Pathology of endocrine system

Pituitary gland
Wt 600mg in male, and 800mg in female.
It has two components:
The Adenohypophysis and the neurohypophysis.

Pathology:
Any abnormality in the functions, secretion of hormones will be expressed by either increase (Hyperpituitaryism) or decrease (Hypopituitaryism), while the local effects are:
1- Enlargement of sella turcica.
2- Visual field impairment due to local effect on optic chiasma.
3- Increase I.C.P lead to headache, vomiting or fit

Pituitary Adenoma:
Etiology:
Is not fully understood, it may be hyper stimulation of hypothalamic releasing factors. It is either non-functioning or functioning.

Types of pituitary adenoma:
1- Somatotropic adenoma (STH cell, result in increase secretion of GH which cause gigantism if occurs before closure of epiphysis (during childhood). Or it may cause acromegaly in the adulthood period that result in large hands bone, feet and jaw, there is also enlargement of internal organs, cardiomegaly and hypertension.
Patient with untreated acromegaly have approximately twice the expected mortality rate, mainly from cardiovascular diseases.
Abnormal glucose tolerance with Diabetes mellitus in minority of cases.

2- ACTH type which lead to Cushing's disease due to excessive glucocorticoid secretion adrenal gland in about 2/3 of cases this is due to excessive stimulation of the adrenal secondary to hypersecretion of ACTH by the pituitary.

3- Prolactinoma; Hyperprolactinaemia: in women excessive Prolactine secretion is often associated with Amenorrhoea and infertility while it is asymptomatic in males or occasionally causes infertility.
4-Gonadotrophs tumors: Increase in FSH lead to hypogonadism in males, with no effect in females.
5-Null cell adenoma, no hormone secretion.
**Gross features of pituitary adenoma:**
These tumors are small soft brownish and surrounded by thin capsule, they are liable for hemorrhage or infarction

**Microscopic features:**
these adenomas consist of cells closely resembling one or the other of the pituitary cells. Occasionally more than one type occurs. The constituent cells are arranged in solid groups with intervening fine vascularized stroma. Glandular or papillary arrangement may be seen.

**Hypopituitarism**

**Causes:**
1. Destruction or tumor of pituitary stalk or hypothalamus.
2. Sheehan's syndrome (post partum pituitary necrosis).
3. Pituitary surgery or irradiation.
4. Trauma, inflammation including autoimmune hypophysitis, supracellular tumor e.g. Craniopharyngeoma

**Thyroid gland:**
It is situated just below the cricoid cartilage, it is the only endocrine gland which is situated close to the surface and in site where any increase in size is visible.
It consists of two lateral lobes joined by the isthmus.
50% of people have a pyramidal lobe above the isthmus.
Wt is 15-25gm

**Histology:**
Consists of many follicles lined by cuboidal epithelium which contain varying amount of colloid (storage form of thyroglobulin). Among the follicular cells in the middle and upper portions of the lateral lobes are scattered C cells which produce Calcitonin.
The follicular cells produce the hormones:
T3: Tri-iodothyronine
T4: Tetra-iodothyronine. It is responsible for metabolism of proteins and carbohydrates.

**Hyperthyroidism:**

**Causes of hyperthyroidism:**
1- Toxic nodular goiter.
2- Adenoma (Toxic nodule)
3- Hashimoto's thyroiditis.
4- Increase TSH by pituitary adenoma.
5- Excessive production of thyroxin due to administration of large amount of iodine to patient with large nodular goiter.
Hypothyroidism:
In adults called Myxoedema.
Causes:
- Autoimmune thyroiditis.
- After thyroidectomy.
- Hypopituitarism.
Cretinism: due to severe hypothyroidism in infancy.

Non-toxic nodular goiter:
Is the commonest lesion in thyroid pathology and it reflects compensatory thyroid hyperplasia in the context of absolute or relative iodine deficiency.

