L4: Adrenal Gland

Surgery Team
MED 433

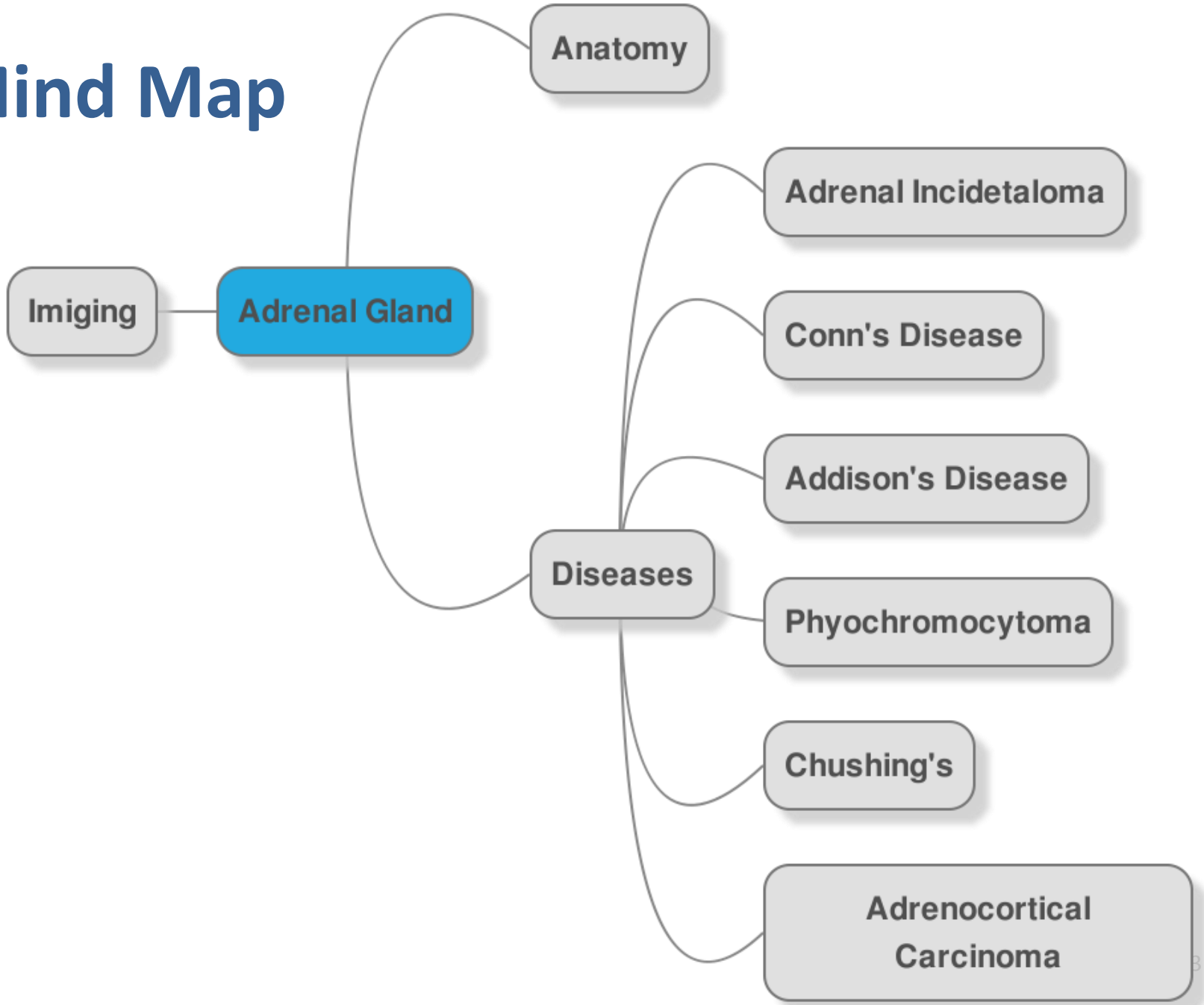
MED 433

Objectives :

Color Index: Slides & Raslan's () | Doctor's Notes | Extra Explanation | Additional

This work is based on doctor's Slides +Notes and Raslan's only (Does not include the book)

