Steroid Use in Veterinary Emergency and Critical Care

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Types of Steroids

- Corticosteroids → glucocorticoids
- Mineralocorticoids
- Anabolic-androgenic steroids (Anabolic)

Glucocorticosteroids

- Produced in the cortex of adrenal glands
- Cortisol (hydrocortisone) most common endogenous glucocorticoid
  - Catabolic steroid
  - Breakdown proteins
- Exogenous glucocorticoids given for disease
  - More potent than cortisol (Prednisone, Dexamethasone, etc)
- 10% of circulating cortisol free
  - Remaining bound to plasma proteins
    - Corticosteroid-binding globulin (transcortin)
- All body cells contain glucocorticoid receptors
  - Massive physiologic response
Glucocorticoid Effects on Metabolism

- Stimulates gluconeogenesis → liver
  - Lipids
  - Amino acids
- Stimulates amino acid production
  - Extrahepatic tissue
    - Substrates for gluconeogenesis
- Inhibits glucose uptake → muscle and adipose tissue
- Promotes glucose conservation
- Promotes fat → adipose tissue
  - Lipolysis → fatty acids for energy production
  - Glycerol released → substrate gluconeogenesis

Glucocorticoid Effects on Inflammation

- Potent anti-inflammatory
- Glucocorticoids reduce expression of
  - Cytokines
  - Chemokines
  - Adhesion molecules
  - Other inflammatory proteins
  - Prevent recruitment of inflammatory cells to sites of inflammation
- Glucocorticoids promote cell proptosis
  - Inflammatory cells
- Bind glucocorticoid receptor (GR)
  - GR up-regulates expression anti-inflammatory proteins
    - Transactivation
    - Represses expression of pro-inflammatory cytokines
    - Transrepression

Glucocorticoid Effects on Immunity

- Glucocorticoids suppress the immune system
  - Retard healing
- Suppress cells that promote immune response
  - Mediators (cytokines)
  - Proteins (adhesion proteins)
- Suppress cell-mediated immunity
  - Inhibit genes code for cytokines
    - Interleukin 1-6, 8-10
    - IFNg
- Suppress humoral immunity
  - B cells → smaller amounts IL-2 and IL-2 receptors
  - Diminish B cell clone expansion
  - Antibody synthesis
  - Fewer IL-2 → fewer T-lymphocytes cells active
- Glucocorticoid-induced proptosis
Mineralocorticoids

- Produced in the cortex of adrenal glands
  - Just like glucocorticoids!
- Aldosterone is primary endogenous mineralocorticoid
- Glucocorticoids circulate approximately 100x more than mineralocorticoids
- Used in the maintenance of minerals in the body
  - Sodium [Na+]
    - Passive potassium [K+] secretion
- Due to affect on minerals $\Rightarrow$ affects body fluid content
  - Retention of sodium $\Rightarrow$ retention of fluids

The Androgen Group- Anabolic Steroids

- Sex hormones
  - Testosterone
  - Estrogen
  - Progesterone
- Anabolic steroid
  - Build up of proteins
- Often used in reproduction
  - Small and large animal
- Can be used to treat incontinence in spayed females
- Not used in Emergency and Critical Care Medicine

When to use Glucocorticoids

- Prescribed often for chronic disease process
  - Asthma, IBD, etc
- Used in acute onset of severe inflammation
  - Anaphylaxis $\Rightarrow$ sometimes!
  - Asthma
  - Immune-mediated disease process
  - Brachycephalic Syndrome
  - Used in severe lack of glucocorticoids
  - Addison’s disease
- Used in refractory septic cases
  - CIRCI patients
Glucocorticoids in Anaphylaxis

- **Anaphylaxis** → severe and profound Type 1 hypersensitivity reaction
  - **Symptoms**
    - Tachycardia, hypotension, and bronchospasm
  - **Mechanism**
    - Massive mediator release
- **Treatment of choice typically Epinephrine**
  - **Alpha 1 and 2 adrenergic receptors** → increase blood pressure and coronary perfusion
  - **Beta 1 adrenergic receptors** → positive inotropic and chronotropic cardiac effects
  - **Beta 2 adrenergic receptors** → reduce release of pro-inflammatory mediators
- **Crystalloids given IV**
  - **Maintain intravascular fluid volume**
- **Antihistamine (Diphenhydramine)**
  - **Decrease ongoing histamine release**
- **Glucocorticoids once cardiovascular collapse reversed**
  - **Help to control ongoing anaphylaxis**
    - **Persistent mediator release**

