Endocrine Glands

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Endocrine Pathology

Organs
• Pituitary
• Thyroid
• Parathyroids
• Adrenals
• Pancreas

Diseases
Non-neoplastic
• too much hormone
• too little hormone

Neoplastic
• benign
• malignant

Pituitary Introduction

Anterior pituitary (adenohypophysis)
• Acidophil cells….secrete GH, and prolactin.
• Basophil cells …. Secrete ACTH, TSH, LH, and FSH
• Chromophobe cells do not secrete
• Controlled by hypothalamus.
**Posterior pituitary (neurohypophysis)**
- Oxytocin, ADH (vasopressin)
- Hypothalamus makes them
- Posterior pituitary stores them

**Hyperpituitarism**
- Definition: too much anterior pituitary hormone(s)
- Most common cause: pituitary adenoma
- Pituitary adenoma symptoms:
  - None, for a while
  - Endocrine abnormalities
  - Mass effects
- Many types
  - Produces gigantism or acromegaly
  - Other findings
    - diabetes mellitus
    - hypertension
    - arthritis
    - gastrointestinal carcinoma

**Acidophil adenoma**
- **Growth Hormone Adenoma**
  - Gigantism
  - Acromegaly
Other Pituitary Adenomas
• Prolactinoma…. Amenorrhea & galactorrhea
• ACTH-producing…Pituitary chushing
• FSH-LH-producing
• TSH-producing
• Non-functioning

Hypopituitarism
• Definition: too little anterior pituitary hormone(s)
• Causes
  – Pituitary destruction
  – Ischemic necrosis….usually after post-partum hemorrhage
• Symptoms usually insidious
  – Dwarfism
  – Loss of libido, menstrual abnormalities
  – Hypothyroidism
  – Adrenal insufficiency

Tumors of the anterior pituitary
Pituitary Adenoma

Gross Appearance
Adenomas appear as a lobulated
mass covered by a thin, attenuated shiny capsule.

M/E
- According to the cell type,
adenomas may be Chromophobe
75%" acidophil 20% or basophil adenoma 5% 
- The tumor is composed of a monomorphic cells forming solid groups,
  small acinar or papillary structures.
A tumor derived from epithelial remnants of Rathke’s Pouch.

Craniopharyngioma arises in children and young adults and is always **benign**

- **Gross Appearance**
  - Tumor is multilobated, cystic, and calcified.

*C/S* reveal multiple cystic areas containing oily fluid. Some areas appear yellow and glistening due to cholesterol crystal deposits.

**2-Craniopharyngioma**

*M/E*

Squamoid and columnar epithelium lining cystic spaces filled with oily fluid

**Effects**

- Compression of the pituitary gland

**2-posterior pituitary hypo function**
  - Diabetes insipidus results from a deficiency in ADH production or release
- Presents with polyuria and polydipsia
- Patient is unable to concentrate urine due to lack of ADH.

3- Adenocarcinoma of pituitary gland
Rare, destroy the base of the sella turcica and extend to the nasopharynx

**Thyroid Pathology**

**Introduction**
Hyperthyroidism
Hypothyroidism
Non-neoplastic diseases
Neoplasms

**Hyperthyroidism**

*A hypermetabolic state caused by \( \uparrow \) thyroid hormones.*

**Cardiac:** rapid pulse, arrhythmias

**Neuromuscular:** tremor, emotional lability

**Eye:** lid lag

**Skin:** warm, moist

**Gastrointestinal:** diarrhea

**Skeletal:** osteoporosis

**Thyroid storm:** \( \uparrow \uparrow \uparrow \) thyroid hormone

**Hypothyroidism**

*A hypometabolic state caused by \( \downarrow \) thyroid hormones.*

**Slowing of mind and body**

**Myxedema:** deepened voice

**Cardiac:** slow pulse

**Gastrointestinal:** constipation

**Skin:** dry, cool, pale

**Cold intolerance**

**Delayed reflexes**
Thyroiditis
Types:
1- Autoimmune thyroditis
   Hashimoto's Thyroiditis
2- Subacute Granulomatous Thyroiditis (DeQuervain throditis)
3- Reidel thyroditis
4- Infectious thyroditis (acute and chronic)

Hashimoto's Thyroiditis
- An auto-immune thyroiditis
- The most common cause of Hypothyroidism.
- Female to male ratio is 10:1
  • Pathogenesis
    • The autoimmune process arises from activation of CD4 (helper) T lymphocytes sensitized to thyroid antigens
    • These CD4+ cells stimulate proliferation of autoreactive cytotoxic (CD8+) T cells, which attack thyrocytes.
    • Activated CD4 cells also recruit autoreactive B cells to produce antibodies against thyroid antigens.