Mind Map


Anatomy
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Conn's Disease
Addison's Disease
Diseases
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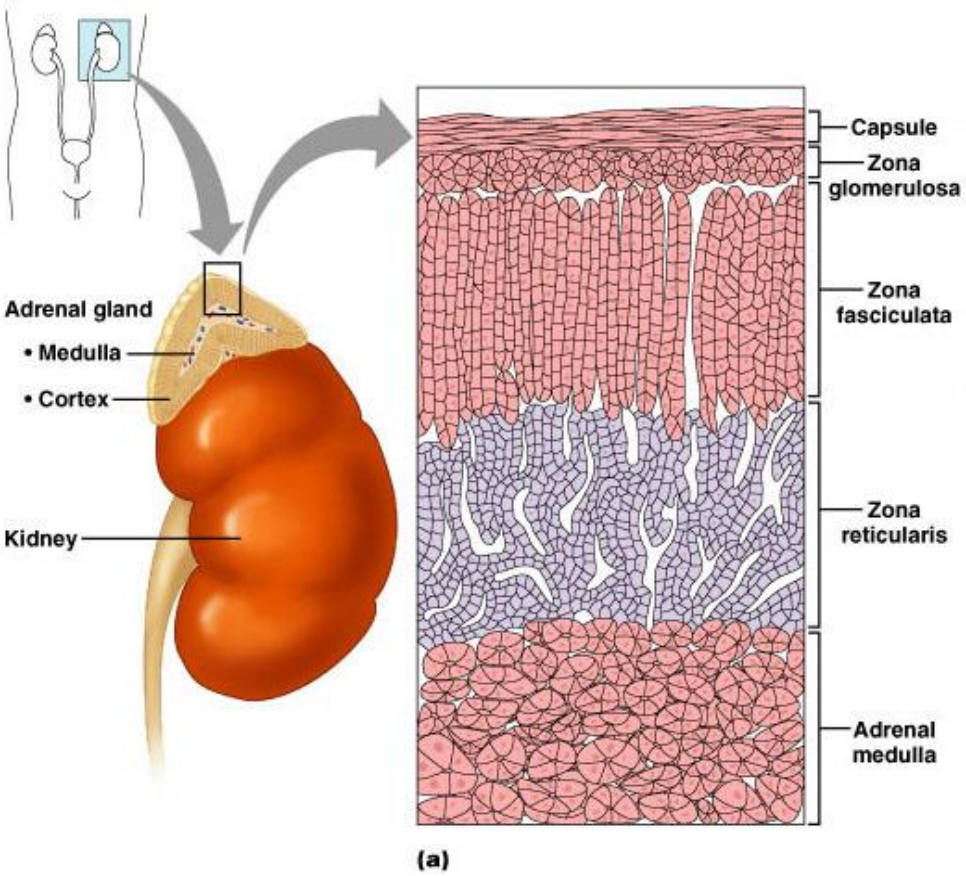
Adrenocortical Carcinoma

Adrenal Gland



- Can not be palpated normally; if it was palpable, it's most likely cancer.

- Each gland has 3 arteries and one vein. Arteries comes from:
  - Inferior phrenic : superior suprarenal artery
  - Abdominal aorta : middle suprarenal artery
  - Renal artery : inferior suprarenal artery

Zona glomerulosa →Mineralocorticoids (Aldosterone)
Zona fasciculata →Glucocorticoids (Cortisole)
Zona reticularis →Androgens
Medulla → 20% norepinephrine, 80% epinephrine

The adrenals are located deeply (retroperitoneal organs), which makes it difficult to remove them.
One approach: from the back below 12th rib, enter fascia surrounding adrenal gland > not applicable to all adrenals e.g. big adrenals

Adrenal Gland Imaging

CT Scan (The gold standard)

To differentiate between benign and malignant

❖ Benign

- Intensity, texture similar to liver
- Low attenuation
- Homogeneous
- Smooth border , Smooth contour
- < 4 cm in greatest dimension (the first criteria to be checked and then the others, size should be less than 4)

❖ Malignant

- High attenuation (>30 HU)
- Heterogeneous
- Irregular borders
- Local/ vascular invasion
- Lymphadenopathy
- Metastases.
- Large size (>6cm)

Tissue biopsy will give you a definite diagnosis (if it's a benign or malignant mass)

MRI

CT still gold standard but if MRI is available, it'll give a better picture

Nuclear Scan

If you suspect pheochromocytoma, to look at the function of the mass and to see the uptake of the gland

