**High Aldo** (First: rule exogenous mineralocorticoid intake then Screen: check Aldo and Renin then Confirm: Salt Suppression Test, etc NB avoid aldo-blockers, ACEI/ARB/DRI, diuretics, BB, etc b/c can affect lab values therefore for >6wks, the only drugs you can use are AB/CCB)

- 1° Hyperaldosteronism 2/2 High Aldo and thus Low Renin (Plasma Aldo Concentration / Plasma Renin Activity >20)
  - (1) Exogenous Mineralocorticoid
  - (2) Solitary Adenoma aka Conn's Syndrome (30%) or Carcinoma (rare) (more dramatic Sx, + Adrenal MRI mass), Tx: Laparoscopic Unilateral Adrenalectomy
  - (3) Bilateral/Unilateral Adrenal Hyperplasia (70%) (less dramatic Sx, -Adrenal MRI mass), Tx: Spirinolactone NB surgery is not effective, NB much more prevalent than previously thought accounting for possible 5% of all hypertensive pts!!!
  - (4) Glucocorticoid Remediable Aldosteronism (rare)
  - (5) ACTH Dependent Promoter Rearrangement (rare)
  - NB many times hyperplasia is focal and adenoma is so small that is missed on imaging therefore if imaging is equivocal consider adrenal vein sampling for more accurate results (high one vein = adenoma vs high both veins = hyperplasia) or just medically Tx and see what happens as contrast often causes adrenal hemorrhage/infarction
- 2° Hyperaldosteronism 2/2 High Renin and thus High Aldo (=20) NB high ACTH not only stimulates cortisol but also aldosterone
  - (1) Renin Tumor
  - (2) Anything that stimulates RAAS like decreased EAV, HyperK, etc
- Psuedohyperaldosteronism 2/2 something else w/ equally Low Aldo and Low Renin (=20)
  - (1) High Cortisol State NB cortisol actually has >100x affinity for aldo receptors than aldo but it doesn't cause aldo effects b/c the receptor has an enzyme (11beta-DSH converts cortisol to cortisone therefore converts cortisol to premature form) which breaks down cortisol but (a) when you have very high levels of cortisol as in Cortisol Syndrome you overwhelm this enzyme and cause hyperaldo effects, (b) when you have the enzyme inhibitor, glycyrrhizinic acid, which is present in licorice, RedMan chewing tobacco, etc endogenous levels of cortisol create an effect, (c) when you have a congenital deficiency of 11beta-DSH (aka Apparent Mineralocorticoid Excess (AME)) endogenous levels of cortisol create an effect
  - (2) CAH (refer to hypoadrenalism states, only the rarer enzyme deficiencies not the most common 21-hydroxylase, where precursors can no longer go thru cortisol/DHEA and thus all are shunted thru aldosterone pathway)
  - (3) Liddle's Syndrome (constitutively activated (aka w/o Aldo) ENaC)
  - (4) Geller's Syndrome (altered activity of MR such that progesterone can bind it and cause HTN esp during pregnancy)

**High Cortisol aka Cushing's Syndrome** (First: rule out exogenous glucocorticoid intake then Screen: check Cortisol and ACTH and 24-Urine Free Cortisol (nl 20-60mcg/d) then Confirm: ON Low Dose Dexamethasone Suppression Test (give 1mg at MN and check serum cortisol at 8am nl <1.8mcg/dL) as false high levels can be seen in certain conditions (obesity, alcoholism, depression, etc))

