

Cushing's Syndrome

A disease of **excess cortisol**, it's caused by one of four conditions:

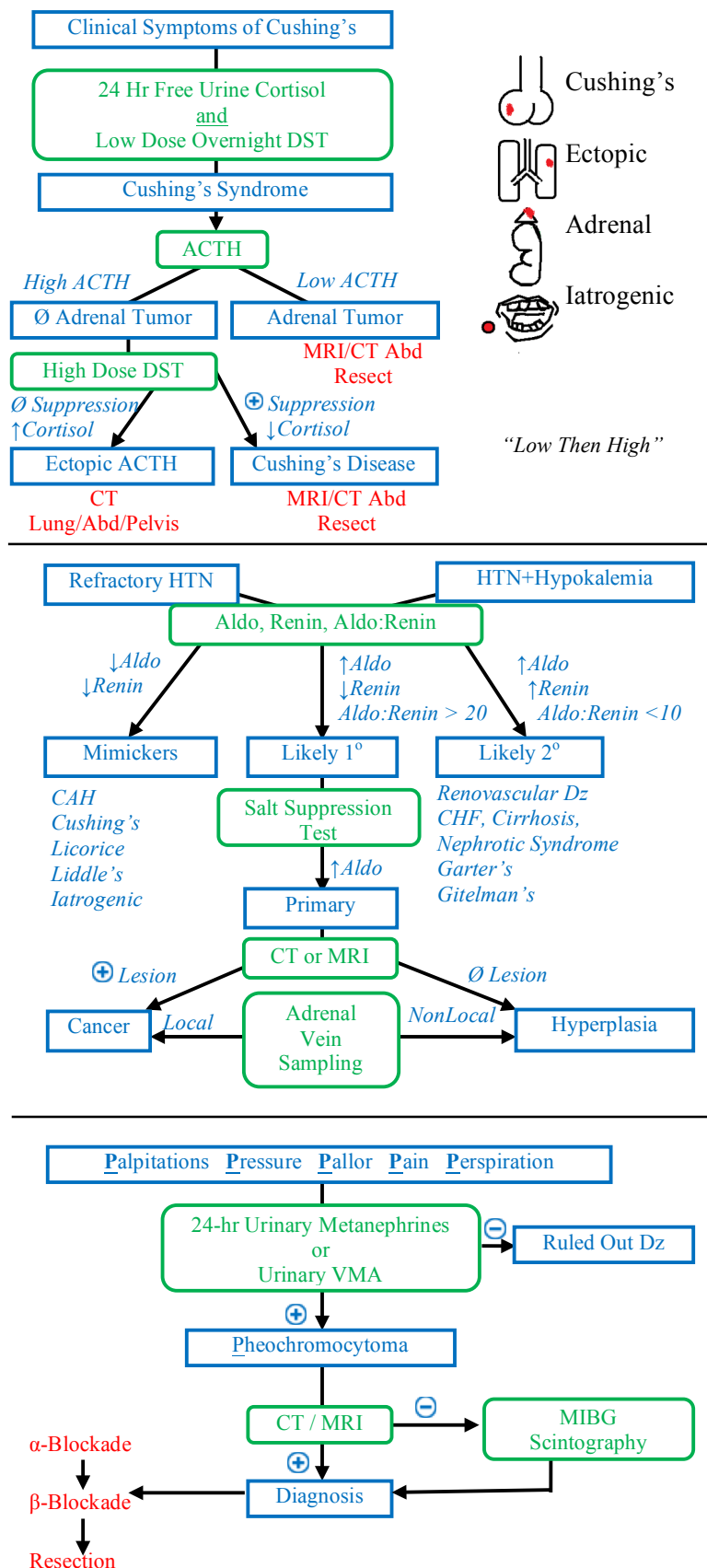
1) **Iatrogenic** (most common, taper off to fix), 2) **Pituitary tumor** (Cushing's disease), 3) **Adrenal Tumor**, or 4) **Ectopic ACTH**. The patient will present with a "Cushingoid appearance": **central obesity, moon facies, extremity wasting, a buffalo hump, glucose intolerance or diabetes, and hypertension**. When faced with this condition, get a **24-hr free cortisol level and confirm with 1mg Low Dose Dexamethasone Suppression test**. If cortisol is  $\uparrow$  it's  $\oplus$  Cushing's. Follow that with an **ACTH** level to distinguish adrenal ( $\downarrow$  ACTH) from extra-adrenal ( $\uparrow$  ACTH). If adrenal, spot it with a **CT/MRI of the Adrenals**. If extra-adrenal, perform a **high dose dexamethasone suppression test** to determine pituitary (suppresses) vs ectopic ( $\emptyset$  suppression). Confirm pituitary Cushing's with an **MRI** followed by transsphenoidal resection. If ectopic, find it with **CT/MRI** of 1) Chest (**Lung Ca**), 2) Abd (**Pancreatic ca**), then 3) Pelvis (adrenals). Remember "Low-Dose ACTH Then High-Dose."

