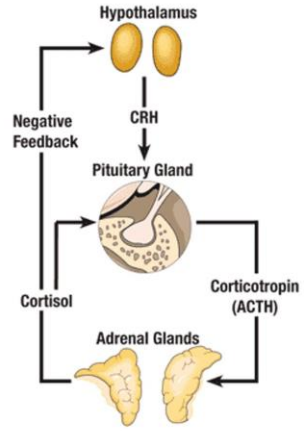
Quick Guide to Hypoadrenocorticism (Addisons)

I. Physiology Review

- **a.** Cortisol and aldosterone are produced in adrenal cortex
- **b.** Cortisol
  - **i.** Functions
    1. Carbohydrate, lipid, and protein metabolism
    2. Modulation of immune function
    3. Ensure proper production of catecholamines and function of adrenergic receptors
  - **ii.** Concentration determined by negative feedback of the hypothalamic-pituitary-adrenal axis
  - **iii.** Hypothalamus produces CRH causing anterior pituitary to produce ACTH
  - **iv.** ACTH stimulates zona fasciculata and zona reticularis to produce and release cortisol

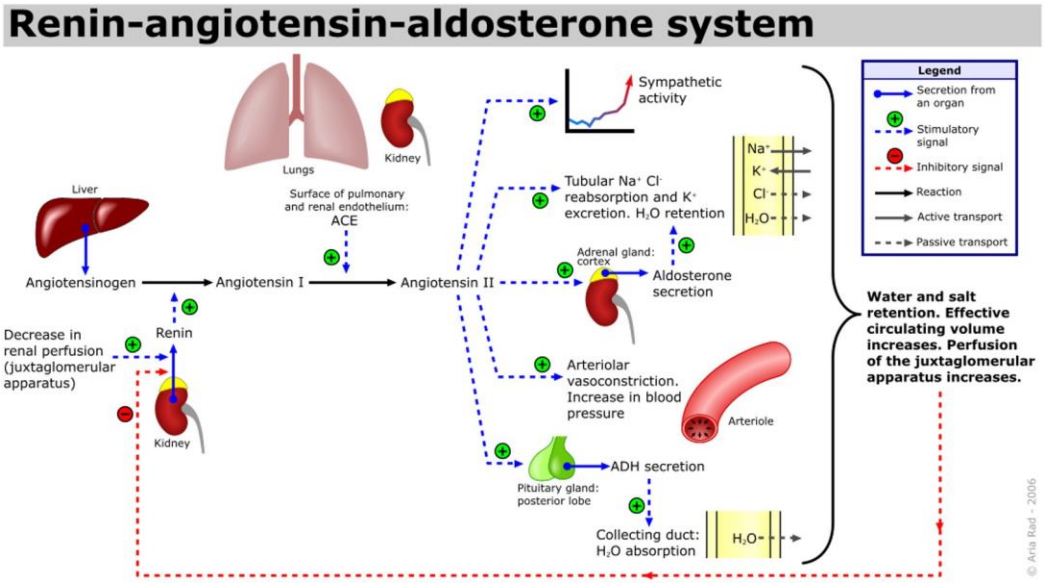
Figure 1. Normal function of hypothalamic-pituitary-adrenal axis.



CRH: corticotropin-releasing hormone.

- **c.** Aldosterone
  - **i.** Released from zona glomerulosa
  - **ii.** Maintains normovolemia and increases potassium excretion
  - **iii.** Hypovolemia results in Renin release which then results in Angiotensin II causing aldosterone release

iv. Aldosterone results in Na+2 reabsorption and K+ excretion in collecting ducts of kidneys



II. Hypoadrenocorticism

a. Primary- adrenal cortical dysfunction, glucocorticoid and mineralocorticoid deficiency
b. Secondary- hypothalamic or pituitary dysfunction resulting in decreased release of CRH or ACTH
    i. Mineralocorticoid deficiency may develop with in weeks or months of secondary diagnosis
c. Clinical Presentation
    i. History
        1. Vague and nonspecific, decreased appetite, lethargy, vomiting, diarrhea, hematochezia, melena, weight loss, polyuria, polydipsia, weakness
    ii. Physical Exam
        1. Poor body condition and coat
        2. Abdominal pain
        3. Dehydration
        4. Collapse
        5. Hypovolemic shock
        6. Bradycardia
        7. Hypothermia
        8. Evidence of GI bleeding
d. Potential Laboratory Findings
    i. Hyponatremia and hyperkalemia
        1. Ratio of <27:1 is highly suspicious

