Brandon Chock, MD // Department of Endocrinology // May 14, 2019

"GLAND" TO MEET YOU

An Introduction to the Adrenal Glands

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CME DISCLOSURE

- Neither faculty or planners of this education have any relevant interests to disclose.

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LEARNING OBJECTIVES

- Adrenal Physiology.
- Glucocorticoids.
  - Physiology.
  - Disorders.
- Catecholamines.
  - Physiology.
  - Disorders.

- Mineralocorticoids.
  - Physiology.
  - Disorders.
- Androgens.
  - Physiology.
  - Disorders.
- Adrenal Adenomas.

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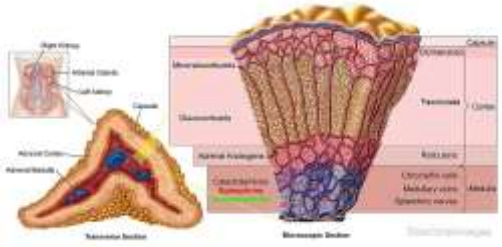
ADRENAL PHYSIOLOGY

ADRENAL ANATOMY



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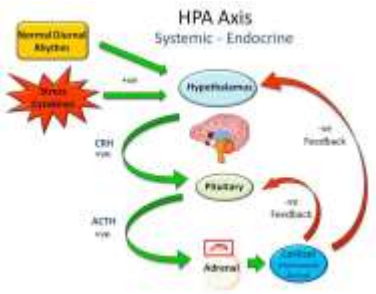
GLUCOCORTICOIDS

GLUCOCORTICOIDS (CORTISOL)

Image Credit: watchesonsteroids.com

- Cortisol helps maintain blood pressure and assist the body's response to stress.
  - Increases glucose production.
  - Inhibits protein synthesis and increase protein breakdown.
  - Stimulates lipolysis.
  - Affects immunologic and inflammatory responses.
- There is a circadian rhythm to cortisol production.
  - Higher cortisol in the morning, lower cortisol in the evening.

GLUCO-CORTICOIDS (CORTISOL)



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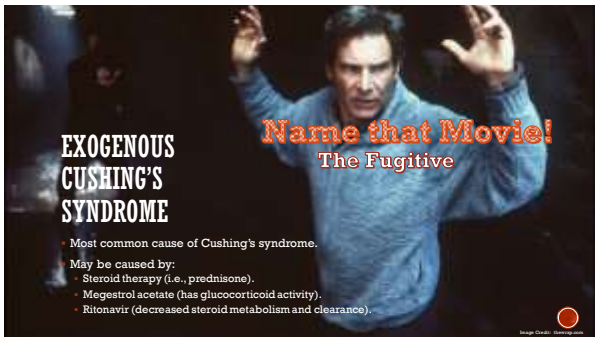
DISORDERS OF GLUCOCORTICOIDS

- Cushing's syndrome.
- Adrenal insufficiency.

CUSHING'S SYNDROME

- Syndrome of excessive cortisol due to:
  - **Exogenous Cushing's syndrome.**
  - **Endogenous Cushing's syndrome.**
  - **Other (Pseudo-Cushing's).**



EXOGENOUS CUSHING'S SYNDROME

- Most common cause of Cushing's syndrome.
- May be caused by:
  - Steroid therapy (i.e., prednisone).
  - Megestrol acetate (has glucocorticoid activity).
  - Ritonavir (decreased steroid metabolism and clearance).

ENDOGENOUS CUSHING'S SYNDROME

- ACTH-Independent (20% of endogenous causes).
  - Adrenal tumors (adenomas/carcinomas).
- ACTH-Dependent (80% of endogenous causes).
  - Pituitary Cushing's disease (85% of ACTH-dependent causes).
  - Ectopic ACTH (15% of ACTH-dependent causes).
    - Most common sites: Lungs, small intestine.
  - Ectopic CRH.

PSEUDO-CUSHING'S

- Psychiatric disorders (depression, anxiety, anorexia/bulimia nervosa).
- Alcoholism and withdrawal.
- Glucocorticoid resistance.
- Polycystic ovarian syndrome.
- Morbid obesity.
- Uncontrolled diabetes mellitus.
- Lipodystrophy.