PET Scan

If you are looking for cancer > hot spots

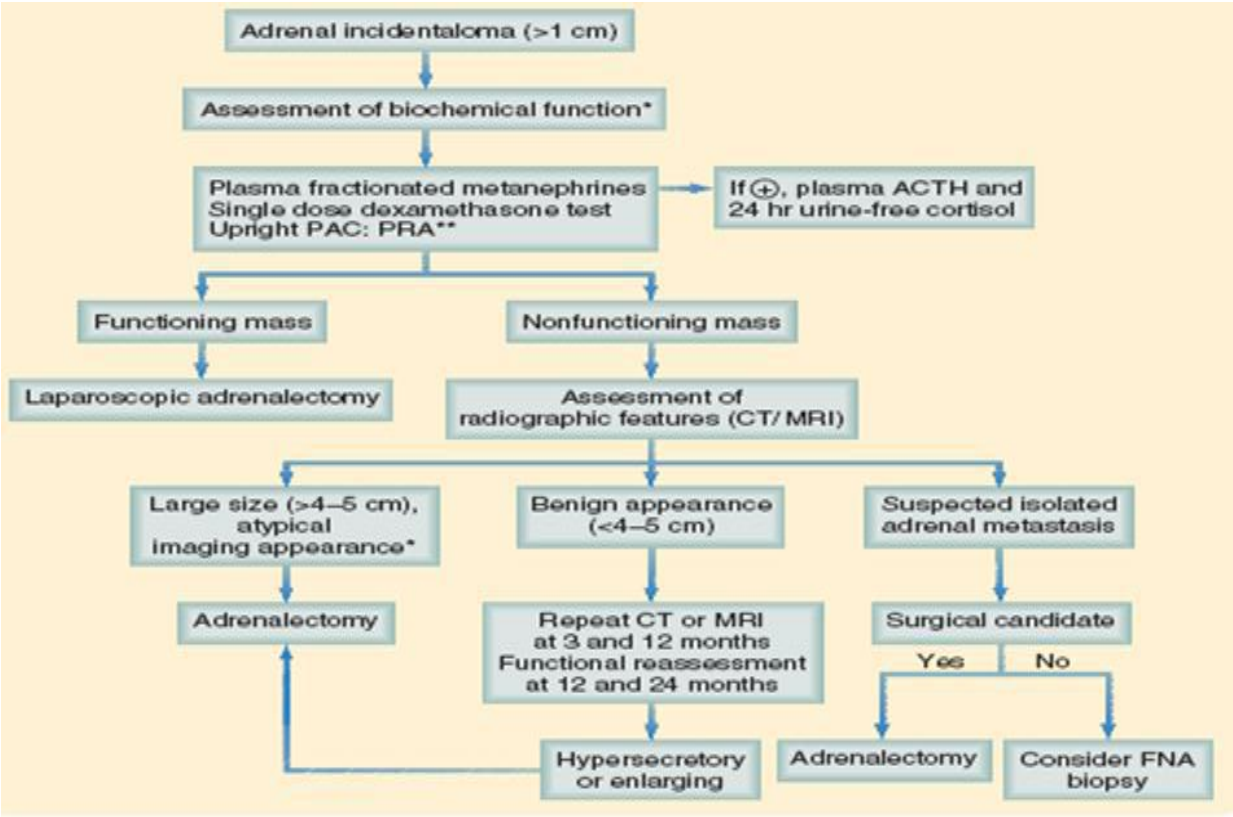
ADRENAL INCIDENTALOMA

- Found in 1-4 % of CT scans.
- Coincidently discovered by radiologic examinations
- Incidence increases with age

Causes

- **Small nonfunctioning adrenal tumors: MOST COMMON (>80%)**
- Subclinical Cushing 5%
- Pheochromocytoma: if functioning, you should interfere regardless of size 5%
- Adrenocortical cancer 5%
- Metastatic carcinoma 2%
- Conn's

Clinical pathway:



*Functioning mass (Surgery), if Not (CT scan)

CT may show:
- Benign appearance (< 4 cm) repeat after 3-12 months.
- If it secretes or has a malignant appearance (surgery).
- Handled based on the Size and function.

HYPERALDOSTERONISM
"Conn's Syndrome"

Causes:

1-Primary hypertension + metabolic alkalosis + with or without hypokalemia

→ primary hyperaldosteronism:

a. Adenoma (Most common)
b. Idiopathic bilateral adrenal hyperplasia.
c. Unilateral adrenal hyperplasia.
d. Adrenocortical carcinoma.
e. Familial (rare)

2-Secondary to any decrease in renal perfusion which causes secondary Hyperaldosteronism:

a. Renal artery stenosis
b. CHF (congestive heart failure)
c. Liver cirrhosis
d. Pregnancy
e. Primary hyperaldosteronism

High aldosterone

Aldosteron effects: Na retention, and K+ & H+ loss

- Na and water retention → ECF volume expansion & HTN
- Hypokalemia → myopathy; muscle weakness
- Acid excretion (H+ secretion from tubules) → metabolic alkalosis

Renin angiotensin system controls aldosterone secretion:

- Renal stenosis → ↓ blood flow to kidney → juxtaglomerular apparatus senses decreased flow (decreased volume) → retain Na+ and water → ECF expansion

So, anything that causes a decrease in renal perfusion can cause secondary hyperaldosteronism

PRIMARY HYPERALDOSTERONISM

It is the excessive production of aldosterone by the adrenal glands independent of any regulation by the renin-angiotensin system.

