Adrenal Glands

429 Surgery Team

Sources: Dr.Areej A. Bokhari & Dr. Abdulaziz Al Saif's lecture

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Team notes are in blue & gray and in boxes

Pages 2-3 are an introduction

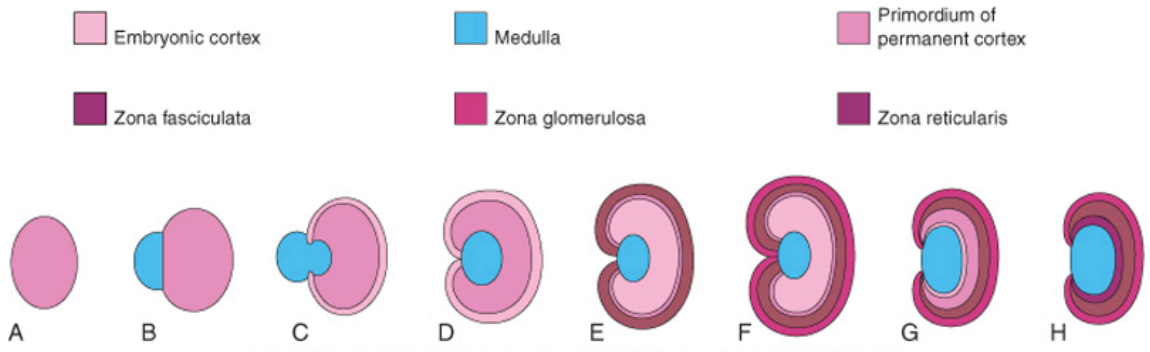
Questions: http://ask.fm/TeamNotes429

ADRENAL GLANDS

INTRODUCTION

- 1563: anatomy
- 1855: Addison described clinical features of the syndrome named after him (primary adrenal insufficiency)
- 1912: Cushing described hyper-cortisolism [Cushing's disease vs. syndrome: Disease problem in pituitary but syndrome anything else apart from pituitary]
- 1934: the role of adrenal tumors in hypercortisolism understood
- 1955: pheochromocytoma was first described by Frankel (before that all patients with this disease died b/c of crisis and there was no treatment)

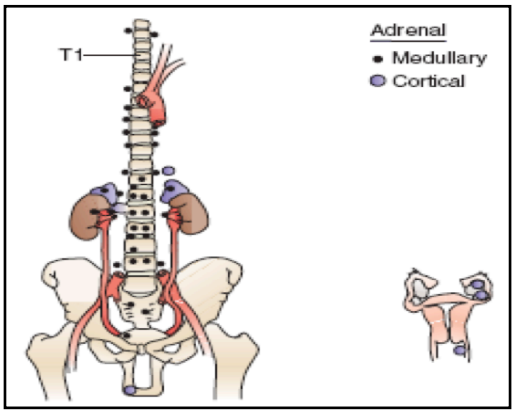
EMBRYOLOGY



Schematic drawings illustrating development of the suprarenal glands. **A,** At 6 weeks, showing the mesodermal primordium of the fetal cortex. **B,** At 7 weeks, showing the addition of neural crest cells. **C,** At 8 weeks, showing the fetal cortex and the early permanent cortex beginning to encapsulate the medulla. **D** and **E,** Later stages of encapsulation of the medulla by the cortex. **F,** Newborn infant showing the fetal cortex and two zones of the permanent cortex. **G,** At 1 year, the fetal cortex has almost disappeared. **H,** At 4 years, showing the adult pattern of cortical zones. Note that the fetal cortex has disappeared and that the gland is much smaller than it was at birth (**F**).

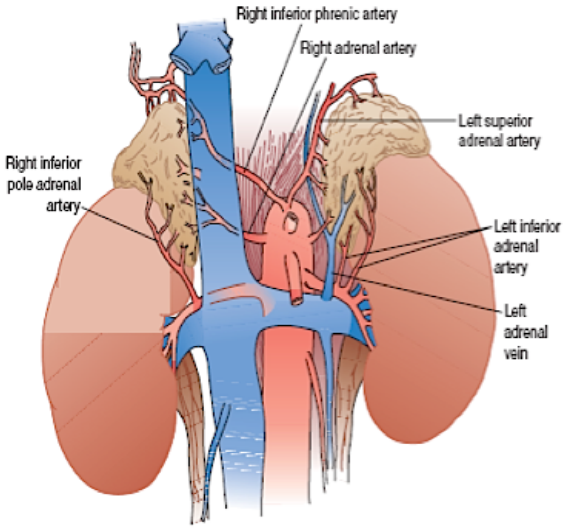
- Paired gland (almost as big as dates)
- Cortex (coelomic epithelium)
  - **Outermost layer: Zona glomerulosa** ➔ Mineralocorticoids
  - **Zona fasciculata** ➔ Glucocorticoids
  - **Innermost layer: Zona reticularis** (3rd year) ➔ Sex hormones
    - Start producing hormone during childhood but v. low levels > not enough to differentiate b/w male and female, but between the ages of 10-12 it starts functioning, finally at the age of 13 differences appear
- Medulla (ectoderm: neural crest)
  - Medulla: secrete 20% nor epinephrine, and 80% epinephrine
- Ectopic tissues: spread in neck & torso (chest, abdomen & pelvis)