Feline Asthma

- **Typically an allergic response**
  - **Altered immunosensitivity of the respiratory tract**
    - **Hyperresponsiveness**
      - **Coughing**
      - **Wheezing**
      - **Expiratory dyspnea**
  - **Diagnosed via physical exam and clinical signs/symptoms**
- **Steroids given to treat the inflammation and hyperresponsive immune system**
  - **If tolerated well → steroids for the rest of the cat’s life**

Immune-Mediated Disease

- **Steroids strong immunosuppressive drugs**
- **Immune-Mediated disease → immune system out of control**
  - **Give immunosuppressive dose of steroids → prevents immune system from wreaking havoc**
- **Hundreds of immune-mediated diseases**
  - **Only a few seen through ECC**
    - **IMHA**
    - **ITP**
Immune-Mediated Hemolytic Anemia

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- IMMUNE-MEDIATED HEMOLYTIC ANEMIA (IMHA)
  - Body's own immune system attacking and destroying red blood cells
  - Destroyed red blood cells release hemoglobin → cause bilirubin release → icterus

  - Physical Exam
    - Tachycardia
    - Tachypnea
    - Pale/Icteric mucous membrane
  - Blood work
    - Decreased PCV/TP
    - Decreased platelet count
    - Decreased PCV/Tp
    - Possible coagulopathy → consumption of clotting factors

IMHA Treatment

- High majority of patients require pRBC transfusion
  - Often need multiple during hospitalization stay
- Oxygen therapy if anemia severe enough
  - No RBCs → no hemoglobin → no oxygen carrying capacity
- Crystalloids to help maintain intravascular volume
- Glucocorticoid steroids started → immunosuppressive dose
  - Commonly start short acting steroid → move to longer acting when patient stabilized
  - Often adjunct with immunosuppressive drugs (i.e. Cyclosporine, Mycophenolate)

Immune-Mediated Thrombocytopenia

- IMMUNE-MEDIATED THROMBOCYTOPENIA (ITP)
  - Immune system attacks and destroys the body's platelets
  - Patients at risk for spontaneous bleeding < 50k platelets

  - Physical Exam
    - Tachycardia
    - Tachypnea
    - Pale mucous membrane
  - Blood work
    - Chemistry may be normal
    - CBC
      - Decreased platelet count
        - little to no clumping
        - Confirm with differential
ITP Treatment

- Transfusions
  - pRBC transfusion
  - Often multiple transfusions required if patient continues bleeding
  - Platelet rich plasma transfusion
  - May bring up platelet count
  - Not always readily available
  - Whole blood transfusion
  - Contains both RBCs for anemia and platelets/clotting factors

- Oxygen therapy
  - Anemia → no oxygen carrying capacity
  - Immunosuppressive dose glucocorticoids
  - Suggestive the immune system to prevent further destruction of platelets
  - Adjunct with immunosuppressive drugs (i.e. Cyclosporine, Mycophenolate)

- Vincristine
  - Chemotherapy drug
  - Stimulation platelet release from bone marrow

Brachycephalic Syndrome

- Brachycephalic Syndrome can affect any brachycephalic breed
  - Pugs, English Bulldog, Pekingese, etc
- Dogs cool themselves off much via panting
- Brachycephalic breeds cannot pant well due to facial structure
- Brachycephalic syndrome occurs
  - Pet gets stressed or hot → starts panting but not enough to relax or cool itself off → pet gets MORE stressed and/or hot → pet pants more, cannot cool → cycle continues
  - Patients often develop laryngeal and pharyngeal edema due to excessive panting
  - Patients can overheat rapidly → temperatures > 105F easily