- Age 30-50 years (middle age group).
- Female > male, 2:1 (females usually more prone to endocrine diseases and cancers).
- Prevalence 5-13%.

Clinical features:

1- **Fatigue** (due to decrease level of K+)
2- **Hypertension** with or without hupokalemia.
3- Weakness, polyuria, parasthesias, tetany, cramps
4- **Metabolic alkalosis**, relative hypernatremia
5- **Elevated aldosterone secretion and suppressed plasma renin activity** (b\c of aldosterone hypersecretion)
6- Usually no edema

Check the level of renin which is increased in secondary hyperaldosteronism and undetectable in the primary disease.

Diagnosis :

A. Screening tests:

1. Plasma Aldosteron Consentration (PAC) / Plasma Renin Activity (PRA) >20 ng/ml
2. Plasma aldosterone > 15 ng/dl **(could mean it's Conn's)**

B. Confirmatory tests:

1. Sodium suppression test (to differentiate between primary & secondary)
2. Urinary aldosterone excretion >14 ug/ 24hr.

C. Others

- Increae urinary K
- CT scan looking for the adenoma **(failure to see an adenoma means there is no tumor and could be Bilateral Adrenal Hyperplasia)**

Treatment and Management:

1. Pre-OP:

A. Stabilize hormonally
B. Correct fluid and electrolytes **(spironolactone)**
C. Cortisol PM before surgery, AM of surgery and during OR.

2. Surgery .

A. **Laparoscopic adrenalectomy**.
B. Open surgery

2. Post-OP. (should give:)

IV cortisol for 24 hours.
IM cortisol 2nd day.
Oral cortisol 3rd day.

Poor wound healing.
If unilateral- steroids weaned, other adrenal takes over 6-12 months.

3. Medical treatment (if surgery is not possible) due to:

A. Unfit patients.
B. Bilateral gland pathology (Bilateral adenoma or hyperplasia)

Prognosis

A. 1/3 of patients will have persistent hypertension
B. K+ levels will be restored (Normal daily activity is restored).

- Some medication induce aldosteronism → stop them and then start screening and confirmatory tests
- If you confirm hyperaldosteronism → do CT
- Venous sampling: catheters all the way to IVC from right & left side → see the gradient
- Lateralization (hormones higher in right than left) → this is the diseased gland → right adrenalectomy
- If no gradient → give medical treatment because you can't take out both adrenals, otherwise you have to replace adrenal hormones i.e. glucocorticoids and mineralocorticoids

- Due to adenoma: 1st correct the hypokalemia (spironolactone) then remove the adenoma.
- Due adrenal hyperplasia (bilateral adrenalectomy)

ADDISON'S DISEASE
"ADRENAL INSUFFICIENCY"

This disease is associated with decrease levels of :
1- glucocorticoids 2- mineralocorticoids 3- androgens.

Etiology of Addison's disease :

1-Idiopathic atrophy:

Autoimmune Antibodies attack adrenal cortex, 90% of tissue are destroyed.

2-TB/fungal infections (histoplasmosis)
3-Iatrogenic causes :adrenalectomy, chemotherapy, anticoagulant therapy.

Signs and symptoms :

1-fatigue, weight loss, anorexia (↓ cortisol)
2-Changes in skin pigment (small black freckles) because of the decreased cortisol which increase ACTH & MSH
3-muscular weakness .
4-fluid and electrolytes imbalance . (hyponatremia,hyperkalemia,hypoglycemia)
5-hais loss , sexual dysfunction and mental illness (anxiety, irritability) (↓ Androgens)
6-salt craving .

Diagnosis :

1-decrease serum cortisol
2-decrease urinary 17-OHCS and 17 KS
3-decrease Na 4-increae K
5-decrease serum glucose .