2. Total values may be normal but ratio is Abnormal
3. Ratios of <24:1 are very specific

ii. Azotemia
iii. Decreased urine specific gravity
1. Indicate mineralocorticoid deficiency
iv. Hypoglycemia
v. Patients with secondary hypoadrenocorticism (glucocorticoid deficiency alone) lack electrolyte changes
vi. Hypercalcemia
vii. Hypoalbuminemia
viii. Hypocholesterolemia
ix. Complete blood count
1. Mild to moderate non-regenerative anemia
2. Anemia maybe masked by dehydration and hemoconcentration
3. Lack of stress response
a. Neutropenia, lymphocytosis, and eosinophilia

e. Electrocardiographic Findings
i. Bradycardia
ii. Diminished or absent P waves
iii. Spiked T waves
iv. Wide QRS complexes
v. PR interval prolongation
vi. Ventricular Fibrillation
vii. Asystole

f. Imaging
i. Radiograph findings
1. Microcardia
2. Decreased size of pulmonary vasculature
3. Small vena cava
4. Microhepatica
ii. Ultrasound
1. Small or absent adrenal glands

III. Diagnosis

a. ACTH Stimulation Test
i. Protocol 1
1. Obtain resting cortisol
2. Administer Cosyntropin IV or IM – 250mcg/dog or 125mcg/cat
3. Post blood sample collection
a. Dogs – post injection 60 minutes
b. Cats – post injection 30 and 60 minutes
ii. Protocol 2 (Dogs)

1. Obtain resting cortisol
2. Administer 5mcg/kg IV
3. Post injection blood sample at 60 minutes

iii. ACTH quantification
1. Helps in differentiating primary vs. Secondary

IV. **Treatment**

a. Fluid Therapy
i. **Correct hypovolemia** or effective circulating volume
1. Administer balanced electrolyte solution (LRS, Plasmalye, Norm-R)
2. **20-40 ml/kg in dogs**
3. **10-20 ml/kg in cats**
4. Reassess perfusion parameters
5. Correcting hypovolemia improves GFR and improves azotemia and promotes kaliuresis (reducing K+)

ii. Ongoing fluid therapy is based on maintenance needs, dehydration deficits, and ongoing loses

b. Hormone replacement
i. Ideally ACTH stimulation and endogenous ACTH testing done prior
ii. Glucocorticoid Supplementation during crisis
1. **Dexamethasone 0.1 mg/kg IV bolus followed by 0.05 mg/kg q12h until can transition to oral prednisone**
2. **Hydrocortisone 1.25 mg/kg IV followed by 0.5 to 1.0 mg/kg q6h until transitioned to oral prednisone**
3. **Oral Prednisone**
a. **0.5 to 1.0 mg/kg daily tapering until lowest possible dose most patients require 0.25 mg/k q48 to 72 hours**

iii. Mineralocorticoid Supplementation
1. **Deoxycorticosterone pivalate (DOCP) administered 1.1 to 2.2 mg/kg IM, SQ**
2. Typically q25 to 28 days
3. Can sometimes be stretched out to q 6 to 8 weeks
4. Recheck electrolytes in 14 days, then every 14 days until ratio starts to decrease or patient develops PU/PD

c. Hyperkalemia
i. Consider treatment when >6.5 mEq/L or ECG abnormalities
ii. Fluid Therapy
iii. DOCP administration
iv. Calcium gluconate or Calcium chloride
1. **50 to 100 mg/kg IV**
2. Restores membrane excitability

v. Insulin and Dextrose

1. **Regular Insulin 0.25 to 0.5 u/kg IV and 1 to 2 gram dextrose per unit administered**

vi. Sodium Bicarbonate

1. **1 mEq/kg IV**

d. Hypoglycemia

i. Dextrose 0.5 to 1 g/kg IV

e. GI disturbances

i. Acid reducers

1. PPI preferred over H2 antagonists
2. Omeprazole/Pantoprazole 1 mg/kg
3. Famotidine 1 mg/kg q12h

ii. Anti-emetics

1. Maropitant 1 mg/kg q24h
2. Dolasetron 0.6 to 1 mg/kg q24h
3. Ondansetron 0.1 to 1 mg/kg q8h

iii. Pro-kinetics

1. Metoclopramide 0.4 to 0.5 mg/kg q8h IM, SQ or CRI at 1-2 mg/kg/day

f. Antibiotics

i. Consider broad spectrum antibiotic therapy for patients with evidence of shock on presentation with persistent GI signs

1. Ex: 1st generation cephalosporin, ampicillin