SYMPTOMS/SIGNS OF CUSHING'S SYNDROME

- Most specific symptoms/signs:
  - Low potassium.
  - Bruising.
  - Osteoporosis.
  - Proximal Muscle Weakness.
  - Striae.
- Other:
  - Hirsutism/acne.
  - Central obesity.
  - Plethora (skin redness from increased blood flow).
  - Moon facies.
  - Dorsal fat pad.
  - Impaired glucose tolerance.
  - Menstrual irregularities.
  - Emotional lability.
  - Low libido.
  - Increased risk of thrombotic events.

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CUSHING'S SYNDROME SCREENING (NEED TWO ABNORMAL TESTS)

- **24 hour urine free cortisol.**
- **1-mg dexamethasone suppression test.**
  - 1-mg dexamethasone administered at 11 PM and cortisol is measured the next morning at 8 AM.
  - Cortisol > 5 mcg/dL suggests Cushing's syndrome, < 1.2 mcg/dL rules out Cushing's syndrome.
- **Midnight salivary cortisol.**
  - > 7.5 mcg/dL suggests Cushing's syndrome.
- **48-hour low dose dexamethasone suppression.**
  - Dexamethasone 0.5 mg every six hours for two days.
  - AM cortisol less than 1.8 mcg/dL at 24 or 48 hours makes it 98% certain Cushing's syndrome is not present.

CUSHING'S SYNDROME DIAGNOSIS (ACTH LEVEL)

- ACTH < 10 pg/mL = ACTH independent.
  - Adrenal MRI or CT.
- ACTH > 20 pg/mL = ACTH dependent.
  - Pituitary MRI.
  - Intrapetrosal sinus sampling.
    - ACTH is measured after CRH is given and compared to the peripheral blood to distinguish pituitary-dependent disease from ectopic ACTH.
  - 8-mg overnight dexamethasone suppression test.
  - CRH stimulation test.
  - Metyrapone test.
  - If ectopic ACTH suspected – chest/pancreas CT/MRI, serum calcitonin, gastrin, and 24 hour urine metanephrines/catecholamines.

TREATMENT OF CUSHING'S SYNDROME

- Surgery
  - Indicated for identified tumors.
  - Bilateral adrenalectomy in severely ill patients, young women who wish to get pregnant, or occult/metastatic ectopic ACTH if patient does not respond to medical therapy.
- Medical Therapy
  - Antifungal: Ketoconazole (drug of choice; impairs steroidogenesis).
  - Metyrapone (Impairs steroidogenesis).
  - Mitotane (Cytotoxic to the adrenal cortex).
  - Etomidate (Intravenous anesthetic agent).
  - Mifepristone (Antagonizes glucocorticoid receptor).
  - Cabergoline (Inhibits ACTH production).
  - Pasireotide (Somatostatin receptor agonist that inhibits ACTH production).
- Radiotherapy (if not surgical candidate)

ADRENAL INSUFFICIENCY

- Primary Adrenal Insufficiency (Addison's Disease).
  - Adrenal gland dysfunction.
- Secondary Adrenal Insufficiency.
  - ACTH deficiency.
- Tertiary Adrenal Insufficiency.
  - CRH deficiency.

PRIMARY ADRENAL INSUFFICIENCY (ADDISON'S DISEASE)

- Autoimmune adrenalitis (most common cause).
- Bilateral adrenal hemorrhage or thrombosis.
  - From trauma, acute stress, coagulopathy or adrenal tumors.
- Metastatic cancer (lymphoma, lung, breast, colon, renal).
- Infection (Tuberculosis).
- Adrenalectomy.
- Infiltrative disease (hemochromatosis, amyloidosis, sarcoidosis).
- Medications.
  - Etomidate, ketoconazole, metyrapone, aminoglutethimide, rifampin, mitotane, suramin, opiates, megestrol acetate, ritonavir, fluticasone.
- Congenital Disorders.

SECONDARY ADRENAL INSUFFICIENCY

- Radiation therapy.
- Withdrawal from long-term glucocorticoids.
- Metastatic disease to the pituitary.
- Pituitary surgery.
- Lymphocytic hypophysitis.
- Infiltrative disease (sarcoidosis, histiocytosis X).
- Infection (tuberculosis, histoplasmosis, HIV, CMV, toxoplasmosis).
- Sheehan's syndrome (massive blood loss in peripartum period).
- Severe head trauma.

