Adrenal gland
2 in one endocrine organs
Cortex & medulla
Different (distinct):
embryologic, anatomic, histologic &
secretory features

Embryology
Cortex: originates from mesodermal tissue near the gonads.
Therefore, ectopic adrenocortical tissue may be found in the ovaries, cord & testes.

Adrenal medulla: ectodermal in origin - from neural cortex.
Neural crest cells - migrate to the paraaortic & paravertebral areas & towards the mediad aspect of
the developing adrenal cortex to form the medulla most extraadrenal neural tissue regresses, but
may persist at several sites.

Zuckerkandl organ: largest extra-adrenal neural tissue;
located to left of aortic bifurcation near the int. Mesenteric A(IMA) origin.
Ectopic Adrenal medullary tissue may also be found in: neck, urinary bladder & paraaortic regions

ANATOMY
The adrenal glands paired, retroperitoneal organs.
located superiorly and medially to the kidneys at the level of the eleventh ribs.
Size: 5x3x1 cm
weight: 4 to 5 g.
The right gland: pyramidal shaped and lies in close proximity to the right hemidiaphragm, liver, and
inferior vena cava.
The left adrenal: closely associated with the aorta, spleen, and tail of the pancreas.

Blood supply: Each gland is supplied by three groups of vessels:
- the super. adr. a. from the inferior phrenic artery,
- the middle adr. a. from the aorta
- the infer. adr. a. from the renal artery.
Other vessels from the intercostal & gonadal vessels may also supply the adrenals.

R. ad. Vein- short- IVC
Left Ad. Vein-longer - L renal vein

Color: cortex-yellow because of high lipid content
Medulla-reddish brown.
Cortex 80-90% . Medulla 10-20% of the gland

Histology
- Cortex - 3 layers(GFR)
A- Outer- zona glomerulosa: small cells secret aldosterone (mineralocorticoid hormone).
B- Middle layer: zona fasciculata-larger , faomy cell - glucocorticoids
C- Inner layer: zona reticularis — smaller cell - adrenal androgens
Medulla: polyhedral cells. Arranged in cords. (Chromaffin cells - stain specially with chromium salts.

Mineralocorticoids
Action
Aldosterone- ON collecting ducts of kidneys
• promote; absorption of Na & H2O
  Excretion of K & Hydrogen

Control of secretion:
1-Changes in extracellular voume via the renin-angiotensin system.
2-ACTH has a negligible role
3-increased Plasma K.
4-Decreased plasma Na

↑ Aldosterone                  ↓ Aldosterone
↑ K⁺                           ↑ Na⁺
↓ Na⁺                           Adrenalectomy
Stress

Aldosterone function(cont.)
• It helps control blood volume via renin-angiotensin system:
  • Fall in Renal perfusion → Juxta-glomerular apparatus → ↑Renin→Angiotensinogen
    →angiotensinogen I → angiotensinogen II( by ACE) →Vasoconstriction(↑ BP)
  • Adrenal cortex(↑ aldosterone)→Kidney tubules& sweat glands) → ↑ Na⁺ ,Cl⁻, H2O
    reabsorption→ ↑ plasma osmotic pressure→ ↑ADH →Blood volume

Action of angiotensin II:
1- arterial & venous vasoconstriction.
2- ↑ Aldosterone
3- ↑ADH
4- ↑ thirst

Hyperaldosteronism
Aldosterone excess.
I⁰ or 2⁰
2⁰ Hyperaldosteronism-
causes :1- CHF(congestive heart failure
  2- liver cirrhosis
Similar features to I⁰ Hyperaldosteronism except renin & angiotensin are ↑d & edema is a feature

I⁰ Hyperaldosteronism(PHA)
Aldosterone producing
Adenoma( Conn’s syndrome)- most common
Bilat .Hperplasia -2 subtypes- micronodular-20-40 %
    macronodular —rare

Adenoca-rare

PHA
• Def. HT+ hypokalemia + Hypersecretion of aldosterone
• Hypokalemic PHA- --2% of HT
• Normokalemic PHA----12% of HT
• Presentations:
  • Age :30-50 y
  • Sex : F > M
  • HT
  • M. weakness, headaches, polydipsia, pokyuria& nocturia.
  • Dx: raised plasma aldosterone+ suppressed plasma renin+ ↓S.K
• Localization of lesion: CT scan, MRI locate adenoma(usually <1 cm)
- Rx preoperative preparation (with spironolactone + K supplementation)
- + removal of affected adrenal gland.