- They are located deeply (retroperitoneum), which makes it difficult to remove them
- One approach: from back below 12th rib, enter fascia surrounding adrenal > not applicable to all adrenals e.g. big adrenals & difficult to learn



ANATOMY

- Differences b/w Lt. and Rt. adrenal:
  - Lt has a long vein and drain to renal vein but
  - Rt. everything goes to major vessels and if pulled, it may injure the IVC directly!
  - If you want to sample?
    - Rt.: take from **Rt. adrenal** vein
    - Lt.: take from **Lt. renal** vein
  - Blood supply relative to its size and weight: it has the highest blood supply
- 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



- **The Adrenal glands are:**

Small in size and surrounded by major blood vessels as following: any tear causes a huge hemorrhage

- IVC around the right gland
- Renal vein around the left gland

- **In adrenalectomy:**

- Half of the operation is exposure; to remove all tissues around adrenal, especially in pheochromocytoma you don't touch adrenal b/c it leads to huge secretion> severe shooting of hypertension
- Right side work on liver: cut coronary ligament, triangular ligament, and retract liver> so it's easier on this side b/c you just push the liver up
- Left side: Retract spleen, splenic flexure until you reach left adrenal
- The rest of operation tie the artery that supplies the gland, tie the vein which drains the gland and pick it up
- So with all these structures surrounding the glands, the operation is difficult and dangerous

PHYSIOLOGY

- Adrenal cortex
  - Aldosterone
  - Cortisol
  - Sex steroids
- Adrenal medulla:
  - Noradrenaline (20%)
  - Adrenaline (80%)

The precursor for all these hormone is cholesterol and in each layer there is an enzyme converting it to the appropriate hormone & there is a limiting step > once a disease affects it, it leads to over-secretion in one way and problem in the other way.

HORMONAL PATHWAY

[Don't memories the pathway (slides 9 & 10)]

- Addison's: absence of cholesterol side chain cleaving enzyme
- 17a-hydroxylase deficiency: no sex hormones – instead: overproduction of aldosterone

ADRENAL IMAGING

1. CT scan: to differentiate between benign and malignant
    - Benign
        - Intensity, texture similar to liver
        - Low attenuation
        - Homogeneous one color, there is no hypo & hyper density at the same time
        - Smooth border
        - Smooth contour
        - < 4 cm in greatest dimension first we look for size then to other criteria
    - Malignant lesions:
        - High attenuation (>30 HU) [hyper-vascular – more white]
        - Heterogeneous
        - Irregular borders
        - Local/ vascular invasion
        - Lymphadenopathy
        - Metastases.
        - Large size (>6cm) [Indicate malignancy irrespective]
2. MRI. (CT still gold standard if MRI available it'll give a better picture)
3. Nuclear scan. (If you suspect pheochromocytoma - to look at the function of the mass > see uptake of gland)
4. PET scan. (If you are looking for cancer > hot spots)

Tissue biopsy will give a definite diagnosis (if it benign or malignant mass) - but CT can give you an indication