On epidemiological grounds there are:
1- Endemic goiter: which usually occurs in mountainous areas, far from the sea in such places > 10% of population are affected.
   As prophylaxis measure introduction of iodized salt help in controlling such condition.
2- Sporadic non-toxic goiter due to lack of iodine in individual patients.

Causes:
1- Poor dietary intake of iodine
2- Inherited deficiency of enzymes involving in biosynthesis of thyroxin.
3- Ingestion of specific chemicals interfere with thyroid hormone synthesis like vegetable, cabbage, brussel sprouts and excessive florid in water
4- Drugs like para amino salicylic acid and sulphonylurea.
5- Autoimmune thyroiditis.

Gross:
The gland is enlarged with obvious nodular configuration and marked asymmetry and nodularity.

Microscopically: Variable sized follicles with increases number of acini lined by flattened to low cuboidal.

Thyroiditis:
The most common clinical significant condition are:

Autoimmune thyroiditis: diseases which are characterized by lymphoid infiltration of the gland and by presence of circulating autoantibodies to various components of thyroid follicular cells.
   TSI thyroid stimulating immunoglobulin are TSH-receptor antibodies which activate the receptor and stimulate secretion of thyroid hormone with resultant hyperthyroidism.
   Other autoantibodies called (TGI) caused goiter of Hashimoto's disease.
**Hashimoto's thyroiditis:**
Mainly of middle age group women female: male is 20:1.  
HLA DR5 correlation  
Painless goiter, euthyroid at early stage and hypothyroidism in 80% of cases.  
**Grossly:** enlarged fleshy soft.  
**Microscopically:** it is widely infiltrated and replaced by lymphoid cells, plasma cells and macrophages and even germlinal center formation. The thyroid follicular cells are enlarged with eosinophilic granular cytoplasm due to accumulation of mitochondria, this is known as Askanasy cell changes, fibrosis also prominent. Most patient show high titer of microsomal antibodies and 50% of patients show antibody to thyroglobulin occasionally presented with hyperthyroidism which may be due to presence of TSI.

**Graves disease**
It is characterized by
- diffuse thyroid hyperplasia and hyperthyroidism.  
- Female affected more than male.  
- 20-40Y is the range of occurrence.  
- Prevalence of HLA-DR3.  
- Exophthalmos (protrusion of globe) probably due to presence of Ab. Against extraocular muscles.  
- Peritibial Myxoedema (unknown cause)

**Microscopically:** hyperplastic epithelium with papillary infolding and little colloid storage and lymphocytic infiltration. Before surgery patient usually treated with antithyroid drugs with or without iodine which may alter the picture of histopathology

**Thyroid tumors:**  
The commonest cause of enlargement or nodular enlargement of the gland is multinodular goiter which form 70% of cases, other are tumors.

**Benign tumors:**

**Adenoma:**
- the commonest thyroid neoplasm  
- Frequent in females over 30Y age  
- May cause hyperthyroidisims so called toxic adenoma showing a hot nodule on thyroid scan due to increase iodine uptake.

**Gross:** usually encapsulated and compress the surrounding normal gland, haemorrhage and fibrosis may be present.
Histopathologically: microfollicular pattern with little colloid storage, other variety may present also that have marked colloid storage called colloid adenoma
Pathogenesis: irradiation
Activation of oncogene called PTC papillary thyroid chromosome.

Malignant tumors:
Papillary carcinoma:
It forms 70%-80% of thyroid cancer, affecting young adults (30-40Y) and more common in women.
Exposure of head and neck to irradiation during first and second of life may cause papillary carcinoma.
Gross: It is found as a nodule, may be very small and found by careful dissection, may be multi focal which is most probably due to intraglandular lymphatic metastasis. Lymphatic spread could be found in 40% of cases at the time of diagnosis
Histologically: well formed papillae with fibro vascular areas. Optically clear nuclei or grooved (ground glass appearance Sclerons and calciphertes (Psammoma bodies)
Prognosis: five year survival rate approach 90% without evidence of metastasis.