TERTIARY ADRENAL INSUFFICIENCY

- Withdrawal from long-term glucocorticoid use.
- Hypothalamic tumors.
- Infiltrative diseases.
- Cranial irradiation.

ADRENAL INSUFFICIENCY SYMPTOMS/SIGNS

- Weakness.
- Fatigue.
- Anorexia.
- Weight loss.
- Nausea/vomiting.
- Abdominal pain.
- Constipation.
- Loss of axillary/pubic hair.
- Orthostatic hypotension.
- Salt craving.
- High potassium.
- Low sodium.
- Low glucose.
- Hyperpigmentation.
- Anemia.

ADRENAL INSUFFICIENCY TREATMENT

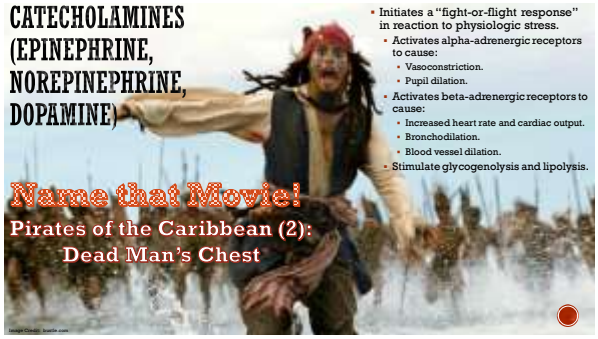
- Glucocorticoid replacement.
  - Hydrocortisone (most common).
  - Prednisone.
  - Dexamethasone.
- Mineralocorticoid replacement (i.e., fludrocortisone) if primary adrenal insufficiency.
- "Stress dose" steroids are required during any medical stress.
  - Steroids should be doubled or tripled for illnesses, trauma, surgical procedures, and labor/delivery.

ADRENAL CRISIS

- Medical emergency due to severe adrenal insufficiency.
- Five S's of adrenal crisis management:
  - **S**alt (Normal saline).
  - **S**ugar (5% dextrose added to normal saline).
  - **S**teroids (hydrocortisone 100 mg IV every 8 hours, or dexamethasone).
  - **S**upport (ICU care).
  - **S**earch for precipitating illness.

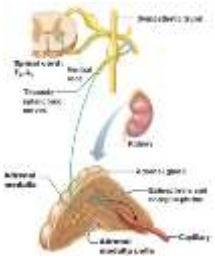
CATECHOLAMINES

CATECHOLAMINES (EPINEPHRINE, NOREPINEPHRINE, DOPAMINE)



- Initiates a "fight-or-flight response" in reaction to physiologic stress.
  - Activates alpha-adrenergic receptors to cause:
    - Vasoconstriction.
    - Pupil dilation.
  - Activates beta-adrenergic receptors to cause:
    - Increased heart rate and cardiac output.
    - Bronchodilation.
    - Blood vessel dilation.
  - Stimulate glycogenolysis and lipolysis.

CATECHOLAMINES (EPINEPHRINE, NOREPINEPHRINE, DOPAMINE)



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PHEOCHROMOCYTOMA/PARAGANGLIOMA

- **Pheochromocytoma:** Adrenal medullary tumor.
- **Paraganglioma:** Extra-adrenal pheochromocytomas.
  - 10% of pheochromocytomas.
  - Familial paraganglioma is an autosomal dominant disorder characterized by paragangliomas of the skull base, neck, thorax, abdomen, pelvis, and urinary bladder.
- **Rule of 10s:** 10% are extra-adrenal, 10% are bilateral, 10% are familial, and 10% are malignant.

PHEOCHROMOCYTOMA: ASSOCIATED SYNDROMES

- Multiple Endocrine Neoplasia.
  - MEN 2A: Pheochromocytoma, hyperparathyroidism, medullary thyroid cancer.
  - MEN 2B: Pheochromocyotma, medullary thyroid cancer, neuromas.
- Carney's triad: Paraganglioma plus tumors of the stomach, lungs, and testicles.
- Neurofibromatosis 1: Pheochromocytoma, café-au-lait spots, neurofibromas, eye tumors.
- Von Hippel-Lindau syndrome: Pheochromocytoma, eye and brain tumors.

