

Suspected relative adrenal insufficiency in a critically ill cat

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Key Points

- The specific mechanism for the development of RAI is unclear, and is likely multifactorial, but may include elevated cytokine levels and other inflammatory mediators
- Sepsis Case and systemic inflammatory response syndrome (SIRS) are the most common underlying causes of RAI
- Eosinophilia is uncommon in critically ill patients, but if present should raise the index of suspicion for RAI

Case Summary

- **8y MC DSH**
- **HBC**
- **rDVM x2d**
 - **Laterally recumbent, severe degloving wound RF, generalized abrasions**
 - **RR: 60bpm, HR 200 bpm, T 97.6F**
 - **PCV: 24%, TS 6.0g/dL**
 - **IVF, cefazolin (22mg/kg IV q8h), butorphanol 0.2mg/kg IV q4h, O₂, active warming (circulating water blanket)**
- **Referred for management of anemia and wounds**
 - Quiet, responsive
 - T: 102.3F, R 220bpm, RR: 36bpm
 - **BP; Doppler 76mmHg**
 - **PCV: 17%, glu: 190mg/dL, lac 5.9mmol/L, hyponatremia 143 mEq/L, hypochloremia 104mmol/L**
 - **Leukocytosis with band neutrophils and toxic changes**
 - Hyperbilirubinemia, inc ALT/AST
 - Concentrated urine, bilirubinuria
 - PT: n, aPTT 144 (70-120s)
 - TxR: microcardia, poss consistent with hypovolemia
 - AUS: severe body wall thickening, otherwise wnl (adrenals not visualized)
 - **Admitted to ICU**
 - **25mL/kg 0.9% NaCl bolus, then 4mL/kg/hr**
 - **pRBC: 1 unit, type-specific**

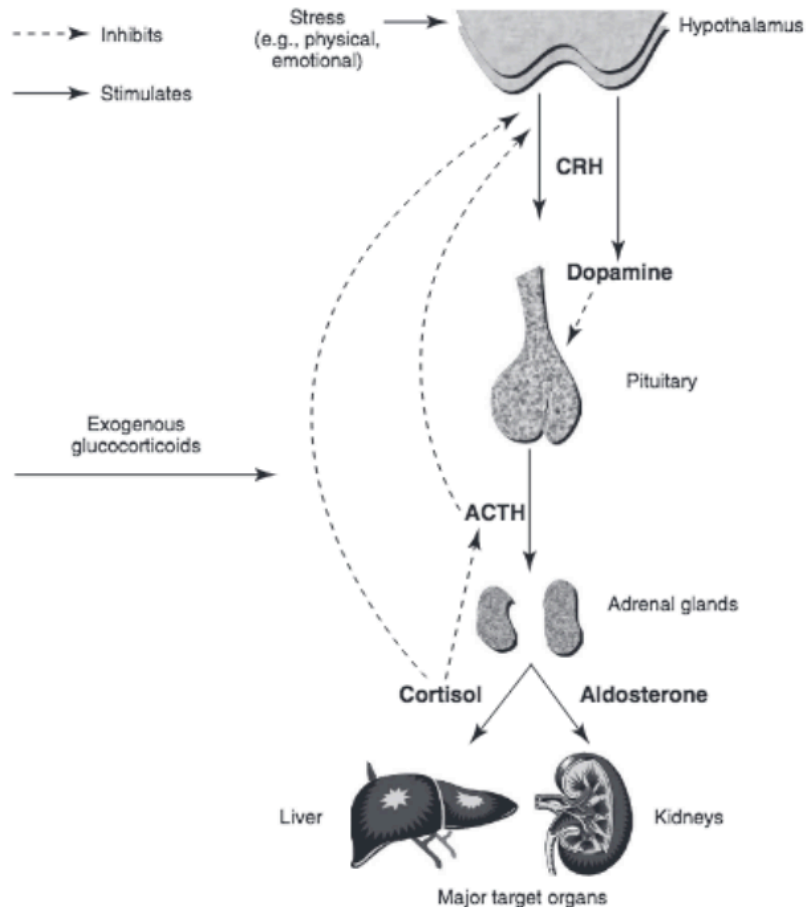
- **Buprenorphine 0.01mg/kg IV q6h**
- **BP -> 120mmHg, HR -> 180bpm. T -> 99.5F**
- Propofol sedation (4mg/kg IV): wound care, urinary cath
- Cefazolin, enrofloxacin
- **Demeanor improved x2d**
- **Day 3: caudal abd pain: body wall hernia, with bowel and u bladder entrapment**
- **PCV: 22%, TS 5.0g/dL, PT/aPTT: n**
- Hydromorphone, midazolam, ketamine: prepubic tendon rupture. Liver biopsy obtained, jug cath and e-tube placed
- **Intraop: Doppler BP <70mmHg despite 42mL/kg LRS. Dopamine (6-12mcg/kg/min), titrated to BP >70mmHg**
- **Postop: dopamine 10mcg/kg/min, IVF to maintain CVP 8-10cmH2O, PCV 18%, TS 4.5g/dL, FFP 6mL/kg IV**
- **ACTH stim, dexamethasone 0.08mg/kg IV (pred 0.5mg/kg equivalent)**
- **BP 'rapidly' improved and dopamine d/c. 24h post-dexamethasone, BP 150mmHg without dopamine**
- **Uneventful recovery**
- **Day 4: PCV/TS 19%/4.2g/dL. CBC: WBC 14.4k/mL with eosinophilia. Toxic changes present. Icteric plasma.**
- Liver biopsy: moderate to severe canalicular cholestasis, mild multifocal hepatocellular necrosis, and mild diffuse hepatocellular vacuolar change
- **Pred tapered over 2w. Full recovery at home**