ADRENAL DISEASE

Most common

INCIDENTALOMA

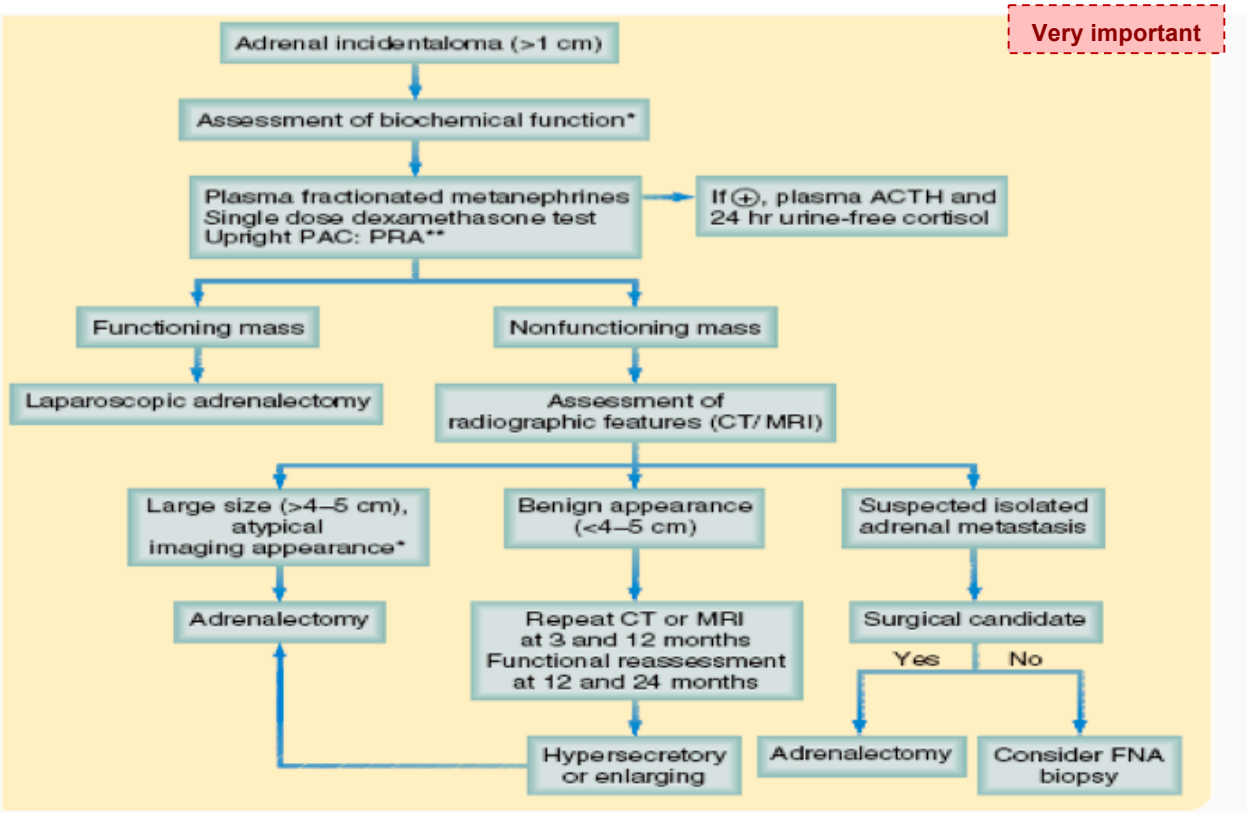
- Found in 1-4 % of CT scans
- Incidence increases with age
- **Small nonfunctioning adrenal tumors**: MOST COMMON
    - Subclinical Cushing 5%
    - Pheochromocytoma>it's functioning u have to interfere regardless of size 5%
    - Adrenocortical cancer 5%
    - Metastatic carcinoma 2%
    - Conn's
- Some with subclinical secretions of hormones (Usually missed by patient and physician)
- Adrenocortical carcinoma (Small percentage)
- Metastases

They do CT for other reasons, and then -incidentally- they find an adrenal mass. Usually asymptomatic or very few symptoms - so patients don't complain of it

- What do you do if you find an incidentaloma? You assess function
- How do you manage it? (Do you forget about it > that depends on?)
    - If it is functioning > you have to interfere
    - If it's non functioning look at the SIZE

CLINICAL PATHWAY

Very important



PAC: PRA for Conn's. Metanephrine: look for pheochromocytoma. Single dose dexamethasone: for Cushing's.

- Radiographic features: if mass is 4 cm but has irregular borders, high attenuated, lymph node involvement, this is cancer and needs surgery
- In adrenals, anything > 6 cm → remove it (most likely cancer but rule out other possibilities and see if patient is fit for surgery or not)
- Benign appearance, 4-5 cm (equivocal or confusing cm), non functioning → repeat workup in 3 months, if it increased in size or turned out to be functioning → remove gland
- Any functioning mass that's causing a pathology (symptoms) → remove gland
- If unfit patient → biopsy → determine type of cancer → give medical treatment to slow it down (but usually, these pt. die even before getting complications)
- Why don't we take a biopsy from the beginning?
    - In pheochromocytoma, if we perform a biopsy, the pt. may die on the table (Metanephrine → Hypertensive crisis with cardiac arrhythmia → cardiac arrest

HYPERALDOSTERONISM (CONN'S)

CAUSES

1- Primary
    a. Adenoma (Most common)
    b. Idiopathic bilateral adrenal hyperplasia.
    c. Unilateral adrenal hyperplasia.

d. Adrenocortical carcinoma.
e. Familial (rare)

2- Secondary
   a. Renal artery stenosis
   b. CHF
   c. Liver cirrhosis
   d. Pregnancy

High aldosterone

- Na and water retention + K^+ loss → 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

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

PRIMARY HYPERALDOSTERONISM

- 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: "patients will mostly present with fatigue (weakness b/c of ↓K^+) & persistent HTN (uncontrolled, even w/3-4 medications)"
  - HTN (hypertension) with or without hypokalemia IMP
  - Weakness, polyuria, paresthesias, tetany, cramps
  - Metabolic alkalosis, relative hypernatremia
  - Elevated aldosterone secretion and suppressed plasma renin activity (b\c of aldosterone hypersecretion)

DIAGNOSIS

PAC: Plasma aldosterone concentration
PRA: Plasma renin activity

- Screening tests:
  - PAC (ng/dl) / PRA (ng /ml) >20 (ordered by the endocrinologist not the surgeon)
  - Plasma aldosterone > 15 ng/dl (could mean it's Conn's)
- Confirmatory tests:
  - Sodium suppression test (to differentiate b\w primary & secondary)
    - In primary secretion is not affected ≠ in secondary secretion is suppressed
  - Urinary aldosterone excretion >14 ug/ 24hr

- In endocrine diseases the rate-limiting step that is responsible for –ve feedback is the suppressor
- E.g.: dexamethasone is actually corticoid
- Confirm then differentiate 1ry from 2ry by suppression tests