Interventions:

- **Life long hormone replacement**
- Change dose for stress
- Also need mineralocorticoid-(FLORINEF)
- Do not fast or ignore meals ☺
- Eat between meals and snack.
- Eat diet high in carbs and proteins.

- Wear medic-alert bracelet with Kit of 100mg hydrocortisone IM in you pocket **(take it or people give you during adrenal crisis)**
- Keep parenteral glucocorticoids at home for injection during illness.
- Avoid infections/stress.

Complications:

1. Adrenal crisis.
2. Electrolyte imbalance.
3. Hypoglycemia.

PHEOCHROMOCYTOMA

Rare, benign tumor of the adrenal medulla.

Epidemiology:

- Less than <0.1% of patients with hypertension, and not common in our community.
- Most occur sporadically (no genetic predisposition) .
- Associated with familial syndromes, such as:
- Multiple endocrine neoplasia type2 (MEN2A) 40% and MEN 2B
  - Reckling-hausen disease
  - Neurofibromatosis type I
  - Von-Hippel-Lindau disease

  90% of patients with pheochromocytoma are hypertensive (Once you diagnose the patient for the first time with HTN you HAVE to perform an US to the abdomen)
- Hypertension is less common in children
- In children, 50% of patients have multiple (bilateral) or extra-adrenal tumors.

If you suspect pheochromocytoma, you must admit the patient and deal with him very carefully. Patient could die from very high BP.

Rule of 10s:

- 10% malignant
- 10% familial
- 10% bilateral
- 10% multiple tumors
- 10% extra-adrenal

("all places including head and neck" but the commonest is the abdomen, that's why we have to do US for the abdomen).

PHEOCHROMOCYTOMA

Signs and symptoms:

Clinical findings are variable:

- **Episodic or sustained hypertension (hallmark)**

(Triad of palpitation, headache, and diaphoresis)

- Anxiety, tremors and weight loss.
- Dizziness, nausea, and vomiting
- Abdominal discomfort, constipation, diarrhea, Visual blurring.
- Tachycardia, postural hypotension.
- Hypertensive retinopathy (in short period of HTN history, few years only!).
- NE and Epinepherine released sporadically.
- Elevated urinary catecholamines or their metabolites, hyper-metabolism,
- hyperglycemia

Some patients can present with septic shock, if you can't explain it → suspect pheochromocytoma.

Diagnosis:

- 24 hour urine of metaniphrine s and VMA "vanillylmandelic acid" (metabolite of Epinepherine). ***Initial test***
- CT to locate tumor ***Best test***

Characteristic bright appearance on T2-weighted MRI.

- History and physical exam.
- Hyperglycemia (and they cannot maintain fasting; they become hypoglycemic –"we can differentiate it from Cushing").
- Asymmetric uptake on MIBG nuclear scan:
  - Particularly useful for extra-adrenal, multiple, or malignant pheochromocytoma
  - Not useful for sporadic biochemical syndrome with unilateral mass

Rule out other causes of hypertension ,Hyperthyroidism , Anxiety disorder and Carcinoid syndrome.

PHEOCHROMOCYTOMA

Interventions :

A. Pre-Operative:

1- **Alpha-Blocking** agent (Minipress "Prazosin") to decrease BP. (at least 2 weeks before the surgery)
2- **Beta-Blocking** agents to decrease BP & force of contraction
3- Diet which is high in vitamins, minerals, calories, no caffeine
4- Sedatives .

B. During Surgery:

Give REGITINE (Phentolamine, which is irreversible alpha-blocker) and NIPRIDE (Sodium Nitroprusside, Relaxes vascular smooth muscle by producing nitric oxide) to prevent hypertensive crisis.

C. Post-Operative:

- BP may be increased initially, but can decreased severely.
- Volume expanders.
- Vasopressors.
- Hourly input and output measurement.
- Observe for hemorrhage **(Any patient with low post-operative BP, always suspect hemorrhage)**

Considerations:

- Avoid arteriography or fine-needle aspiration as they can precipitate a hypertensive crisis
- Early recognition during **pregnancy is important because if left untreated,** half of fetuses and nearly half of the mothers will die.
- Patients with pheochromocytoma usually die of high blood pressure, as the adrenal gland itself is very sensitive if it was to be touched in surgery and there will be a surge of secretions, which leads to a severe increase in blood pressure leading to a BP of 250 leading to intracranial hemorrhage! then Death!