Question:

1. Describe an ACTH stim suggestive of RAI.
 - Diagram the hypothalamic-pituitary-adrenal axis, and what the ACTH stim is assessing.

Answers:

1. Describe an ACTH stim suggestive of RAI in felines.
 - a. Normal range baseline cortisol levels
 - b. Post-stimulation sub-reference range cortisol levels
 - c. (post-stimulation cortisol change (Δ cortisol) of $<9\text{mg/dL}$ -- humans)
 - d. Post recovery and cessation of prednisone normal ACTH stim
2. Diagram the hypothalamic-pituitary-adrenal axis, and what the ACTH stim is assessing.



- a. Assessing response of the adrenal glands to synthetic ACTH administration

Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: Consensus statements from an international task force by the American College of Critical Care Medicine

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Objective

- To develop consensus statements for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients

Participants

- A multidisciplinary, multispecialty task force of experts in critical care and international experts in endocrinology

Design/Methods

- Review of published literature and expert opinion
- The strength of each recommendation was quantified using the Modified GRADE system
 - Classifies recommendations as strong (grade 1) or weak (grade 2) and the quality of evidence as high (grade A), moderate (grade B), or low (grade C) based on factors that include the study design, the consistency of the results, and the directness of the evidence

Results

- Critical illness-related corticosteroid insufficiency (CIRCI): the dysfunction of the hypothalamic-pituitary-adrenal axis that occurs during critical illness
- CIRCI is caused by adrenal insufficiency together with tissue corticosteroid resistance and is characterized by an exaggerated and protracted proinflammatory response
- CIRCI should be suspected in hypotensive patients who have responded poorly to fluids and vasopressor agents, particularly in the setting of sepsis
- Diagnosis of tissue corticosteroid resistance remains problematic
 - Adrenal insufficiency in critically ill patients is best made by a Δ total serum cortisol of $<9\text{g/dL}$ after ACTH administration or a random total cortisol of $<10\text{g/dL}$
- The benefit of treatment with glucocorticoids at this time seems to be limited to patients with vasopressor-dependent septic shock and patients with early severe acute respiratory distress syndrome ($\text{PaO}_2/\text{FIO}_2$ of <200 and within 14 days of onset)
- ACTH stim should not be used to identify those patients with septic shock or acute respiratory distress syndrome who should receive glucocorticoids
- Hydrocortisone (200 mg/day, four divided doses -or- as a CRI of 240 mg/day for >7 day for septic shock

- Methylprednisolone (1mg/kg/day for >14 days is recommended in patients with severe early acute respiratory distress syndrome)
- Glucocorticoids should be weaned and not stopped abruptly
- Reinstitution of treatment should be considered with recurrence of signs of sepsis, hypotension, or worsening oxygenation
- Dexamethasone is not recommended to treat CIRCI
 - Leads to immediate and prolonged suppression of the HPA axis (limiting the value of ACTH testing)

Background

- Severe illness and stress strongly activate the hypothalamic-pituitary-adrenal (HPA) axis and stimulate the release of ACTH from the pituitary, which in turn increases the release of cortisol from the adrenal cortex
- This is an essential component of the general adaptation to illness and stress and contributes to the maintenance of cellular and organ homeostasis
- Adrenalectomized animals succumb rapidly to hemorrhagic and septic shock, and steroid replacement is protective in these situations
- Adrenal failure is reported with increasing frequency in critically ill patients with septic shock, severe community-acquired pneumonia, trauma, head injury, burns, liver failure, HIV infection, pancreatitis, after cardiac surgery, after the use of etomidate, and in brain-dead organ donors
 - May be associated with structural damage to the adrenal gland, pituitary gland, or hypothalamus
 - However, many critically ill patients develop reversible failure of the HPA axis
- Diagnosis and management of this disorder remains controversial, with poor agreement among the experts