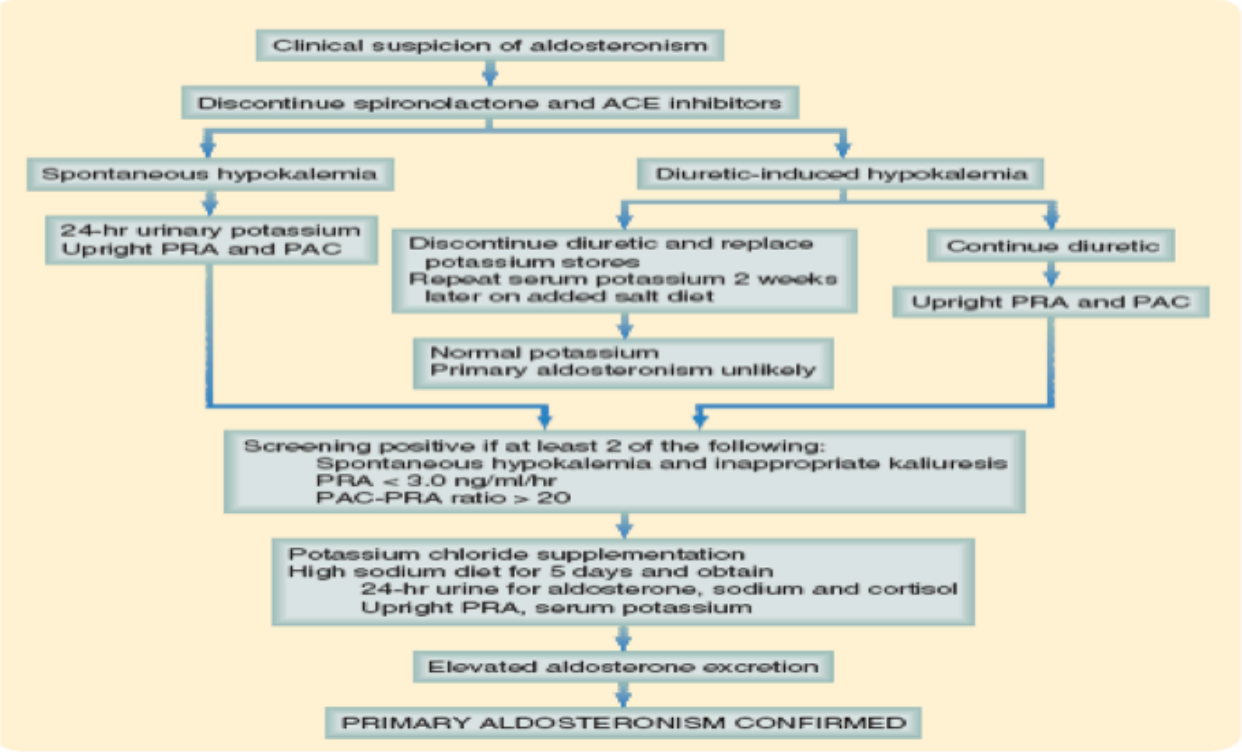
TREATMENT AND PROGNOSIS

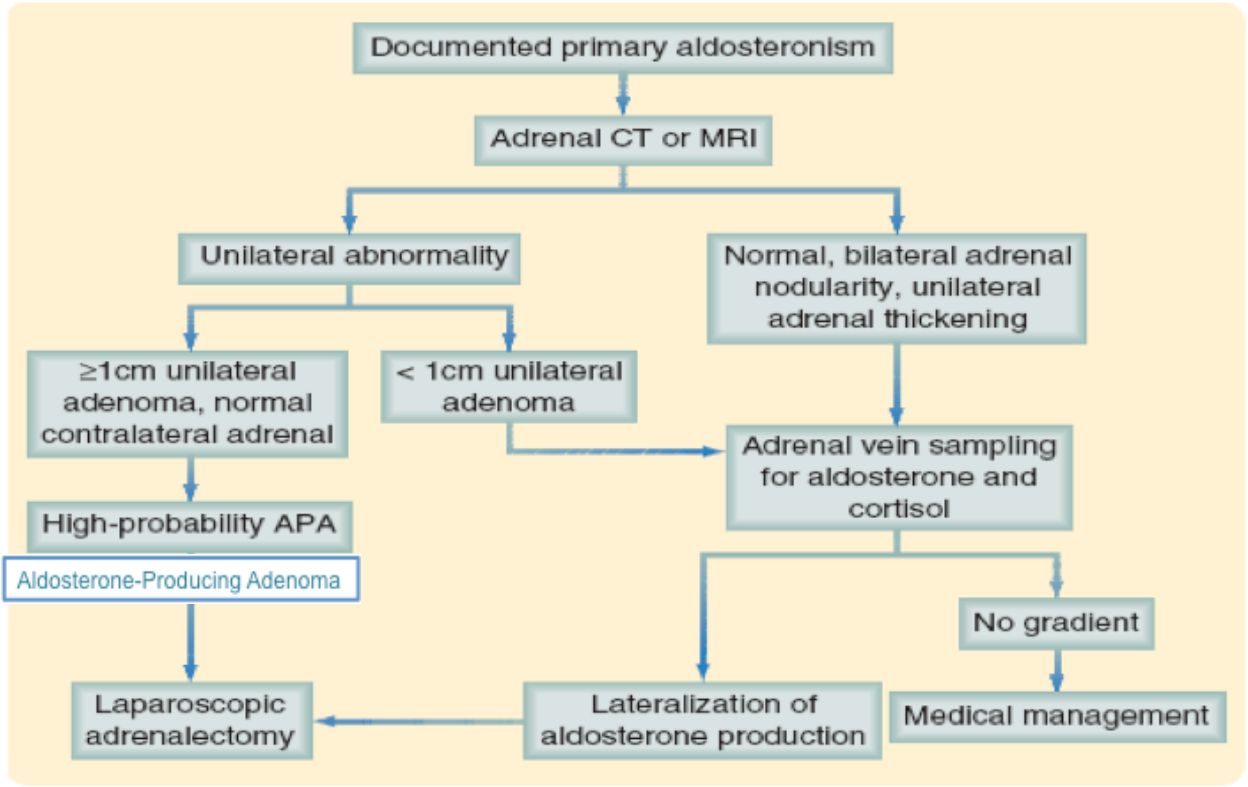
- Pre-operative preparation:
  - Spironolactone:
    - Competitive aldosterone antagonist (corrects pathology caused by aldosterone by binding to its receptors)
    - Promotes K retention (K^+ sparing diuretic)
    - Reduces extracellular volume
    - Reactivates the renin-angiotensin-aldosterone system
  - Amiloride: not as common as spironolactone
  - Other K^+ sparing diuretics
- Surgery:
  - Laparoscopic adrenalectomy
  - Open surgery
- Medical treatment (if surgery is not possible):
  - Unfit patients.
  - Bilateral ald. (Bilateral adenoma or hyperplasia and pt doesn't want to go to full list of replacement)