PHEOCHROMOCYTOMA: SYMPTOMS AND SIGNS

- Sudden severe headaches.
- Diaphoresis.
- Palpitations.
- Hypertension.
- Anxiety.

PHEOCHROMOCYTOMA: DIAGNOSIS

- Initial screening:
  - Plasma free metanephrines (15% false positive rate).
  - 24 hour urine metanephrines.
  - Possible test interference:
    - Blood pressure medications (alpha1 blockers, alpha2 agonists, calcium channel blockers, ACE inhibitors, beta-blockers).
    - Bromocriptine.
    - Antidepressants/antipsychotics.
    - Physiologic stress.
- Imaging
  - CT scan of the adrenal glands (average tumor size is 4.5 cm).
  - MIBG scan may reveal metastases.
- Adrenal vein sampling.

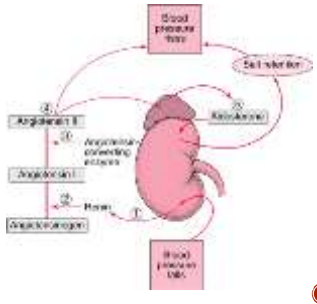
PHEOCHROMOCYTOMA: TREATMENT

- Surgical resection is the only definitive treatment.
  - Pre-operative alpha blockade reduces the incidence of intraoperative hypertensive crisis and postoperative hypotension.
    - Phenoxybenzamine (long-acting alpha blocker).
    - Prazosin (short-acting antagonist).
  - Phentolamine 5 mg IV bolus can be used for intraoperative hypertensive crisis.
    - Nitroprusside, nicardipine, nitroglycerine, and urapidil IV are other alternatives.

MINERALOCORTICOIDS

- Sodium and water retention by the kidneys.
  - Increases blood pressure.
- Potassium secretion by the kidneys.
  - Decreases serum potassium.

MINERALO-CORTICOIDS (ALDOSTERONE)



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HYPERALDOSTERONISM

- Primary hyperaldosteronism (high aldosterone, low renin).
  - Aldosterone-producing adenomas (Conn's syndrome) - 50%.
  - Adrenal hyperplasia - 50%.
  - Rare:
    - Familial hyperaldosteronism.
    - Adrenal carcinoma.
    - Ectopic aldosterone secretion (kidneys, ovaries).
- Secondary hyperaldosteronism (high aldosterone, high renin).
  - Renovascular hypertension and aortic stenosis (compromising renal vascular flow).
  - Diuretic use.
  - Renin-secreting tumors.
  - Severe left ventricular failure.

HYPERALDOSTERONISM: SIGNS/SYMPTOMS/COMPLICATIONS

- Hypertension (most common presenting sign).
  - Seen in 3 – 15% of patients with hypertension.
- Low potassium (although up to 50 – 75% may be normal).
- Metabolic alkalosis.
- Low magnesium.
- Increased left ventricular wall thickness and reduced diastolic function.
- Endothelial dysfunction, predisposing to atherosclerosis, hypercholesterolemia, type 2 diabetes mellitus, and metabolic syndrome.
- Atrial fibrillation.
- Cerebral hemorrhage/infarction.
- Renal insufficiency.

HYPERALDOSTERONISM: DIAGNOSIS

- Screening: Mid-morning aldosterone/plasma renin activity ratio.
  - Ratio greater than 20 in setting of aldosterone greater than 15 ng/dL is suggestive of primary hyperaldosteronism.
  - Patient should have normal potassium and be off of medications that may affect testing for up to six weeks.
- Who to Screen:
  - Moderate, severe, or resistant hypertension.
  - Hypertension and spontaneous or diuretic-induced hypokalemia.
  - Hypertension with adrenal incidentaloma.
  - Hypertension and family history of early-onset hypertension or cerebrovascular accident at a young age (< 40 years).
  - All hypertensive first-degree relatives of patients with primary hyperaldosteronism.

