Endocrine Crises

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Endocrine Crises

- Rare
- Highly lethal
- Elusive
- Easily treatable
Outline

1. **Thyroid**
   1. Thyroid storm
   2. Myxedema coma

2. **Parathyroid**
   1. Severe hypercalcemia secondary to 3° hyperparathyroidism

3. **Adrenal**
   1. Addisonian crisis
   2. Steroids in septic shock
   3. Pheochromocytoma crisis
Thyroid Hormone Physiology

- **Tyrosine**
  - Monoiodotyrosine (MIT)
  - Diiodotyrosine (DIT)

- **Thyroid peroxidase**
- **Dietary Iodide**
- **PTU**
- **NaI**
- **Steroids**

- **Thyroid**
- **Peripheral tissues**
  - $T_4$
  - $T_3$
Thyroid Storm

- Exacerbation of hyperthyroidism in response to metabolic stress (e.g., trauma, surgery, critical illness)

- First recognized during thyroidectomy in unprepped Grave’s patients

- Uncommon

- Life-threatening (mortality 20%)
Thyroid Storm
Classic Presentation

• Fever (106°F)

• Abnormal mental state (anxiety – coma)
  – Diagnosis unlikely if normal mentation

• High-output cardiac failure: Tachyarrhythmias, CHF

• GI distress

• TSH undetectable; T3 > T4

• ↑ WBC, LFTs, calcium, glucose
Thyroid Storm
Atypical Presentations

• Normothermia, normoglycemia, lactic acidosis, MODS

• Elderly: Apathetic storm; weakness and emotional apathy
Thyroid Storm
Treatment

• **Prevention**
  – Adequate preparation of patient undergoing surgery for hyperthyroidism
  
  – Best indicator of appropriate preparation for surgery: TSH
  
  – T3 is the most important number to assess in patients who require surgery relatively quickly
Thyroid Storm  
Treatment  

- **Inhibit hormone synthesis**: PTU 1000 mg load then 300 mg PO q6H  
- **Blunt end-organ effects**: Beta blocker: Propranolol vs. esmolol 250 mcg/kg load then 50 mcg/kg/min  
- **Inhibit hormone release**: NaI 500 mg IV q8h  
- **Inhibit peripheral conversion**: Dexamethasone 2 mg q6  
- Treat precipitating problem
Myxedema Coma

• Exacerbation of hypothyroidism in response to metabolic stress (e.g., trauma, surgery, critical illness)

• Long-standing, neglected, untreated hypothyroidism

• Uncommon (1:1,000,000); Predominantly elderly women presenting in the winter

• Life-threatening (mortality 50%)

• Sunitinib (Sutent)
Myxedema Coma
Symptoms/Diagnosis

- Hypothermia $T<35^\circ C$
- Disorientation $\rightarrow$ coma
- Non-pitting total body edema
- Macroglossia
- Ileus
- Bradycardia $\rightarrow$ heart block
- Free $T_4 < 10$ mcg/dL
- TSH usually increased but unreliable ($1^\circ$ vs. $2^\circ$ hypothyroidism)
- Anemia, hyponatremia, hypoglycemia
Myxedema Coma

Treatment

• Levothyroxine (T₄)
  – Bolus 100-500 mcg IV
  – Maintainence 50-100 mcg until symptoms resolve

• Support organ failure

• Coexisting glucocorticoid deficiency common (~33%); give steroids
Sick Euthyroid Syndrome

- ? Pathologic vs. adaptation to critical illness

- Progressive, sub-acute deterioration of thyroid function

- Early: decreased peripheral conversion of T4 → T3, usually iatrogenic (medication induced)

- Late: Reduced concentrations of TSH, T4, & T3

- Treatment unclear
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GUT-mediated Ca\textsuperscript{2+} absorption

KIDNEY
- Activation of VitD
  - \( \uparrow \text{Ca}^\text{2+} \) resorption
  - \( \downarrow \text{PO}_4\text{2-} \) resorption

PTH

BONE
Stimulate osteoclasts

PO\textsubscript{4}\textsuperscript{-2}

Vit D

Ca\textsuperscript{2+}

PO\textsubscript{4}\textsuperscript{-2}

Ca\textsuperscript{2+}

Ca\textsuperscript{2+}

PO\textsubscript{4}\textsuperscript{-2}
Hyperparathyroidism

- **Primary**: Pathology originates within the parathyroid gland(s); Adenoma (85%), hyperplasia (15%), carcinoma (1%).

- **Secondary**: Overzealous response to hypocalcemia of non-parathyroid etiology, most commonly renal failure. Resolves with resolution of non-parathyroid pathology.

- **Tertiary**: Chronically stimulated gland(s) develop autonomous function despite resolution of non-parathyroid pathology. *Severe hypercalcemia*
Life-threatening tertiary hyperparathyroidism in the critically ill

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Presented at the 47th Annual Meeting of the Midwest Surgical Association, Mackinac Island, Michigan, August 15–18, 2004

- Shock → fluid sequestration → hypoprotienemia, hypocalcemia
- Acute renal failure → ↓ Vit D hydroxylation, ↓ Ca reabsorption
- Secondary → tertiary hypoparathyroidism with severe hypercalcemia
- Presents as refractory hypercalcemia, bradycardia, asystole
Severe Hypercalcemia

Treatment

• **Volume Expansion**

• **Diuresis**
  – urine output ~ 250ml/hr
  – Begin only after adequate hydration has been achieved

• **Definitive therapy = bisphosphonates**
  – Pamidronate 90 mg IV (maximal effect takes 72 hours).
Adrenal Insufficiency