- **All pheochromocytoma should be excised.**
- **Contraindications to surgery:**
  - **Metastatic disease (because we cannot control it)**
  - **Without proper α- blockade surgery is contraindicated**

Cushing's Syndrome

- **Increase secretion of cortisol.**
- 4 times more frequent in females, usually Occurs at 35-50 y.o
- And we should differentiate between Cushing's syndrome and Cushing's disease:
    1. **Cushing's syndrome:** Term used to describe a group of symptoms that occur when a persons' cortisol levels are too high
    2. **Cushing's disease:** When Cushing's syndrome is secondary to pituitary adenoma (with ↑ secretion of ACTH)

Etiology

- **Primary:** tumor on the adrenal cortex
- **Secondary:** tumor on the anterior pituitary gland (Cushing's disease)
- Ectopic ACTH secreting tumor (lung, pancreas)
- **Iatrogenic:** Steroid administration

Signs & Symptoms

Increase Protein Catabolism

- Muscle Wasting,
- Poor Wound Healing
- Loss of collagen support (thin, fragile skin, bruises easily)

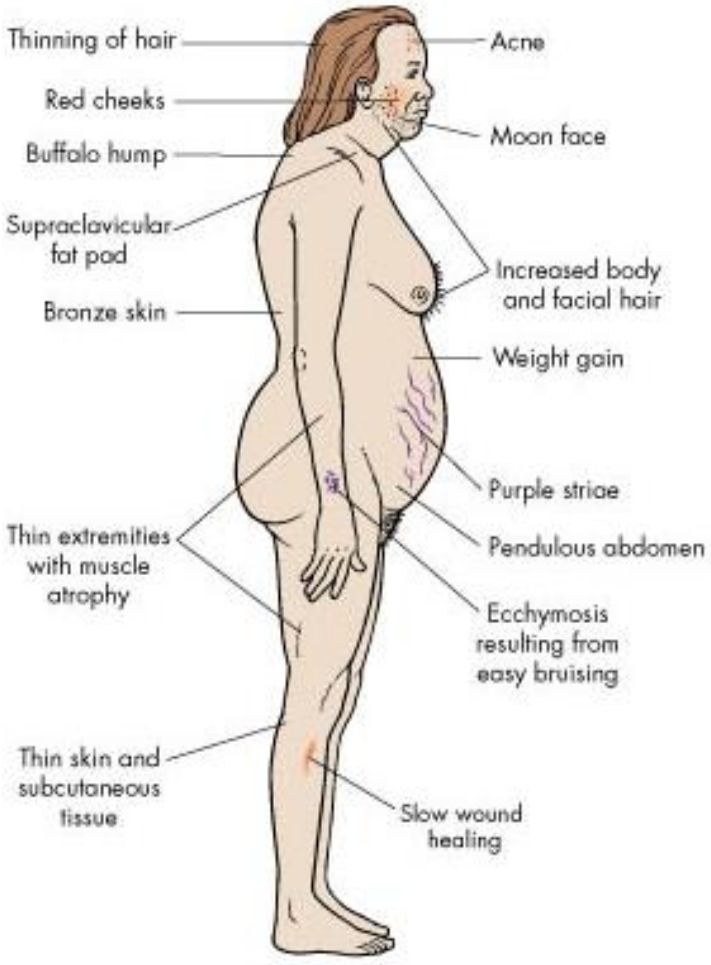
Increase CHO Metabolism

- Hyperglycemia (Can cause Diabetes)
- Polyuria

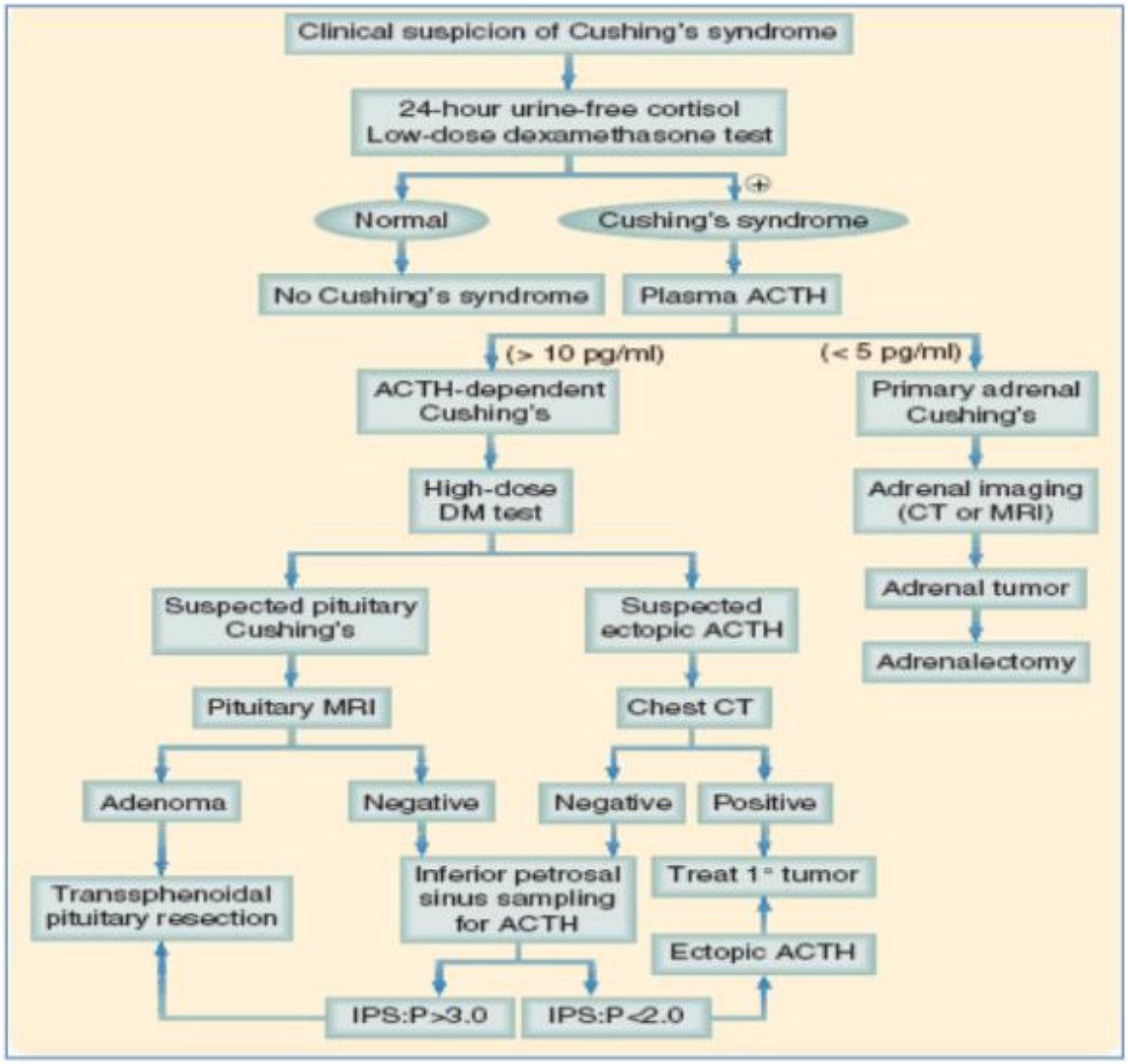
Increase Androgen Secretion

- Excessive hair growth, receding hairline.
- Acne, Change in Voice

Signs & Symptoms



Clinical Pathway



Adrenocortical Carcinoma

Essential features:

❖ Variety of clinical symptoms through excess production of adrenal hormones.
❖ Complete surgical removal of the primary lesion and any respectable metastatic sites has been the mainstay of treatment.

Epidemiology:

❖ These tumors are rare; (1—2 cases per million persons in the US)
