoma
- B. Follicular carcinoma
- C. Anaplastic carcinoma
- D. Medullary carcinoma

16-papillary carcinoma usually metastasize through lymphatics?

- A. True
- B. False

17-A 56 male have past history of well-differentiated thyroid carcinoma, presents with swelling in his neck, biopsy was done and showed poor differentiated pleomorphic giant cells. What is the most likely diagnosis?

- A. Follicular carcinoma
- B. Papillary carcinoma
- C. Anaplastic carcinoma
- C. Medullary carcinoma

18-In the patient described in Q7, what other microscopic features you will observe?

- A. Well-defined, intact capsule
- B. Spindle cell with a sarcomatous appearance
- C. Psammoma bodies
- D. Orphan Annie eye

19-A 50 years old woman come to the hospital with severe goiter then appear to have iodine deficiency .Histological examination of the thyroid shows follicular cells invading the blood vessels. What is the most likely diagnosis?

- A. Papillary carcinoma
- B. follicular carcinoma
- C. Anaplastic carcinoma
- D. Medullary carcinoma

20-In follicular thyroid carcinomas there is mutation in?

- A. In the PI-3K/AKT signaling pathway
- B. RET gene
- C. P53 tumor suppressor gene

21-Medullary carcinoma derived from follicular epithelium?

- A. True
- B. False

22-A 36-year-old woman presents with swelling in her neck. Physical examination reveals a non-tender nodule in the left lobe of the thyroid. The thyroid nodule is found to be “cold” by radioiodine test. And a section stained with Congo red reveals birefringent amyloid stroma. What is the most likely the diagnosis?

- A. Follicular carcinoma
- B. Medullary carcinoma
- C. Anaplastic carcinoma
- D. Papillary carcinoma

Question	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Answer	B	A	D	D	B	B	D	A	C	B	A	B	B	A	A	A	C	B	B	A	B	B

Thank You & Good Luck