PROGNOSIS

- 1/3 of pts: persistent hypertension
  - "Tell the patient about this complication. Surgery may either cure or reduce the amount of antihypertensive medications needed"
- K level will be restored "Patient will be very active again"

CLINICAL PATHWAY





- 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 TTT b\c you can't take out both adrenals, otherwise you have to replace adrenal hormones i.e. glucocorticoids and mineralocorticoids

PHEOCHROMOCYTOMA

When there is a patient with pheochromocytoma in the ward everyone is ready -physician, surgeon, anesthetist, ICU physician- to arrange an ICU bed, administer him α- & β-blockers, and prepare the OR. Why? B/c they might lose him if BP shoots up > bleeding > death!

EPIDEMIOLOGY:

- Less than < 0.1% of patients with hypertension (not common in our community)
- 5% of tumors discovered incidentally on CT scan (less than 4-5 cm but functioning)
- Most occur sporadically (no genetic predisposition)
- Associated with familial syndromes, such as:
  - Multiple endocrine neoplasia type 2 (MEN 2A & 2B); present in **40%** of MEN pts
  - Recklinghausen disease (Neurofibromatosis type I)
  - von Hippel-Lindau disease

- 90% of patients with pheochromocytoma are hypertensive
    - Hypertension is less common in children
- In children, 50% of patients have multiple or extra-adrenal tumors (so check MIPG nuclear scan to detect the exact location of the tumor)

SYMPTOMS AND SIGNS

Clinical findings are variable

If you suspect pheochromocytoma DO NOT treat as out patient

Patient can die in crisis

- Episodic or sustained hypertension (jumping HTN on and off)
- Triad of **palpitation, headache, and diaphoresis**
- Anxiety, tremors and weight loss
- Dizziness, nausea, and vomiting
- Abdominal discomfort, constipation, diarrhea. "That anything goes with hit and runs "
- Visual blurring
- Tachycardia, postural hypotension
- Hypertensive retinopathy (in short period of HTN history)

Case example: patient diagnosed with HTN only 3 yrs ago, ophthalmologist examines him and observes full blown retinopathy.

ESSENTIAL FEATURES

- Episodic **HEADACHE** (due to HTN), excessive **SWEATING**, **PALPITATIONS**, and **VISUAL BLURRING**
- **HYPERTENSION**, frequently sustained, with or without paroxysms IMP!
- Postural tachycardia and hypotension
- Elevated urinary catecholamines or their metabolites, hyper-metabolism, hyperglycemia
- Rule of 10s: IMP!
    - 10% **malignant**
    - 10% **familial**
    - 10% **bilateral**
    - 10% **multiple** tumors
    - 10% **extra-adrenal** "all places including head and neck" but the commonest is the abdomen "so when we do CT for the adrenals and we don't find anything - we do nuclear scan and check abdomen then act accordingly"

10% is an acceptable percentage in most surgical conditions e.g.