❖ Bimodal occurrence **"in the very young and the very old“,** with tumors developing in children < 5 years of age and in adults in their fifth through seventh decades of life.
❖ Male to female ratio is 2:1, with functional tumors being more common in women
❖ **Left adrenal involved slightly more often than the right (53% vs. 47%);** bilateral tumors are rare (2%).
❖ 50—60% of patients have symptoms related to hypersecretion of hormones (most commonly Cushing's syndrome and virilization).
❖ Feminizing and purely aldosterone-secreting carcinomas are rare.
❖ **50% of patients have metastases at the time of diagnosis**
❖ It is very difficult to diagnose, because the symptoms appear when it is too late (*like pancreatic cancer).*

Signs & symptoms:

❖ Symptoms of specific hormone excess (e.g. cortisol excess, virilization, hypertension)
❖ Palpable abdominal mass **"because the mass is very big"**
❖ Abdominal pain
❖ Fatigue, weight loss, fever, hematuria

Adrenocortical Carcinoma

Lab findings:

All laboratory abnormalities depend on hormonal status of tumor

- Elevated urinary free cortisol or steroid precursors
- Loss of normal circadian rhythm for serum cortisol
- Low serum adrenocorticotropic hormone (ACTH)
- Abnormal dexamethasone suppression test
- Elevated serum testosterone, estradiol, or aldosterone levels

- Right sided surgeries are always more difficult than left sided ones; because the right tumors go to the IVC directly, creating big thrombi and that makes the surgery more difficult **(so you have to restrict part of IVC then remove the thrombus then anastomose it again)**
- All tissues involved should be removed, such as part of kidney or part of liver or maybe lymph nodes.