Gross
1- Early... there is symmetrical enlargement of the gland
- The affected areas are white gray or yellow brown and firm
- They lack the glistening appearance of colloid.
2- Late... The gland becomes symmetrically atrophic
   ...MlE
   - Some acini are atrophied. Other acini show regenerative changes and lined by large cubical cells with deeply eosinophilic granular cytoplasm (Askanazy or Hurthle cells).
- Inflammatory cells (lymphocytes, plasma cells, macrophages) and fibrosis around the acini

**Complication**

1- Hypothyroidism 2- Lymphoma

**Subacute Granulomatous “DeQuervain” Thyroiditis**

- A self-limited disorder in which patients present with a tender thyroid.
- May have a viral etiology, since it commonly follows an upper respiratory infection or mumps.
- Scattered follicles are surrounded by histiocytes, multinucleated giant cells, and lymphocytes – producing a granulomatous appearance.

**Reidel thyroditis**

- Rare of unknown cause affect both sexes.
  - The gland is hard and adherent to the surrounding structures due to dense fibrosis

**Goitre**

- **Definition**: Non inflammatory, non neoplastic enlargement of the thyroid gland
- **Classification**
- Simple (non toxic)...diffuse and multinodular
- Toxic.... Primary and Secondary

Simple (non toxic)
Enlargement of the thyroid without toxic manifestation

Causes
1. Absolute iodine deficiency: in area away from seas or due to intake of goitrogenic agents e.g. cabbage and hard water
2. Relative iodine deficiency due to increase demand for thyroxine in pregnancy, at puberty and during lactation

Pathogenesis
- In nontoxic goiter, the capacity of the thyroid to produce thyroid hormone is impaired.
- Resulting increased secretion of TSH leads to enlargement of the gland, which maintains the euthyroid state.
- Simple nodular thyroid enlargement tends to be familial, suggesting a genetic factor in the disorder.

Pathology
- Non-toxic goiter may be diffuse (early) or multinodular (chronic cases).
- Diffuse nontoxic goiter characterizes the early stages of the disease.
- The gland is diffusely enlarged
- Microscopically exhibits hypertrophy and hyperplasia of the follicular epithelial cells.
- At this stage, the amount of colloid in the follicles is decreased.

Multinodular nontoxic goiter
- Multinodular nontoxic goiter reflects more chronic disease.
- The enlarged gland becomes nodular, and the cut surface is typically studded with numerous irregular nodules.
- When these nodules contain large amounts of colloid, the thyroid tends to be soft, glistening, and reddish.

- **Microscopically**, nodules vary considerably in size and shape. Some are distended with colloid; others are collapsed.
- Large colloid-containing follicles may fuse to form even larger colloid cysts.
- Lining epithelial cells are flat to cuboidal.
- The individual follicles or groups of follicles are separated by dense fibrosis.
- Hemorrhage, chronic inflammation and dystrophic calcifications are common.

**Complication**

1. Pressure effects: on trachea, esophagus and recurrent laryngeal nerve
2. some of these nodules may become hyperfunctioning and cause secondary hyperthyroidism (no exophthalmos)
3. malignancy: rare in 2% of cases.

**Toxic goiter**

**Two types:**

- **Primary toxic goiter** exophthalmoic goiter or grave’s disease
- **Secondary toxic goiter**: toxic nodular goiter
Grave's disease

- Organ specific autoimmune disease, affecting young females.
- Due to auto-antibodies (LATS; Long Acting Thyroid Stimulating) antibodies.
- They stimulate TSH receptors leading to diffuse hyperplasia and hyper functioning thyroid acini with excess thyroid hormone secretion

Pathological Features

Grossly
- The thyroid is symmetrically enlarged.
- Cut surface is firm and dark red.
- Loss of the normal translucence of stored colloid. The gland appears fleshy.