- Incidence of hereditary breast Ca 10%
- Incidence of medullary thyroid carcinoma 10 %

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EXTRA-ADRENAL

Very **RARE**

- Abdomen (75%) [Closest to normal site so it is the most common]
- Bladder (10%)
- Chest (10%)
- Pelvis (2%)
- Head and neck (3%)

WORK-UP

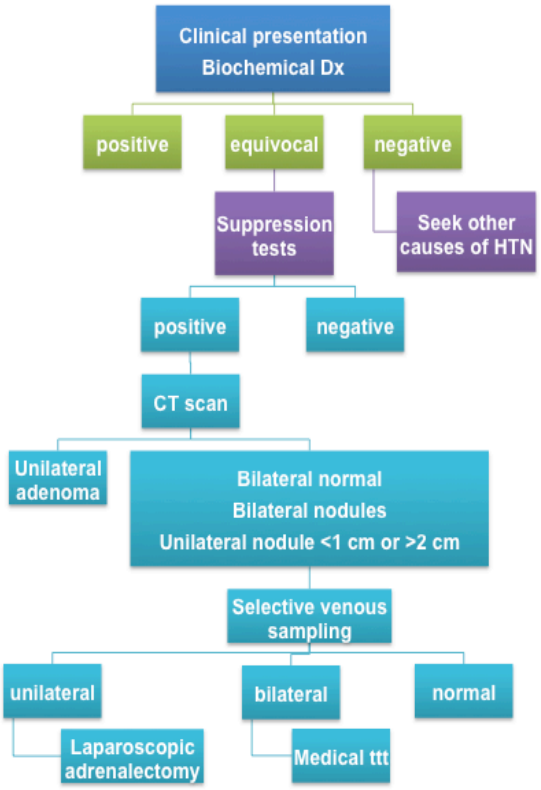
- History and physical exam
- Suspect pheochromocytoma based on symptoms
- CT, MRI, or other scans
- Plasma and urine studies (metanephrines, catecholamines, VMA)

- Begin treatment with a-blockers
- Possible MIBG scan
- Operative excision of tumor

LABORATORY FINDINGS

- Hyperglycemia "and they can not maintain fasting; they become hypoglycemic – we can differentiate it from Cushing"
- Elevated plasma metanephrines
- Elevated 24-hour urine metanephrines and free catecholamines
- Elevated urinary vanillylmandelic acid (VMA)
- Elevated plasma catecholamines

RECALL: Adrenaline:
- Lipolysis & proteolysis (catabolism), gluconeogenesis
- Hyperglycemia: Due to α2-adrenergic inhibition of insulin release, epinephrine-induced inhibition of glucose uptake, α-adrenergic stimulation of hepatic glucose production and β-adrenergic receptor desensitization



IMAGING

- Adrenal mass seen on CT or MRI
- Characteristic bright appearance on T2-weighted MRI
- Asymmetric uptake on MIBG nuclear scan
  - *Particularly useful for extra-adrenal, multiple, or malignant pheochromocytomas*
  - Not useful for sporadic biochemical syndrome with unilateral mass

CONSIDERATIONS

- **AVOID arteriography** or fine-needle aspiration as they can precipitate a hypertensive crisis IMP!
- Early recognition during **pregnancy** is key because if left untreated, half of fetuses and nearly half of the mothers will die (hypertensive crisis could kill the mother or fetus)

Rule out:

- Other causes of hypertension
- Hyperthyroidism
- Anxiety disorder
- Carcinoid syndrome

TREATMENT

ADMISSION

- **HYPERTENSIVE CRISIS** (can develop multisystem organ failure, mimicking severe sepsis)
  - Some patients can present w/septic shock, if you can't explain it → suspect pheochromocytoma

MEDICAL

- **α-Adrenergic blocking agents** should be started as soon as the biochemical diagnosis is established to restore blood volume, to prevent a severe crisis, and to allow recovery from the cardiomyopathy
- Good alpha and beta-blocker control → smooth anesthesia, smooth surgery, and smooth recovery after.

SURGERY

- Indications:
  - All pheochromocytoma should be excised
- Contraindications:
  - Metastatic disease "b\c we cannot control it"
  - Inadequate medical preparation (a-blockade) "has to be adequate to avoid cardiomyopathy and vasoconstriction"