MEDICATION EFFECTS ON ALDOSTERONE/RENIN

Medication	Renin	Aldosterone	Aldosterone/Renin Ratio	Impact on Diagnosis
Beta-blocker and clonidine	Decreases	No change	Increases	False positives
ACE inhibitor and Angiotensin II antagonist	Increases	Decreases	Decreases	False negatives
Dihydropyridine Calcium Channel Blocker	Increases (acutely only)	Decreases (acutely only)	Decreases (acutely only)	Rarely, false negatives
Diuretic	Increases	Increases	Decreases or no change	Possible false negatives
Spironolactone or Eplerenone	Increases	Increases	Decreases	False negatives
NSAID	Decreases	Increases	Increases	False positives

HYPERALDOSTERONISM: DIAGNOSIS

- Salt-loading confirms the diagnosis of primary hyperaldosteronism.
  - Patients given normal saline infusion of 2 liters over four hours or sodium chloride tablets 12 grams daily for three days.
  - Plasma aldosterone > 5 ng/dL after saline infusion or 24 urine aldosterone > 10 mcg/day (with urinary sodium greater than 200 mEq/day) after oral salt loading confirms primary hyperaldosteronism.
- Imaging:
  - CT scan to evaluate for aldosterone-producing adenomas in primary aldosteronism.
  - Renal artery imaging if secondary hyperaldosteronism.
- Adrenal vein sampling distinguishes adenoma from hyperplasia.
  - After ACTH stimulation, a ratio of aldosterone:cortisol ratios greater than 4:1 is consistent with unilateral disease.

HYPERALDOSTERONISM: TREATMENT

- Surgery: Unilateral adrenalectomy.
- Medical Therapy:
  - Potassium-sparing diuretics.
    - Preferred therapy for those with high surgical risk or bilateral hyperplasia.
    - Spironolactone: Mineralocorticoid receptor antagonist.
    - Amiloride: Sodium epithelial channel inhibitor.
  - Selective Mineralocorticoid Receptor Antagonist: Eplerenone.
  - Calcium channel blockers.
  - ACE inhibitors.

HYPOALDOSTERONISM

- Hyperreninemic Hypoaldosteronism (high renin and low aldosterone):
  - Autoimmune destruction of the zona glomerulosa.
  - Aldosterone synthase mutation.
  - Drugs (heparin, cyclosporine).
  - Critical illness.
- Hyporeninemic Hypoaldosteronism (low renin and low aldosterone):
  - Diabetic nephropathy.
  - Amyloidosis.
  - Myeloma.
  - Lupus.

HYPOALDOSTERONISM: SYMPTOMS/SIGNS

- Hypotension.
- Dizziness.
- Salt-craving.
- Weight loss.
- Anorexia.
- Dehydration.
- Hyponatremia.
- Hyperkalemia.
- Metabolic acidosis.

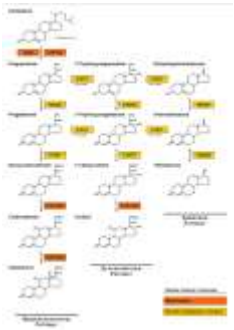
HYPOALDOSTERONISM: DIAGNOSIS/TREATMENT

- Diagnosis
  - Low aldosterone in the setting of other suggestive clinical symptoms and signs.
- Treatment
  - Fludrocortisone.

ANDROGENS

ANDROGENS

- Production is driven by ACTH.
- DHEA (dehydroepiandrosterone) and DHEA sulfate are the primary adrenal androgens.
  - Converted to androstenedione, testosterone, and estrogen to exert androgenic effects.



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HYPERANDROGENEMIA: SYMPTOMS/SIGNS

- Males (few effects).
  - Acne.
  - Early puberty.
  - Decreased testes size, testicular testosterone secretion, and spermatogenesis (from inhibiting gonadotropins).
- Females.
  - Hirsutism.
  - Acne.
  - Male-pattern baldness.
  - Menstrual irregularities,
  - Infertility.
  - Virilization.

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ADRENAL HYPERANDROGENEMIA: CAUSES

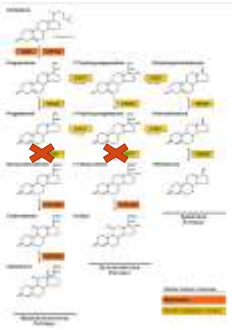
- Premature adrenarche.
- Adrenal adenoma/carcinoma.
- Bilateral macronodular adrenal hyperplasia.
- Congenital adrenal hyperplasia.
- ACTH-dependent Cushing's syndrome.
- Glucocorticoid resistance.