Imaging:

- Evaluation of adrenal glands with **CT** or MRI (adrenocortical carcinomas are typically iso-dense to liver on T1-weighted MRI, and hyper-dense relative to liver on T2-weighted MRI images).

MRI more accurately gauges the extent of any intracaval tumor thrombus.

Considerations:

- Mean diameter of adrenal carcinoma at diagnosis is 12 cm (black size 6cm to 12cm is malignant (remove it). black size 2cm to 4cm is cyst)
- Radiographic evaluation of suspected metastatic sites for purposes of staging should be considered prior to thought of any surgery.
- **We should rule out: Pheochromocytoma.**

Summary

From the Textbook :

Management of adrenal pathologies

- Hyperfunctioning benign adrenal masses should be removed surgically (phaeochromocytoma, cortisol secreting adenomas and Conn's syndrome). The laparoscopic approach is the preferred one
- Careful preoperative assessment to exclude multiple hormone secretions from a single or bilateral adrenal masses must be undertaken (e.g. a phaeochromocytoma that is also secreting cortisol)
- In primary hyperaldosteronism (Conn's syndrome) preoperative selective venous sampling from both adrenals should be considered to confirm the site of maximal secretion. It can be misleading to assume this will be the side with the mass lesion in it
- Incidentally found adrenal masses must be investigated for possible hypersecretion of all adrenal hormones prior to their removal or a decision to leave them in situ and follow up.
- Have a low threshold to remove non-functioning incidentalomas > 3.5 cm in size, as the incidence of adrenocortical carcinomas increases significantly above this size
- Only biopsy an adrenal mass if you think it is due to a metastasis from a previous known malignancy. Always exclude a phaeochromocytoma before biopsy of any adrenal mass.

Notes from the doctor:

- **Any adrenal mass, ask yourself:**
  1. **Is it functional or not?**
  2. **Is it malignant ?**
  3. **Is it pheochromocytoma?**

- **Secondary masses in adrenal, Look for primary tumor in:**
  Kidney, Lung, Breast, Melanoma

MCQs

Q1: A 30-year-old pregnant women complains of headaches, restlessness, sweating, and tachycardia. She is 18 wk pregnant and her blood pressure is 200/120 mm Hg. Appropriate workup might include:

a) Exploratory laparotomy
b) Mesenteric angiography
c) Head CT scan
d) Abdominal CT scan
e) Abdominal ultrasonogram

Q2: The most likely diagnosis in a patient with hypertension, hypokalemia, and a 7 cm suprarenal mass is:

a) Hypernephroma
b) Cushing's disease
c) Adrenocortical carcinoma
d) Pheochromocytoma
e) Carcinoid

Q3: A 49-year-old obese man has become irritable, his face has changed to a round configuration, he has developed purplish lines on his flanks, and he is hypertensive. A 24-hour urine collection demonstrates elevated cortisol levels. This is confirmed with bedtime cortisol measurements of 700 ng/mL. Which of the following findings is most consistent with the diagnosis of Cushing disease?

a) Decreased ACTH levels
b) Glucocorticoid use for the treatment of inflammatory disorders
c.) A 3-cm adrenal mass on computed tomography (CT) scan
d. Suppression with high-dose dexamethasone suppression testing
e.) A 1-cm bronchogenic mass on magnetic resonance imaging (MRI)

Q4: A 34-year-old woman presents with hypertension, generalized weakness, and polyuria. Her electrolyte panel is significant for hypokalemia. Which of the following is the best initial test given her presentation and laboratory findings?

a) Plasma renin activity and plasma aldosterone concentration
b) Urine electrolytes
c) Plasma cortisol level
d) Overnight low-dose dexamethasone suppression test
e) Twenty-four-hour urinary aldosterone level

Ans: Q1:e , Q2:c , Q3:d , Q4:a

Cushing disease is cortisol excess caused by an ACTH-hypersecreting pituitary adenoma. In these patients the ACTH level is normal or elevated and cortisol is suppressed with administration of high-dose dexamethasone

Thank You..

Done By :
Abdulaziz Al-Sudairi
Fahad Al-Qahtani

Revised By:
Faisal S. AlGhamdi

surgery433@gmail.com