**Cushing’s syndrome**
- Def. clinical syndrome produced by excess circulating glucocorticoid.
- Can occur due to excess:
  - B - Glucocorticoid alone

**Causes:**
- I- ACTH- dependent : 85%
  - 1- pituitary lesions- adenoma
  - 2- ACTH producing tumors (e.g. Oat cell Ca. of lung)
- II- ACTH-independent 15%
  - 1- steroid administration
  - 2- Adrenal Ca. or adenoma

**Clinical features of Cushing’s syndrome**
- 1- Truncal obesity
- 2- Skin changes: facial plethora. Acne, striae. Hirsute (hair growth), easy bruising.
- 3- HT
- 4- edema
- 5- DM
- 6- M. weakness
- 7- CNS- Psychosis. depression/mania
- 8- Menstrual changes- irregularity/ impotence
- 9- Osteoporosis
- 10- hypokalemia

**Dx**
- 24-h urinary free cortisol ↑ in Cushing’s syndrome
- Overnight dexamethasone suppression test:
  - in non-affected patient, 2mg dexamethasone given at midnight will reduce the morning plasma cortisol level, but is not reduced in Cushing’s syndrome.
  - Morning & evening plasma cortisol measurement: a loss of the circadian variation.

**Investigations of the cause of Cushing’s syndrome**
1- Plasma ACTH level
2- Adrenal CT scan
3- Pituitary CT scan
4- CXR- for ACTH producing bronchogenic Ca.

**Rx**
Treat the cause
• **Pituitary:**
  1- Trans-sphenoidal excision of pituitary adenoma.
  2- Ext. irradiation (can take years to work)
  3- Yttrium irradiation

**Adrenal:**
1- Resection of adenomas & carcinomas.
2- Bilateral adrenalectomy: indications;
   a- When other measures have failed.
   b- ACTH producing tumor is not found.
   c- Severe Cushing’s syndrome requiring rapid Rx.
   d- bilateral adrenal nodular hyperplasia.

**Adrenocortical Insufficiency (Addison’s disease)**
- **Causes:**
  1- Bilat. Adrenalectomy
  2- Infection (e.g. T.B, Histoplasmosis)
  3- Metastatic deposits within the adrenal glands.
  4- Amyloidosis.
  5- Sudden cessation of steroid therapy.
  6- Sarcoïdosis
  7- Meningococcal septicemia -> bilat. Adrenal infarction (named; Waterhouse-Friderichsen syndrome. rapidly fatal unless immediately treated
  8- Autoimmune disease
  9- HIV infection
  10- Haemorrhage

**Presentations**
- Acute ad.insufficiency:
  - Shock+ Fever + nausea, vomiting, abdominal pain, hypoglycemia & electrolyte disturbance.
  - DDX- Acute abdomen
- Chronic ad insufficiency:
  - Postural hypotension + pigmentation of the buccal mucosa & skin.
  - Other symptoms: weakness, loss of body hair, drowsiness, confusion & coma.
  - Hyponatremia, Hyperkalemia, hypoglycemia – commonly found

**Dx**
- Basal ACTH level: high + low cortisol level
- ACTH stimulation test (short Synachthen test)- which does not raise the plasma cortisol level in affected patients

**Mx**
- Patients with acute hypotension: iv fluid (3L N/S /6h+ 100mg hydrocortisone qds.
- Long-term replacement therapy: hydrocortisone 20mg morning + 10mg in the evening + fludrocortisone (0.1mg)
- Surgical patients- who usually take steroids long-term: must be given hydrocortisone 100mg with their premedication & thereafter 6hourly until they are able to resume their normal dose of hydrocortisone