Hyperaldosteronism

Aldosterone causes resorption of Na and H<sub>2</sub>O producing an expanded vascular volume and hypertension by  $\uparrow E_{Na}$  in the collecting tubules, trading Na for K. This produces a **refractory HTN** or a **Diastolic HTN and Hypokalemia**. Differentiate between: **primary** (a tumor or adenoma called **Conn's Syndrome**) where aldosterone production is independent of Renin, **secondary** (renovascular disease, edematous states of CHF, Cirrhosis, Nephrotic Syndrome) where the production of aldosterone is dependent on renin and is an appropriate response to  $\downarrow$  renovascular flow, and **mimickers** (CAG, Licorice, or exogenous mineral corticosteroids). When suspected, perform 8am levels for **Aldosterone, Renin, and Aldo:Renin Ratio**. Ensure any hypertension medication is discontinued (ACE, CCB, Diuretics confound the test). If **elevated** ( $>20$  Aldo and  $>20$  Aldo:Renin), it's likely **primary**. Confirm with the **salt suppression test** (where aldosterone will not decrease after a 200g Na load). The tumor is found by **CT** or **MRI**. If early AM levels are  $\emptyset$  **elevated** a different disease is likely provoking the aldosterone increase.

Pheochromocytoma

An overproduction of **catecholamines** produces either a **sustained refractory HTN** or **Paroxysmal Five P's** which are 1) **Pressure** (HTN), 2) **Pain** (Headache or Chest Pain), 3) **Pallor** (vasoconstriction), 4) **Palpitations** (tachycardia, tremor), and 5) **Perspiration**. This follows the rule of 10 percents (excellent pimping question, useless for practice). Screen for this disease with **24 hr urinary metanephrines or Urinary VMA** (metanephrines is better, VMA is cheaper). If  $\oplus$ , do an **MRI/CT of the pelvis**. They should be easy to spot. If not, a **MIBG Scintigraphy** can be done. The treatment is **resection** but with caution; touching one can cause release of catecholamines. Pretreat first with  $\alpha$ -blockade to prevent unopposed  $\alpha$ -action with  $\beta$ -blockade, then  **$\beta$ -Blockade**, then **surgery**.