ADRENAL HYPERANDROGENEMIA: DIAGNOSIS

- Diagnosis
  - High DHEA-S > 500 mg/dL suggests adrenal tumor.
  - CT scan or MRI to localize adrenal tumor.
- Treatment
  - Surgery for adrenal tumor and Cushing's syndrome.
  - Glucocorticoid (and possibly mineralocorticoid) treatment for congenital adrenal hyperplasia.

CONGENITAL ADRENAL HYPERPLASIA

- Autosomal recessive disorders that involve a deficiency or relative defect in cortisol and/or aldosterone synthesis.



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CONGENITAL ADRENAL HYPERPLASIA

21-Hydroxylase Deficiency

- 90% of CAH cases.
- Aldosterone and cortisol deficiency.
- Increased androgens.
- Virilization in females.
- Precocious puberty in males.

NON-CLASSIC CAH

- "Late-onset" CAH.
- Production of normal amounts of cortisol and aldosterone at the expense of mild to moderate overproduction of sex hormone precursors.
- Variable degrees of androgen excess.
- Sometimes asymptomatic.

CONGENITAL ADRENAL HYPERPLASIA: DIAGNOSIS

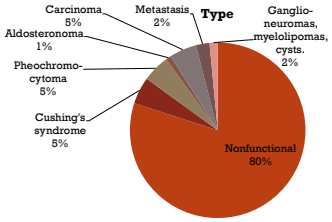
- Screening may involve a 17-OH progesterone check in the early morning (6 – 8 AM).
- Cosyntropin stimulation testing with checks of 17-OH progesterone and other steroid levels can confirm the diagnosis.

CONGENITAL ADRENAL HYPERPLASIA: TREATMENT

- Treatment for adrenal insufficiency is indicated in those with classic congenital adrenal hyperplasia.
- Symptomatic non-classic CAH can be treated with low-dose glucocorticoid therapy (i.e., dexamethasone 0.25 mg daily) or antiandrogen therapy (i.e., spironolactone).
- Goal is 17-OH progesterone between 400 – 1200 ng/dL and normal androstenedione.

ADRENAL ADENOMAS

ADRENAL INCIDENTALOMAS



EVALUATION

- Biochemical:
  - Cushing's syndrome screening.
  - Pheochromocytoma screening.
  - Hyperaldosteronism screening (only if history of hypertension).
  - DHEA-S (optional).
- Radiographic:
  - CT scan of adrenal glands.
    - On CT scan with contrast, < 10 Hounsfield units and wash out more than 50% on delayed scans strongly suggest a benign lesion.

TREATMENT AND FOLLOW-UP

- Surgery is indicated for adrenal mass > 4 cm (due to increased risk of cancer), functional mass, and adrenocortical carcinoma.
- For those not going to surgery:
  - CT scan should be repeated at 3 – 6 months and then annually for 1 – 2 years.
  - Hormonal evaluation should be performed annually for 5 years.

RESOURCES

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- Auchus, R. and J. Findling, *Primary Aldosteronism*, in *ENDO2011 Meet-The-Professor & Clinical Case Management Handouts*. 2011.
- Ayala, A., *Primary Hyperaldosteronism*. 2010.
- Ayala, A., *Syndromes Resulting from Increase Mineralocorticoid Action: Primary Aldosteronism and Related disorders*. **Section 4-5**: p. 857-865.
- Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, Husebye ES, Merke DP, Murad MH, Stratakis CA, Torpy DJ. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016 Feb;101(2):364-89.
- Catecholamine. Encylcopaedia Britannica. https://www.britannica.com/science/catecholamine. 2019.
- Chakera, A.J. and B. Vaidya, *Addison disease in adults: diagnosis and management*. Am J Med, 2010. **123**(5): p. 409-13.
- Cook, D.M., *Short and Long Term Issues in Postoperative Pituitary Assessment*, in *ENDO2010 Meet-The-Professor & Case Management Forum Handouts*. 2010.
- Cosman, F., et al., *Effects of teriparatide in postmenopausal women with osteoporosis on prior alendronate or raloxifene: differences between stopping and continuing the antiresorptive agent*. J Clin Endocrinol Metab, 2009. **94**(10): p. 3772-80.
- *Endocrine Secrets*. Fifth ed, ed. M.T. McDermott. 2009, Philadelphia: Mosby Elsevier. 573.
- Esposito D, Pasquali D, Johannsson G. Primary Adrenal Insufficiency: Managing Mineralocorticoid Replacement Therapy. J Clin Endocrinol Metab. 2018 Feb1;103(2):376-387.
- Farrugia FA, Martikos G, Surgeon C, Tzanetis P, Misiakos E, Zavras N, Charalampopoulos A. Radiology of the adrenal incidentalomas. Review of the literature. Endocr Regul. 2017 Jan 1;51(1):35-51.