- 1° Hypercortisol 2/2 High Cortisol and Low ACTH
  - (1) Exogenous Glucocorticoids
  - (2) Solitary Adenoma/Carcinoma, (rare), confirm mass w/ CT-A/P adrenal protocol or NP-59 (iodomethylnorcholesterol) Scan, NB adenomas have low DHEA/small-nonpalapable/less-Sx while carcinomas have high DHEA/large-palpable/more-Sx, Tx: total unilateral adrenalectomy, pathway inhibitors (mitotane/ketoconazole/metyrapone)
- 2° Hypercortisol 2/2 High ACTH and thus High Cortisol then perform ON High Dose Dexamethasone Suppression Test (give 8mg at MN and check serum cortisol at 8am) to determine likely location of ACTH production and then proceed with imaging of appropriate area, NB if you can't confirm the above malignancies then consider a Bilateral Inferior Petrosal Sinus Vein Sampling (**BIPSVS**): ratio of petrosal/peripheral ACTH where >2 indicates high ACTH being made by pituitary
  - (1) >50% Suppression (b/c at very high doses that tumor can be inhibited) = ↑ Endogenous ACTH by Cushing's Disease (65%): Pituitary Adenoma, Dx: MRI, Tx: TSS if not successful then XRT if not successful then medical adrenalectomy w/ mitotane/ketoconazole/metyrapone if not successful then surgical bilateral adrenalectomy w/ subsequent HRT
  - (2) <50% Suppression (b/c even at very high doses that tumor cannot be inhibited) = ↑ Ectopic ACTH by Paraneoplastic Malignancy (15%): SCLC, Bronchial Carcinoid, Islet Cell Tumor, Medullary Thyroid Carcinoma, Pheo, Dx: CT, Tx: depends on exact malignancy

**High DHEA-S**

- Congenital Adrenal Hyperplasia (CAH) (refer)

**High Epi**

- Pheochromocytoma
  - Mechanism
    - Neural crest cells differentiate into adrenal medullary chromaffin cells (tumor: pheochromocytoma) sympathetic ganglia (tumor: neuroblastoma, paragangliomas, paraganglioneuromas) and CNS (tumor: ?)
    - These cells produce all different types of amines (Epi, NEpi, and Dopamine) and is highly variable as to which one predominates
  - Epidemiology
    - Only 0.05% of hypertensive pts you think have pheo actually have pheos!!!
    - 10% have unique features (10% Rule)
      - 10% extra-adrenal (esp para-ganglia at Organ of Zuckerandle at Aortic Bifurcation)
      - 10% recur (esp if extra-adrenal)

        - 10% familial (esp MEN-2A/B, NF-I, Von Hipple Lindau, Familial Carotid Body Tumors)
        - 10% malignant (esp if they secrete dopamine)
        - 10% bilateral/multiple
        - 10% asymptomatic
        - 10% pediatric
- Symptoms
    - Adult
        - *Paroxysmal/Severe/Resistant* HTN
        - Classic Triad: HAs + Diaphoresis + Palpitations (~90% sens/spec in pts w/ HTN above)
        - Common: Tachy-Arrhythmias esp during surgery or when taking meds (antidepressants, metoclopramide, naloxone, etc), D-CM, Pulmonary Edema, Tremor, Pallor, Anxiety, Weight Loss, Fever, Orthostatic Hypotension 2/2 Hypovolemia, etc (NB not flushing) DDx: hyperthyroid, carcinoid, hypoglycemia, menopause, etc
        - Rare: pheos sometimes create other random hormones like VIP, ACTH, Glucagon causing other random Sx
        - NEpi causes HTN while Epi causes HypoTN therefore some pheos have normal BP
    - Child
        - *Sustained* HTN
- Diagnosis (NB not specific as other conditions can be associated w/ above etc and not sensitive as pheos are sporadic)
    - Screen: Spot Plasma or even better 24-Hour Urine (b/c secretion is sometimes intermittent) Fractionated Metanephrines (aka Metanephrine & Normetanephrin) and Catecholamines (Epi and NorEpi)
        - NB pt must be at rest and off labetalol/TCAs/Tylenol (all other antihypertensives are fine?)
        - NB Spot Plasma Vanillyl-Mendaleic Acid (VMA) is no longer used anymore
    - Confirm: CT (best for adrenal pheo) vs MRI (best for extra-adrenal pheo) then do PET Scan for assessing mets
        - NB $I^{131}$-Meta-Iodo-Benzyl-Guanidine ($I^{131}$-MIBG) Scan if equivocal
        - NB Clonidine Suppression Test or Glucagon Stimulation Test
- Treatment
    - Pre-Op: αB (1° Phenoxybenzamine, 2° Phentolamine, Methyl Tyrosine) and Volume Expansion 2wks pre-op to control HTN then βB (Propranolol, etc) 3d pre-op to control tachycardia
    - Op: venous ligation to prevent Epi surge during surgery followed total unilateral adrenalectomy with gentle removal of gland to prevent Epi release (90% are cured with surgery)
    - Post-Op: continue aggressive fluids to prevent hypoTN
    - Follow-Up: $I^{131}$-MIBG Scan