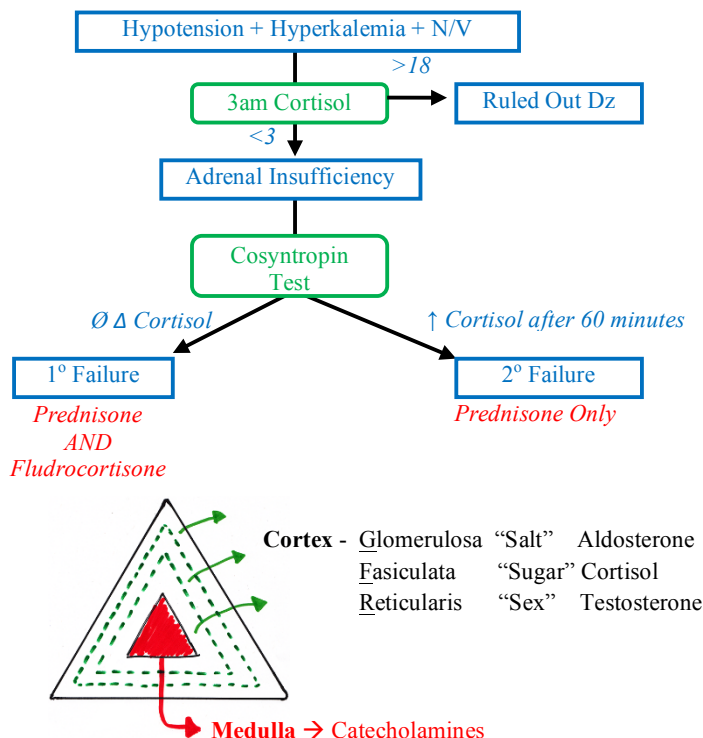
Adrenal Incidentalomas

These are **asymptomatic adrenal masses** found on CT scan for something else - an "incidental finding." It's important to rule out **functioning adenomas** (pheo, aldo, cortisol, androgen) from **nonfunctioning adenomas**. All above findings must be done to rule out Cushing's (DST), Pheo (24-hr urine metanephrines) and Aldo (plasma renin and Aldo). A direct needle biopsy should **NOT be done** until pheo is ruled out. It's ok to **watch and wait** if **<4cm**, but intervene with treatment if **>4cm** or there's an **increase in size over time**.

Adrenal Insufficiency

The loss of adrenal function may be from a variety of **etiologies**, and may be sudden/acute with multiple **presentations**. The **most common cause** in the US is **autoimmune adrenalitis**; it's **TB worldwide**. In the setting of **sepsis** there may be bilateral adrenal destruction from **hemorrhage** (Waterhouse-Friderichsen). Weir **deposition disease** can also compromise the adrenals (amyloid, sarcoid, and hemochromatosis). In **primary failure** (loss of cortisol, maintenance of ACTH) the symptoms will be **hypotension, fatigue, N/V** of cortisol loss, as well as the **hyperpigmentation and hyperkalemia**. Hyperpigmentation is a result of ACTH production trying to increase cortisol while hyperkalemia is from deficient aldosterone. In **secondary failure**, no ACTH is produced so hyperpigmentation is absent. Because aldosterone production is intact there's also no hyperkalemia. It's key to make sure it's not a primary deficiency so perform a **cosyntropin test** (exogenous ACTH administration). Establish a baseline cortisol in the morning (**<3ug = Dz**, **>18ug = ruled out**). Give the ACTH then reassess in 60 minutes to determine if there's any change in cortisol. (**3, 3, 3 =  $\emptyset$  ACTH problem = 1<sup>o</sup> deficiency**) vs (**3, 3, 20 = ACTH problem, 2<sup>o</sup> deficiency**). Treat this by **giving the steroids** they don't have. **Prednisone** for all types and **fludrocortisone** for primary only (it's a synthetic aldo that has its function retained through the RAAS in secondary).

r/o...	With
Cushing's	Dexamethasone Suppression test
Pheo	24-Hr Urine
Conn's	Aldo/Renin



Dz	Path/Etiology	Presentation	Diagnostic	Tx
<b>Cushing's</b>	Iatrogenic Pituitary Tumor Adrenal Tumor Ectopic Tumor	Obesity, Diabetes Moon Facies, Buffalo Hump	Low Dose Dexa Suppression ACTH levels High Dose Dexa Suppression CT/MRI Abd/Pelvis/Thorax	Stop Steroids or Cut out Tumor
<b>Hyperaldo (Conn's)</b>	1 <sup>o</sup> Dz = Tumor 2 <sup>o</sup> Dz = Systemic Mimickers	Hypertension and HypoK <b>OR</b> Refractory HTN	Aldo, Renin, Aldo:Renin Salt Suppression CT/MRI MIBG Scintillography	Cut out Tumor Fix Systemic Dz
<b>Pheo</b>	Adrenal Tumor	Paroxysmal Pain Pressure Palpitations Pallor Perspiration	24-hr Urinary Metanephrine or VMA Urine CT/MRI	$\alpha$ -Blockade $\beta$ -Blockade Adrenalectomy
<b>Adrenal Insufficiency</b>	Autoimmune Infection Hemorrhage Deposition Disease Pituitary Failure	Hypotension Fatigue Anorexia Nausea/Vomiting Hyperpigmentation	Cortisol Level @ 3am Cosyntropin Test CT/MRI	1 <sup>o</sup> = Prednisone (cortisol) and Fludrocortisone 2 <sup>o</sup> = Prednisone Only