Microscopically,
- The gland is diffusely hyperplastic and highly vascular.
- The epithelial cells are tall and columnar and are often arranged as papillae that project into the lumen of the follicles.
- The colloid tends to be depleted and appears scalloped or (moth-eaten) at the periphery.
- Scattered B and T lymphocytes and plasma cells infiltrate the interstitial tissue and may even aggregate to form germinal follicles.

Hyperplastic acini lined by columnar cells and filled with faintly
stained colloid with peripheral scalloping. The stroma is highly vascular and shows lymphocytic infiltration.

2-Exophthalmos
It is caused by enlargement of orbital extraocular muscles by mucinous edema, accumulation of fibroblasts and lymphocyte infiltration. The increased orbital contents displace the eye forward (proptosis).

3-Diffuse lymphoid hyperplasia: in thymus, tonsil, spleen, gut

4-Left ventricular hypertrophy "thyrotoxic cardiomyopathy."

5-Pretibial myxedema.

6-Increased basal metabolic rate

**Secondary toxic goiter**

Due to:

A. **Toxic nodular goiter**: diffuse, nodular enlargement of the thyroid. Some nodules show hyperfunctioning acini. Other acini are inactive.

B. **Toxic adenoma**: the hyperfunctioning acini are like grave's disease. The remaining thyroid tissue is inactive. Thyroid hormone secretion is autonomous.

**Manifests as hyperthyroidism without exophthalmos.**

**Tumors of the thyroid**

I- Benign

**Follicular Adenoma**

Derived from thyroid follicular epithelial cells. Most common cause of a solitary thyroid nodule.

**Gross** - Solitary nodule, surrounded by a fibrous capsule.
Thyroid adenoma

**M\E**
- **Solid adenoma**
  A- Macrofollicular (colloid) adenoma: formed of acini containing colloid
  B- Microfollicular (Fetal) : formed of small acini with scanty colloid
  C- Hurthle cell adenoma: the acini are lined by
    oncocytic cells

Tumors of the thyroid

**II-** Malignant
- **Primary**
  A- Epithelial...Carcinoma
  B- Mesenchymal....Lymphoma
- **Secondary (Metastatic)...Rare**

**Thyroid Carcinomas**
Most are derived from follicular epithelial cells

**Grossly** Irregular firm
  grayish mass infiltrating
  the thyroid.

**Microscopically... 4 Types**
1. Papillary carcinoma
2. Follicular carcinoma
3. Medullary carcinoma
4. Undifferentiated carcinoma

**Capsular invasion**

**M\E**

1-Papillary carcinoma:
- Most common carcinoma
  - Female predominance
  - Any age
  - Lymphatic spread
- Excellent prognosis
  - Microscopically, 
  - Branching papillae are lined by neoplastic columnar epithelium with clear nuclei (washed out nuclei).
  - Psammoma bodies are evident.

2-Follicular Adenocarcinoma:
- 2nd most common
  - Worse prognosis than Papillary carcinoma
  - These tumors invade blood vessels with hematogenous spread to lung and bone.
M\E -
• Resemble follicular adenomas.
Diagnosis based entirely on demonstration of invasion of blood vessels in region of capsule OR by finding capsular invasion

**Prognosis**... a slowly growing neoplasm that may, however, spread via the bloodstream at an early stage, producing metastases in bone and lungs.
- Lymphatic metastasis to cervical nodes also occurs but to a lesser extent than in papillary carcinoma.

3- **Medullary carcinoma**
Rare, about 5% of thyroid carcinomas.
• It is derived from the calcitonin-secreting parafollicular cells (C cells) of the thyroid.
• 90% of cases are sporadic and 10% are familial
• **Microscopically**, it is composed of small spindle-shaped and polygonal cells arranged in nests, cords, and sheets
  - The stroma contains amyloid material.
• **Prognosis**
  Slow but progressive growth pattern.
• Local invasion of neck structures is common.
• Both lymphatic and bloodstream metastasis occurs.