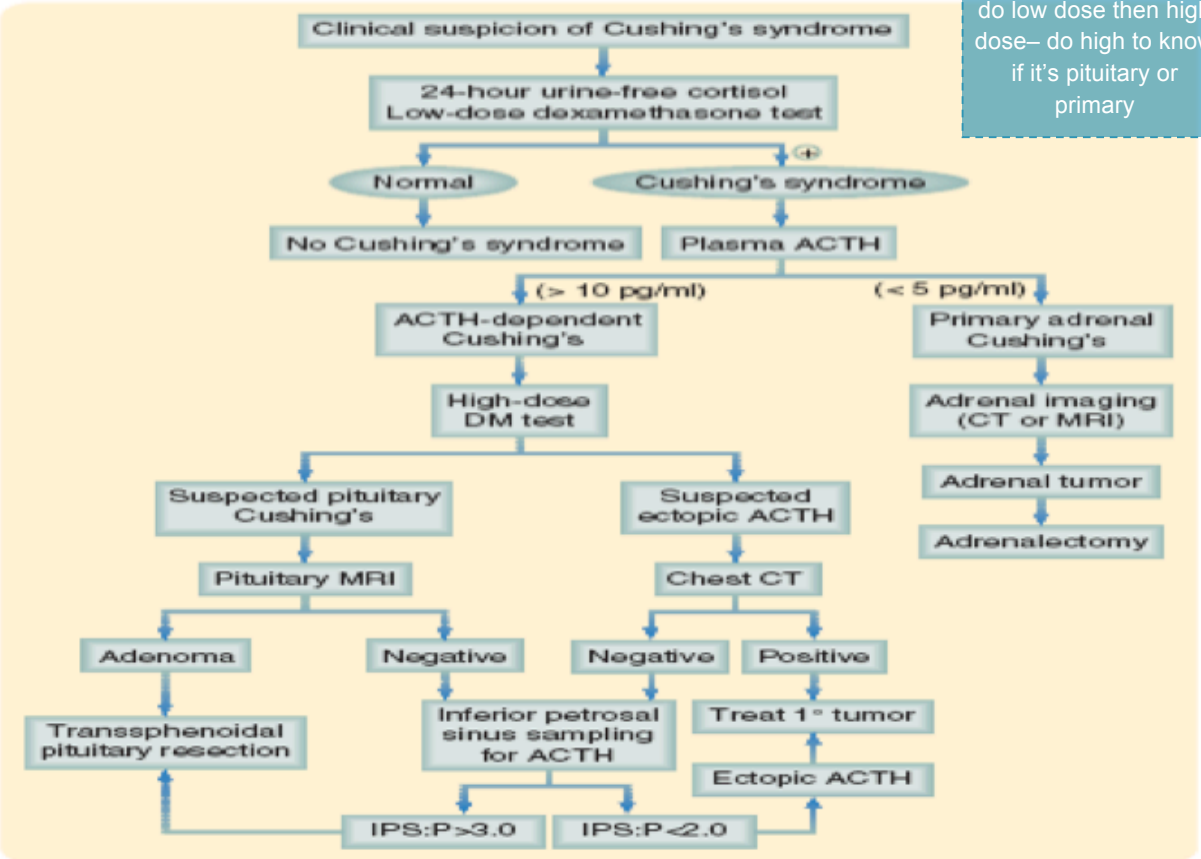
CUSHING'S

Disease Vs. Syndrome

- Cushing disease secondary to pituitary adenoma
- Cushing syndrome secondary to anything else

CLINICAL PATHWAY

Check hormones then do low dose then high dose– do high to know if it's pituitary or primary



- If we suspect Cushing first we do simple **low dose** (screening test) → suppression = normal patient
- If "+ve" (there is no suppression) = Cushing's
- Next step: ACTH dependent or not?
  In **high dose** test: if not suppressed it's either ectopic e.g. pulmonary carcinoma **OR** adrenal tumor (difference is in ACTH level: undetectable in adrenal & very high in ectopic), if pituitary it will be suppressed by high but not low dose dexamethasone
  "All will be suppressed by high dose but there is a difference in the reading – so we do CT chest (for ectopic) & MRI for brain (Cushing's disease) to confirm the diagnosis"

ADRENOCORTICAL CARCINOMA

ESSENTIAL FEATURE

- Variety of clinical symptoms through excess production of adrenal hormones
- Mainstay of treatment: Complete surgical removal of the primary lesion and any respectable metastatic sites
- Adrenocortical carcinoma is v. rare usually **PRESENT LATE WITH METASTASIS** but the only Rx is surgery, which has **high morbidity and mortality**
  - Unless patient is dying! Give supportive Rx
- Difficult to discover early b/c it's retroperitoneal structure

EPIDEMIOLOGY

- These tumors are rare; 1—2 cases per million persons in the United States
- Less than 0.05% of newly diagnosed cancers per year
- Bimodal occurrence "in the very young and the very old pts", with tumors developing in children < 5 years of age and in adults in their fifth through seventh decade of life
- Male: 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 "high testosterone")
- Feminizing and purely aldosterone-secreting carcinomas are rare
- 50% of patients have metastases at the time of diagnosis

SYMPTOMS AND SIGNS

- Symptoms of specific hormone excess (cortisol excess, virilization, feminization)
- Palpable abdominal mass "b\c the mass very big"
- Abdominal pain
- Fatigue, weight loss, fever, hematuria

DIAGNOSIS

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

IMAGING

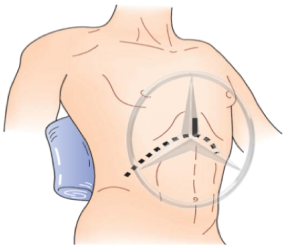
- Evaluation of adrenal glands with CT or MRI (adrenocortical carcinomas are typically iso-dense to liver on T1-weighted MRI, and hyper-dense relative to liver on T2-weighted MRI images)
- **MRI** more accurately gauges the extent of any intracaval tumor **thrombus**

Right tumor > goes to IVC creating big thrombus and that makes the surgery v. difficult. You have to restrict part of IVC, remove the thrombus and anastomose it again, and remove all tissues involved e.g. part of kidney, lymph node, or part of liver