- Common in critical illness (as high as 77% in septic shock)

- **Etiology**
  - Iatrogenic
    - Persists for over a year
  - Infection (Sepsis)
    - Suppression
    - Destruction via massive adrenal hemorrhage (Waterhouse-Friderichsen Syndrome)
  - Trauma
Adrenal Insufficiency
Diagnosis

• Hypotension despite adequate fluid resuscitation and vasopressor therapy

• Hypoglycemia, hyponatremia, hyperkalemia

• **Biochemical Assays:**
  – Random cortisol < 20 mcg/dL
  – Cortisol stimulation test: increase < 9 mcg/dL
  – Free vs. total
  – Etomidate suppresses HPA axis
Adrenal Insufficiency

Treatment

• Hydrocortisone 200-300 mg /day

• Do not wait for the labs to come back

• Probably don’t need to taper if < 7 days

• ? retest after steroids discontinued
Steroids in Septic Shock
Where do we stand?

• **Annan et al. JAMA 2002**
  – Hypotension for 1 hour despite adequate fluid resuscitation and vasopressor therapy
  – Randomization within 3 hours of shock onset
  – Hydrocortisone 50 mg IV q6, fludrocortisone 50 mcg IV qD x 7 days
  – 300 patients, 77% non-ACTH responders
  – Significant mortality reduction overall (61% vs. 55%), driven by non-responders (63% vs. 53%).
Steroids in Septic Shock
Where do we stand?

• **Sprung et al. NEJM 2008**
  – Need for vasopressor for at least 1 hour
  – Randomization within 72 hours of shock onset
  – Hydrocortisone 50 mg IV q6 x 5 days, then tapered
  – 500 patients, 47% non-ACTH responders
  – No mortality reduction (~35%/group) *regardless of response to ACTH-stimulation.*
  – More superinfection in the steroid group
Steroids in Septic Shock
Where do we stand?

• Surviving Sepsis Guidelines 2008

7. We recommend that corticosteroids not be administered for the treatment of sepsis in the absence of shock. There is, however, no contraindication to continuing maintenance steroid therapy or to using stress-dose steroids if the patient’s endocrine or corticosteroid administration history warrants (grade 1D).
Catecholamine Synthesis

Tyrosine

Thyroid hydroxylase

Dopamine

Norepinephrine

Adrenal Medulla

Epinephrine

PNMT

Urine

Normetanephrine

VMA

Metanephrine

Any Chromaffin Tissue

STEROIDS
Pheochromocytoma Crisis

- Rapid, massive release of catecholamines resulting in cardiovascular collapse
- More often triggered vs. spontaneous
  - Stressor (e.g., trauma, surgery, anesthesia, critical illness)
  - Medications
    - Glucocorticoids
    - Beta blockers
Pheochromocytoma Crisis
Diagnosis

• Classically, HTN with triad of headache, palpitations, diaphroresos

• Cardiogenic shock/myocardial ischemia
• Pulmonary edema, respiratory failure
• Rhabdomyolysis/renal failure
• Tachyarrythmias

• Elevated 24-hour urine metanephrines/VMA
• Plasma metanephrine/normetanephrine
Pheochromocytoma Crisis

Treatment

• Volume expansion
• Alpha blockade
• Beta blockade
• Surgical extirpation
Perioperative Stress Dose Steroids: Do They Make a Difference?

Carl J Brown, MD, W Donald Buie, MD, FRCSC, FACS
Perioperative Stress Dose Steroids: Do They Make a Difference?

Carl J Brown, MD, W Donald Buie, MD, FRCSC, FACS

- Increased circulating cortisol helps maintain hemodynamic stability in the face of surgical stress
- Patients treated with long term exogenous steroids have a blunted HPA response to surgical stress
- Case reports have led to the longstanding (>50 years) surgical tenant of “stress dose steroids.”
Risks of Corticosteroids

- Infection
- Hyperglycemia
- Impaired wound healing
- Psychosis
- Pancreatitis
- Neuromuscular atrophy
Perioperative Stress Dose Steroids: Do They Make a Difference?

Carl J Brown, MD, W Donald Buie, MD, FRCSC, FACS


- Original research focusing on human patients treated with steroids who were undergoing an operative procedure.

- One outcome measure had to be blood pressure.

- Methodological quality assessed using the Heyland Criteria.
Perioperative Stress Dose Steroids: Do They Make a Difference?

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- 4,243 → 11 articles
- Variable patient populations, extent of surgery, definitions of outcomes
- 2/11 randomized
Perioperative Stress Dose Steroids: Do They Make a Difference?

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- 2/11 (n=89 & 104): Steroids *withheld* in the perioperative period
  - 2% required rescue steroids for refractory hypotension
- 2/11 (n=18 & 20): Randomized to stress dose vs. pre-operative dose
  - Cardiac and renal transplantation
  - All patients had adrenal suppression (ACTH stim test)
  - No difference in outcomes (BP, HR, hypotensive crisis)
Perioperative Stress Dose Steroids: Do They Make a Difference?

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- 3/11 (n=21, 28, & 84): Followed patients maintained on pre-operative doses
  - No adverse consequences

- 1/11 (n=61): Non-randomized single stress dose vs. pre-operative dose
  - No difference in need for a rescue dose to treat unexplained hypotension
Perioperative Stress Dose Steroids: Do They Make a Difference?

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- **GRADE C**: All patients treated with corticosteroids should be treated with perioperative glucocorticoids at the time of operation.

- **GRADE B**: Patients should be maintained on their preoperative daily dose of steroids throughout the perioperative period.

- Authors are currently conducting an adequately-powered RCT involving IBD patients.