4- **Anaplastic Carcinoma**
• Age above 50 years.
• **Grossly**... A massive infiltrative lesion. It is hard, gritty, and grayish-white and frequently shows areas of necrosis and hemorrhage.
• **Microscopically,**... it is composed of highly malignant-appearing spindle or giant cells, showing extreme pleomorphism and frequent mitotic figures.
- **Prognosis**: aggressive, rapidly growing neoplasms that disseminate extensively.

**Normal thyroid**

- Follicular cells
- Parafollicular C cells

**Follicular adenoma**

- Histologically very similar to normal thyroid
- Fibrous capsule
- Compressed rim of residual normal thyroid

**Medullary C cell carcinoma**

- Amyloid
- Carcinoma cells contain calcitonin

**Papillary carcinoma**

- Epithelial shows many fingerlike growths (hence papillary)

**Anaplastic carcinoma**

- No resemblance to thyroid tissue; may include bizarre giant cells

**Follicular carcinoma**

- Well differentiated, resembles adenoma but with more variability of follicles, plus nuclear atypia and invasion
- Invasion of blood vessel

**Thyroid tumors**
Diseases of suprarenal gland

Suprarenal cortex
Hypofunction

1. **Acute adrenal insufficiency**...

   Waterhouse-Friederichsen Syndrome due to septicemia.

2. **Chronic adrenal insufficiency** "Addison's disease"

   a- Idiopathic Atrophy
   b- Autoimmune disease,
   c- Tuberculosis (20% )
   d- Other - (Amyloidosis, metastatic Carcinoma )

Hyperfunction

*Causes*

1- Cortical hyperplasia       2- Cortical adenoma
3- Cortical carcinoma

Suprarenal medulla

*Tumors*

*Neuroblastoma*

- An embryonal malignant tumor of neural crest origin that is composed of neoplastic neuroblasts and originates in the adrenal medulla & paraganglia

- The peak incidence is in the first 3 years

*Grossly*.... They are round, irregularly lobulated masses.

- The cut surface is soft and friable, with areas of necrosis, hemorrhage, calcification, and cystic change are often present.
Neuroblastoma

Microscopically
It is composed of dense sheets of small, round to fusiform cells with
hyperchromatic nuclei and
scanty cytoplasm mitoses are frequent.
- Characteristic Homer Wright rosettes are defined by a rim of
dark tumor cells in a circumferential arrangement
around a central pale fibrillar core
- Spread
  - Infiltrate surrounding structures and metastasize to regional
    lymph nodes, liver, lungs, bones, and other sites.
- The tumor may differentiate into a ganglioneuroma
- Prognosis
  - Depends on...Age of child, stage, histological differentiation

Pheochromocytoma
- Rare catecholamine-secreting tumors of chromaffin cells of the
  adrenal medulla.
- Tumor may be sporadic or part of multiple endocrine neoplasia
  (MEN)
• In sporadic pheochromocytomas, 10% are bilateral and 10% are in extraadrenal locations; 10% are malignant and 10% occur in children
• Tumor presents with secondary hypertension (episodic or persistent).
• If detected early, pheochromocytomas are amenable to surgical resection, but when left untreated, patients can die of the complications of prolonged hypertension
• **Grossly,**
  - Tumor tends to be encapsulated, spongy, reddish, with prominent central scars, hemorrhage and foci of cystic degeneration.
• **Microscopically,**
  • Typically, circumscribed nests are found
  • Tumor cells may be polyhedral, fusiform, with granular cytoplasm and vesicular nuclei.
  • Cellular pleomorphism is often prominent and may include multinucleated tumor giant cells
Endocrine pancreas

D.M

Insulin secretion and functions

<table>
<thead>
<tr>
<th>After a meal</th>
<th>Liver</th>
<th>Muscle</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High serum insulin level</td>
<td>Increased</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>• In the presence of dietary glucose</td>
<td>Glycogen storage</td>
<td>Glycogen storage</td>
<td></td>
</tr>
<tr>
<td>• Principally anabolic</td>
<td>Lipogenesis</td>
<td>Protein synthesis</td>
<td>Lipogenesis</td>
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<tr>
<td></td>
<td>Decreased</td>
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<tr>
<td></td>
<td>Gluconeogenesis</td>
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<tr>
<td></td>
<td>Ketogenesis</td>
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Diabetes mellitus

Definition:
A clinical state in which glucose metabolism is reduced due to insufficient secretion or inefficient action of insulin.