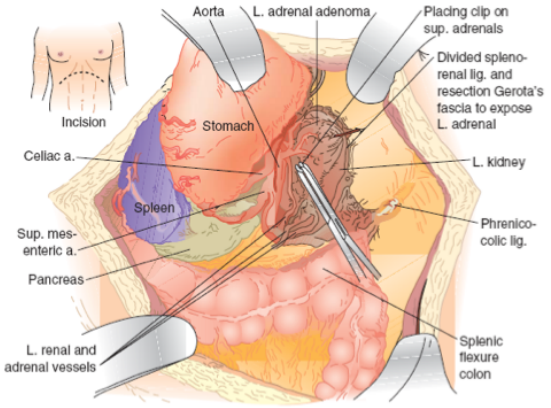
CONSIDERATIONS

- Mean diameter of adrenal carcinoma at diagnosis is 12 cm as we mention early if it more than 6 cm remove it if he was surgically fit
- Radiographic evaluation of suspected metastatic sites for purposes of staging should be undertaken prior to thought of any surgery " like any other tumor u have to use TNM "
- Rule out IMP
    - Pheochromocytoma

OPERATIVE APPROACHES

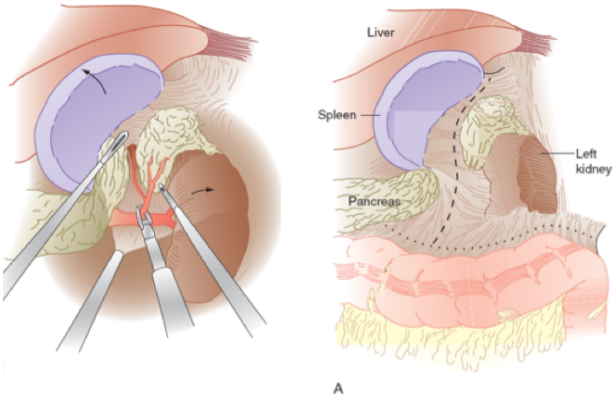


- You have to put a pillow as picture to push things; so the liver can easily be removed and expose the glands
- Mercedes incision, also called Chevron incision that is an inverted V shape "old way not used anymore except in some cases such as bleeding, if you repeat surgery again"
- Incision is big because the target "adrenal" is v. high and deep > so you have to retract liver, ligate vessels …etc
- Surgery of adrenal:
    - Open operation: abdominal, back
    - Laparoscopic: trans-abdominal, back
    - Gold standard for adrenalectomy is laparoscopy IMP!
    - What is the advantage of back laparoscopy "for small tumor" instead of trans-abdominal? Pt can leave on the same day, opposite to trans-abdominal when pt can go home within 24-48 hr
    - Disadvantage of back laparoscopy: it needs a lot of experience
    - Advantages of the robotic adrenalectomy over laparoscopy:
        - Hand movement 360 degree
        - Accuracy, clarity of the picture.
- But there is no difference, so if they ask what is the **gold standard? LAPAROSCOPY**
- Considerations:
    - Choose a good time to do the surgery (1st surgery in day so all staff will be there)
    - Book ICU bed, has to be managed in ICU
    - LINES: Any line you know for e.g. central venous line, arterial line "exact measurement of BP", folly's catheter "urine output", NGT, intra-esophageal temperature monitoring > b/c you want to monitor pt accurately



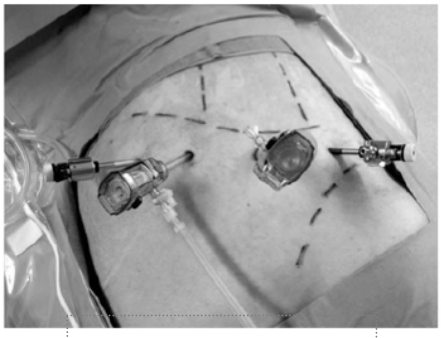
REMEMBER:
- anything functional we remove if the pt fit - if the pt not fit medical
- any thing non functional, small in size we follow up - in b\w we assess growth if it enlarged or secreted
- If > 6 cm we remove

We remove splenorenal ligament then push kidney away to remove adenoma alone.



Adenoma usually gold brown in color

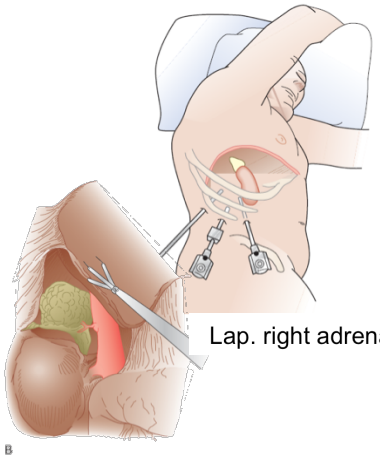
- Open splenorenal ligament then push the liver, pancreas, or stomach to the right side and isolate left kidney with adrenal and clip “ligature” the adrenal vein - we do not bother with the artery; usually very small branches



Lap. left adrenalectomy

How to do?

- 5 ports .5-1 cm
- 2 for the surgeon
- One for camera
- 2 for assistance



Lap. right adrenalectomy: