**Adrenal Disorders in Pediatrics**

Adrenal Gland Physiology:

* + Embryology:
    - Cortex: mesodermal origin. Medulla: neuroectoderm origin (week 8 of gestation)

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| **Anatomy**  Located on top of the upper pole of each kidney | **Adrenal Hormone** | **Function** |
| **Cortex** | | |
| Zona Glomerulosa | *Mineralocorticoid*  Aldosterone | ***SALT***  -Regulate renal retention of sodium and excretion of potassium  -Regulated by renin-angiotensin axis |
| Zona Fasiculata | *Glucocorticoids*  Cortisol | ***SUGAR***  -Stimulate gluconeogenesis, lipolysis, and protein catabolism-Increase excretion of free water  -Anti-inflammatory |
| Zona Reticularis | *Androgens*  DHEA, DHEA-S, Androstenedione | ***SEX***  -Induce virilization (pubic and axillary hair)  -Precursor hormones for extra-adrenal testosterone synthesis and extra-gonadal estrogen synthesis  -Important roles in bone mineralization |
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| **Medulla** | *Catecholamines*  Epinephrine and Norepinephrine | -“Fight or Flight” response to physiological stress  -Neuromodulator that mediate central and peripheral nervous system functions |

* **Adrenal Hyperfunction - Cortisol:**
  + Pertinent History and Exam Findings:
    - History: rapid weight gain, declining growth velocity, headache, fatigue, delayed/arrested puberty, acne, nocturia
    - Exam Findings: hypertension, acne, dorsocervical fat pad, central adiposity, violaceous striae, cushingoid facies, hirsutism
  + Work Up:
    - Initial Screening Labs and Referral to Endocrinology: midnight salivary or serum cortisol, 24 urine free cortisol (with creatinine) level, 1 mg Overnight Dexamethasone suppression test
  + Interpretation of Laboratory Findings**:**
    - Midnight Serum Cortisol level of > 7.5 mcg/dL x 2
    - Midnight Salivary Cortisol > 0.13 mcg/dL x 2
    - 24 hour Urine free cortisol: >70 mcg/m2/day (>3 times the upper limit of normal)
    - Dexamethasone Suppression Test: Cortisol > 1.8 mcg/dL (95% sensitive, 90% specific)
  + Differential Diagnosis**:**
    - Cushing Syndrome: Hypersecretion of cortisol from adrenal glands
      * Adrenal Adenoma, carcinoma, multinodular adrenal hyperplasia, Ectopic ACTH Syndrome
    - Cushing Disease: Pituitary overproduction of ACTH
      * Pituitary Microadenoma or Macroadenoma
      * Ectopic CRH
    - Conn Syndrome: Primary Hyperaldosteronism
    - Virilizing and Feminizing Adrenal Tumors: Androgen excess
* **Adrenal Hypofunction:**
  + Pertinent History and Exam Findings:
    - History: fatigue, weight loss, nausea, vomiting, abdominal pain, weakness, salt craving, headaches, hyperpigmentation, hypoglycemia (pallor, seizure)
    - Exam Findings: hypotension; hyperpigmentation of gums, palmar creases, areolae, and scrotum
  + Work Up:
    - Initial Screening Labs (sent by primary provider): sodium, potassium, glucose, cortisol (7-8 AM), ACTH, Plasma Renin Activity (PRA)
    - Other tests to consider after consultation with pediatric endocrinologist: ACTH stimulation test, 17-OH Progesterone, DHEA-S, adrenal autoantibodies (Anti-CYP11, 21-hydroxylase Ab), very-long chain fatty acids
  + Interpretation of Laboratory Findings: 8 AM Cortisol level <5 mcg/dL (5-10 mcg/dL require further work up with stimulation test)
    - ACTH:
      * Primary AI: >200 pg/mL
      * Secondary AI: <50 pg/mL
    - Electrolytes (can be normal):
      * Primary AI: K+ (high), Na+ (low), Aldosterone (low), glucose (low)
      * Secondary AI: Na+ (low or normal)
    - 17-Hydroxyprogesterone
      * Primary: Normal (Autoimmune), High (Defects of steroid biosynthesis)
      * Secondary: Normal
    - PRA:
      * Primary AI: high
      * Secondary AI: Normal
    - ACTH Stimulation Test: 60 minute cortisol value <18 with a delta change from baseline of <10
  + Differential Diagnosis:
    - Primary (Disease of the adrenal cortex):
      * Autoimmune: Isolated vs. Autoimmune Polyglandular Syndrome (APS 1, APS 2, APS 4, IPEX)
      * Acquired: Hemorrhage, infection, infiltration, medications (etomidate)
      * Defects of steroid biosynthesis: Congenital adrenal hyperplasia, Congenital lipoid adrenal hyperplasia
      * Adrenal Dysgenesis: Adrenal Hypoplasia Congenita, SF-1 deficiency, Pallister- Hall syndrome
      * Metabolic and Cholesterol disorders: X-linked adrenoleukodystrophy, Wolman disease, Smith-Lemli Opitz, Kearns-Sayre
    - Secondary (Disorder of ACTH):
      * Hypopituitarism
      * ACTH Deficiency
      * Familial glucocorticoid deficiency/ ACTH resistance
      * Iatrogenic