RESOURCES

- Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, Stowasser M, Young WF Jr. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016 May;101(5):1889-916.
- Hamrahian, A.H. *Pituitary & Adrenal Disorders*. in *Cleveland Clinic Endocrine Board Review*. 2007.
- Kater, C.E., *Investigating Mineralocorticoid Hypertension*, in *ENDO2011 Meet-The-Professor & Clinical Case Management Handouts*. 2011.
- Katznelson, L., *Value of Medical Therapy before Pituitary Surgery*, in *ENDO2011 Meet-The-Professor & Clinical Case Management Handouts*. 2011.
- Lee, J., *Welcome to Adrenals*. 2009.
- Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, Naruse M, Pacak K, Young WF Jr; Endocrine Society. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014 Jun;99(6):1915-42.
- Mantero, F., *Benefits of Mineralocorticoid Antagonist Therapy*. 2011: Boston.
- Murphy, T.A. *Adrenal Dysfunction*. in *Cleveland Clinic Endocrine Board Review*. 2007.
- Newell-Price, J., *Controversies in Cushing Syndrome*, in *ENDO2011 Meet-The-Professor & Clinical Case Management Handouts*. 2011.
- Nieman, L., et al. *Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline.* J Clin Endocrinol Metab. 2015. **100**(8):p. 2807-2831.
- Nieman, L. and J. Newell-Price, *Cushing's Syndrome: Medical, Surgical and Other Options*, in *ENDO2010 Meet-The-Professor & Case Management Forum Handouts*. 2010.
- Nieman, L. and X. Bertagna, *Medical Treatment of Cushing Disease: Safety and Efficacy*, in *ENDO2011 Meet-The-Professor & Clinical Case Management Handouts*. 2011.

RESOURCES

- Papanicolaou, D., *Cushing's Syndrome*. 2010.
- Simon, D.R. and M.A. Palese, *Clinical update on the management of adrenal hemorrhage.* Curr Urol Rep, 2009. **10**(1): p. 78-83.
- Siraj, E.S. *Endocrinology Board Review*. in *Cleveland Clinic Endocrine Board Review*. 2007.
- Speiser, P.W., et al., *Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline.* J Clin Endocrinol Metab, 2010. **95**(9): p. 4133-60.
- Stowasser, M., et al., *Laboratory investigation of primary aldosteronism.* Clin Biochem Rev, 2010. **31**(2): p. 39-56.
- Young, W.F. *Board Review: Endocrine Hypertension*. in *Cleveland Clinic Endocrine Board Review*. 2007.
- Young, W.F., *Endocrine Hypertension: Then and Now.* Endocr Pract, 2010: p. 1-52.
- Young, W., et al., *Endocrine Self-Assessment Program*. 2010.
- Young, W., et al., *Endocrine Self-Assessment Program*. 2011.
- Young, W.F., *Invasive Dynamic Endocrine Testing*. 2011.
- Young, W.F., *Primary Aldosteronism*, in *ENDO2010 Meet-The-Professor & Case Management Forum Handouts*. 2010.
- Young, W.F., *Work-up of Primary Aldosteronism*. 2011: Boston.
- Zennaro, M.C., M. Caprio, and B. Feve, *Mineralocorticoid receptors in the metabolic syndrome.* Trends Endocrinol Metab, 2009. **20**(9): p. 444-51.