Follicular carcinoma:
• 1/4 of thyroid cancer.
• More aggressive than papillary type.
• Distant blood born metastasis to bone and lung.
Gross: grayish white growth of thyroid, either ass small nodule seem to be encapsulated or obvious invasive mass occupying almost the entire lobe.
Histologically: The pattern is that of adenocarcinoma with considerable range in follicular size and differentiation, so some has trabecular pattern, other produce a well defined follicules containing colloid.
The most important prognostic factor is the extent of invasion: patient with an encapsulated tumor faring better than those which is invasive.

Medullary carcinoma:
• It forms 5-10% of thyroid cancer
• More in females.
Arising from C. cells within the gland, on background of C. cell hyperplasia. So if medullary carcinoma and C. cell hyperplasia could be seen it is important to screen the family members for raised Calcitonin level or other features of tumor so thyroidectomy should be done 10-20% are familial forming part of the MEN2 (Multiple endocrine neoplasia syndrome)
**Gross:** presented as nodule in one lobe or bilateral, soft fleshy or firm gritty.

**Histologically:** It consists of solid irregular group and cords of cells.
Calcitonin immunohistochemistry can be demonstrated in the tumor cells.
Amyloid is identified in 50% of cases.
Spread and metastasis by blood and lymphatics.

**Anaplastic (undifferentiated carcinoma):**
- 5-10% of thyroid carcinoma.
- Mainly in women (60-70) Y
- Grow rapidly and highly malignant often show sign of local and distant metastasis at time of presentation.
**Gross:** bulky mass of thyroid.
**Histology:** poorly differentiated with bizzar giant cells, small cuboidal cell backed together forming cords or clusters within amyloid containing stroma.

**Etiology of thyroid carcinoma:**
- It is unclear weather iodine deficiency have any relation to malignancy in thyroid.
- Radiation increase number of patients after atomic bomb in Hiroshima fallowing head and neck radiation in early childhood.
molecular genetic study show:
80% of follicular carcinoma express activated ras oncogene and in 20% of papillary thyroid carcinoma.

**Adrenal glands:**
They lie above the kidneys and comprise the cortex, derived from the mesoderm of the urogenital ridge and the medulla which is of neuroectodermal origin.
It is divided into head body and tail, medulla present in to head and body.
Wt 4-4.5gm
It is under pituitary control.
Adrenal cortex:
Function: synthesis of steroid hormones and some sex hormones.

**Adrenal tumors:**
**Adenoma:** it may be associated with excessive secretion of cortisone, aldosterone or sex steroids.

**Carcinoma:** some adrenocortical tumors are frankly malignant especially the larger tumors > 100gm.
Adrenocortical hyperfunction:

**Cushing's syndrome:** characterized by excessive circulating glucocorticoid.
- Mostly in women, may be in men rare in children.
- Increase protein breakdown lead to loss of muscle bulk.
- Centripetal deposition of fat resulting in moon face, buffalo-hump and truncal obesity
- Cause abdominal striation due to abnormal collagen maturation.
- Hypertension.
- Osteoporosis.
- Excessive androgen secretion which lead to hirsitism, amenorrhea and virilization.

**Adrenal medulla:**
It consists mainly of
- Pheochromocytes or chromaffin cells which produce adrenal or non adrenal
- Ganglion cells and autonomic nerve fibers.

**Tumors**

A- **Pheochromcytoma:**
It's name due to ability of reducing chrom salt to metallic chrome (Brown).
Arise from Pheochromocytes lead to high secretion of catecholamine.
Causing:
- Hypertension.
- Palpitation.
- Sweating.
- It occurs in both sexes.
- 10% are familial.

**Microscopically:**
Cells arranged in alveolar or trabecular pattern. Surrounded by fibrovascular stroma.
Cells are large with large nuclei and prominent nucleoli, granular cytoplasm. Giant & bizarre cell may be present. Distant metastasis is absolute evident of malignancy. Diagnosis is by detection of VMA vinyl medilic acid in urine.