**Congenital adrenal hyperplasia**
Virilization & adrenal insufficiency in children are pathognomonic.
Autosomal recessive disorder.
Variety of enzymatic defects in the synthesis pathway of cortisol & other steroids. Most freq. 95% is 21-hydroxylase deficiency.
Loss of cortisol -> excessive ACTH -> increases androgen secretion
So; reduced cortisol & aldosterone levels whilst androgens are increased
Dx radioimmunoassay (RIA) of 17-hydroxyprogesterone, which shows elevated levels
Rx—Replacement therapy with Hydrocortisone + mineralocorticoid (fludrocortisone)

**Pheochromocytoma (PCC)**
- Tumor of adrenal medulla, arising from chromaffin cells.
- 0.1-0.6% of HT caused by it.
- 0.05% in autopsy
- Known as 10% tumor because 10% are:
  - Malignant
  - Bilateral
  - Familial
  - Extraadrenal

Extraadrenal sites include: Neck, thorax, Kid, Bladder & sacrum.
Can occur alone or as apart of genetic conditions:
  - Von Hippel-Lindau (VHL) syndrome (Early onset bilateral. Renal tumors + PCC + cerebellar & spinal hemangiomas & pancreatic tumors),
  - Neurofibromatosis (NF) type 1: PCC + fibromas on the skin & mucosa + Café–au-lait skin spots
  - multiple endocrine neoplasia (MEN) type I & II

**Clinical features**
- Excess plasma levels of catecholamines:...
- Hypertension: sustained or intermittent
  - Hyperglycemia.
- Psychological effects. angina. Stroke
- Pathology: soft, vascular tumors with areas of haemorrhage & necrosis.

**Dx & Mx**
- **Dx—** 24-h urinary of catecholamines & VMA (vanillylmandelic acid) measurement shows an elevated result
- CT and MRI are used to localize the tumour once the diagnosis of phaeochromocytoma is made
- **Mx**
- Treatment of choice is adrenalectomy, except in those with metastatic disease or who are unfit for surgery. However, patients must be thoroughly prepared prior to surgery due to potentially fatal changes in CVS which can be occur under anaesthesia and whilst handing the tumour.

**Adrenalectomy for pheochromocytoma**
**Open methods**
**Approaches—** bilat subcostal, transverse epigastric or lumber incisions
**laparoscopic—** intra-abdominal
Preoperative preparation:
- α and β adrenergic blockade (phenoxybenzamine + propranolol)
- α blockade start at least 1 week before surgery, whereas propranolol is started 4 days preoperatively.
- IVU demonstrates the function of the kidneys in case of unavoidable nephrectomy.
Per-operatively:
- Tempered handling of tumor is required to minimize changes in BP.
- Nitroprusside is used iv to control BP intra-operatively.
- Removal of the tumor often precipitates hypotension & is managed with fluids, blood & dopamine.

Incidentaloma
Clinically unapparent mass detected incidentally by imaging studies conducted for other reason
- Incidence:
  - At autopsy - 1.4 - 8.7% (increases with age)
  - 75% are non-functioning adenomas
  - There may be: Cushing’s adenoma, PCC or adrenocortical carcinomas.
- Once incidentaloma diagnosed: answer 2 questions:
  - Functioning adenoma or malignant adrenal tumor is present.
  - Hormonal assessment:
    - 1 mg overnight dexamethasone suppression test
    - 24-h urinary cortisol excretion
    - 24-h urinary excretion of catecholamines, metanephrines, or plasma free metanephrines
    - S.K.plasma aldosterone & plasma renin activity
    - Serum DHEAS (DeHydroEpiAndrosterone-adrenal androgen), testosterone, or 17β-OH estradiol (virilizing or feminizing tumors

Evaluation of malignancy in incidentaloma
- CT scan
- MRI
  - If PCC excluded—Do FNA
  - The likelihood of Ca increases with size (25% malig. If > 4 cm)

Rx
1- Functional adrenal tumors – accordingly
2-Non-functioning tumors:
  A- Size & malignancy
    size > 4 cm or smaller but malignant—surgery
  B-< 4 cm no malig... follow up after 6, 12, 24 months by imaging & hormonal evaluation