Etiology and types:
Primary (idiopathic): Type I and type II.
Secondary: follows pancreatitis, hemochromatosis and associated with endocrinopathies (acromegally, Cushing syndrome, pheochromocytoma and thyrotoxicosis).

<table>
<thead>
<tr>
<th>1. Age</th>
<th>Type I (IDDM)</th>
<th>Type II(NIDDM)</th>
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<tbody>
<tr>
<td></td>
<td>Under 25 years</td>
<td>Above 40 years</td>
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<tr>
<th>2. B. Cell mass.</th>
<th>Reduced</th>
<th>Not reduced</th>
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</thead>
<tbody>
<tr>
<td>3. Insulin secretion</td>
<td>Reduced</td>
<td>Not reduced</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Etiology</th>
<th>Type I (IDDM)</th>
<th>Type II(NIDDM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hereditary</td>
<td>- Autoimmune destruction of surface receptors on most of the B.cells</td>
<td>- Decreased insulin specific surface receptors on most of the body cells</td>
</tr>
<tr>
<td></td>
<td>- Premature aging of body cells including B cells</td>
<td></td>
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</tbody>
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<thead>
<tr>
<th>5- Treatment</th>
<th>Type I (IDDM)</th>
<th>Type II(NIDDM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>By insulin only</td>
<td>- Oral hypoglycemics</td>
<td></td>
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</table>
I. Pancreas:

1- **In type I:** the pancreas is atrophic. M/P: degranulated and destroyed β-cells, lymphocytic infiltration and fibrosis.

   - **2-In type II:** the pancreas is normal. M/P: normal in early stage, later on shows hyalinosis.

2- Disturbance of metabolism (catabolic disturbances)

A. Carbohydrate metabolism:

   - Hyperglycemia due to either decreased glucose utilization or due to glycogenolysis.

   Leads to:

   1. Glucose retention in the tissue (increase the liability to infection).
   2. Glucosuria: leads to osmotic diuresis and dehydration.

B. Fat metabolism:

   Lipolysis leads to

   1. Hyperlipidemia (atheroma formation and fatty infiltration in the parenchymatous organs).
   2. Formation of ketone bodies in the liver with ketoacidosis and coma.

C. Protein metabolism

   Proteolysis leading to

   1. Muscle wasting
   2. Gluconeogenesis
3- Vascular changes:

1- Diabetic macroangiopathy of small arteries: with atheroma formation, usually affect coronaries, cerebral and small arteries of the leg and foot.

2- Diabetic microangiopathy of arterioles and capillaries: leads diabetic nephropathy, retinopathy and neuropathy.

3- Diabetic Glomerulosclerosis: nodular type "Kimmelstiel-Wilson lesion" and diffuse type.

**Diabetic nephropathy**

- In many advanced cases, there is nodular glomerulosclerosis ("Kimmelstiel-Wilson lesion"), with round masses of GBM-mesangial matrix material in the glomerular tufts.
- This histologic picture is highly characteristic of diabetes, and it is usually present if the diabetes has been present for longer than 20 years (sometimes much less).

- Many diabetics have albuminuria (occasionally in the nephrotic range), which progresses over years to renal failure (probably due to the mesangium choking off the glomerular capillaries

  - Atheroma of the renal artery or the segmental branches leads ischemia and hypertension
-Chronic pyelonephritis and pyonephrosis, due to increased liability for infection

Complications of D.M

1. Diabetic coma....(ketoaciditic in type I, hyperosmolar in type II, may be hypoglycemic in overdose treatment of any type)

2. Cardiovascular complications:-
   Ischemic heart disease and peripheral vascular insufficiency
   (trophic ulcers and finally gangrene.)
   Peripheral vascular insufficiency: leads to trophic changes and even gangrene.

3. Renal complications:

4. Increased susceptibility to infection: bacterial, fungal leads to frequent boils, carbuncles or T.B.

5. Peripheral neuropathy

6. Diabetic retinopathy which may end in blindness.