**Neuroblasoma:**
Arising commonly in children, from the primitive cells of the medulla, they are small primitive cells with dark nuclei forming rosettes like structure which surrounding central space filled with neurofibrils Metastasis by lymph node, blood.
ENDOCRINE PANCREAS
DIABETES MELLITUS
This is “a group of metabolic disorders sharing the common underlying characteristic of hyperglycemia.”

Diabetes is an important disease because
1. It is common (affects 7% of the population).
2. It increases the risk of atherosclerotic coronary artery and cerebrovascular diseases.
3. It is a leading cause of
   a. Chronic renal failure
   b. Adult-onset blindness
   c. Nontraumatic lower extremity amputations (due to gangrene)

Classification
Diabetes is divided into two broad classes:
1. Type 1 diabetes (10%): characterized by an absolute deficiency of insulin secretion caused by pancreatic β-cell destruction, usually as a result of an autoimmune attack.
2. Type 2 diabetes (80%): caused by a combination of peripheral resistance to insulin action and an inadequate secretion of insulin from the pancreatic β cells in response to elevated blood glucose levels.
The long-term complications in kidneys, eyes, nerves, and blood vessels are the same in both types.

Pathogenesis
Type 1 diabetes is an autoimmune disease and as in all such diseases, genetic susceptibility and environmental influences play important roles in the pathogenesis. The islet destruction is caused primarily by T lymphocytes reacting against immunologic epitopes on the insulin hormone located within β-cell; this results in a reduction of β-cell mass. The reactive T cells include CD4+ T cells of the TH1 subset, which cause tissue injury by activating macrophages, and CD8+ cytotoxic T lymphocytes; these directly kill β cells and also secrete cytokines that activate further macrophages. The islets show cellular necrosis and lymphocytic infiltration (insulitis). Autoantibodies against a variety of β-cell antigens, including insulin are also detected in the blood and may also contribute to islet damage.

Type 2 Diabetes Mellitus: the pathogenesis remains unsettled. Environmental influences, such as inactive life style and dietary habits that eventuates in obesity, clearly have a role. Nevertheless, genetic factors are even more important than in type 1diabetes. Among first-degree relatives with type 2 diabetes the risk of developing the disease is 20% to 40%, as compared with 5% in the general population.
The two metabolic defects that characterize type 2 diabetes are 1. A decreased ability of peripheral tissues to respond to insulin (insulin resistance) and 2. β-cell dysfunction manifested as inadequate insulin secretion in the face of hyperglycemia. In most cases, insulin resistance is the primary event and is followed by increasing degrees of β-cell dysfunction.

Morphology of Diabetes and Its Late Complications
The important morphologic changes are related to the many late systemic complications of diabetes and thus are likely to be found in arteries (macrovascular disease), basement membranes of small vessels (microangiopathy), kidneys
(diabetic nephropathy), retina (retinopathy), and nerves (neuropathy). These changes are seen in both type 1 and type 2 diabetes. The changes are divided into pancreatic & extrapancreatic

A. Pancreatic changes are inconstant and are more commonly associated with type 1 than with type 2 diabetes. One or more of the following alterations may be present.
1. Reduction in the number and size of islets
2. Leukocytic infiltration of the islets (insulitis) principally by T lymphocytes.
3. Amyloid replacement of islets; which is seen in advanced stages.

B. Extrapancreatic changes
1. Diabetic macrovascular disease
2. Hyaline arteriolosclerosis
3. Diabetic microangiopathy The microangiopathy underlies the development of diabetic nephropathy, retinopathy, and some forms of neuropathy.
4. Diabetic Nephropathy

Ocular Complications of Diabetes: Visual impairment up to total blindness may occur in long-standing diabetes. The ocular involvement may take the form of
a. retinopathy
b. cataract formation
c. glaucoma