Brachycephalic Syndrome Treatment

- Oxygen support!
- If rectal temperature > 106.5F (may change with different literature) → actively cool with water and blankets → cool until rectal temperature reaches 103.5F → stop active cooling → monitor patient doesn’t become hypothermic.
- Patient may need sedation to break cycle!
  - Butorphanol often works very well
  - Acepromazine can be used as well
- Depending on severity intubation may be required → anesthesia necessary
  - Take over patient’s airway
- Low dose of short acting glucocorticoid helps reduce pharyngeal and laryngeal swelling
Glucocorticoids in Addisonian Crisis

- Addison’s Disease
  - Body doesn’t make enough glucocorticoid or mineralocorticoid steroids
    - Typically cortisol and aldosterone

- Patient’s present collapsed
  - Typically severely dehydrated
  - Lack of mineralocorticoids → lack of appropriate fluid retention
  - Often with GI disease (diarrhea)
  - Blood work for typical Addison’s
    - Elevated K+, decreased Na+
    - Hypoglycemia
    - Resting cortisol warranted

Glucocorticoids in Addisonian Crisis (con’t)

- Often administration of fast, short acting steroid
  - Dexamethasone Sodium-Phosphate often chosen
    - Treats the Glucocorticoid!!
      - Most common mineralocorticoid → desoxycorticosterone pivalate
    - Typically given after emergency situation is resolved

- Crystalloids given IV
  - Maintain fluid balance → replace losses → treat dehydration
  - Can give dextrose → hypoglycemia treated with glucocorticoid
  - Electrolytes treated with glucocorticoid

Glucocorticoids in CIRCI

- What is CIRCI??
  - Critical Illness-Related Corticosteroid Insufficiency

- As the name suggests → critically ill patients!
- Severe stress response → adrenals unable to keep up with need
- Cortisol levels lower than needed
- Decreased albumin and corticosteroid-binding globulin (CBG) during severe illness
  - Albumin and CBG bind cortisol
- Due to critical illness
  - Decreased GR sensitivity
  - Decreased tissue response to corticosteroids
Glucocorticoids in CIRCI (con’t)

• Suspect in patients with refractory hypotension
  • Best known guideline for diagnosing CIRCI
  • ACTH stim test \(\rightarrow\) takes time to receive results
• Patients in septic shock
• No improvement with fluids and pressors
• New studies moving AWAY from this diagnosis
  • Still, keep in mind, for now

Treatment of CIRCI

• Recommended treatment
  • Physiologic dose of steroids
  • Hydrocortisone typically chosen \(\rightarrow\) most closely resembles cortisol
• Again...only if refractory to vasopressors and fluids
  • If blood pressure responsive to fluids \(\rightarrow\) NO steroids!

When NOT to use Glucocorticoids

• Trauma \(\rightarrow\) Shock
  • Shock occurs \(\rightarrow\) decreased oxygen delivery to tissues
    • Cardiogenic
    • Septic
    • Distributive
    • Hypovolemic
Glucocorticoids in Thoracic Trauma

• Contraindicated → fallen out of practice and standard of care medicine
  • Proven only to be effective if given directly before a trauma
  • Not helpful!
• Due to effects on immune system → often makes healing and treatment of trauma worse
• Treat the trauma → wounds → fractures → internal injuries

Glucocorticoids in Abdominal Trauma

• Contraindicated → fallen out of practice and standard of care medicine
  • Proven only to be effective if given directly before a trauma
  • Not helpful!
• Due to effects on immune system → often makes healing and treatment of trauma worse
• Treat the trauma → wounds → fractures → internal injuries

Glucocorticoids in TBI

• TBI → Traumatic Brain Injury
  • Steroids given to reduce brain swelling
• CRASH study
  • Patients given steroids → increased mortality
• Pathophysiology why?
  • Still uncertain → no evidence of severe infection or GI bleed
  • Hyperglycemia seen → poor prognostic indicator in TBI
  • Concern for unknown side effects of steroids on neuro status
Presenting to ER for Glucocorticoid Use

- Owners may make mistakes with the prescribed medication
  - Due to the numerous side effects of glucocorticoids → some may be emergent!
- Very important clients be educated on the medications
  - Example: Never stop giving glucocorticoids without a doctor’s permission
    - Taper dose → prevents steroid-induced Addisonian crisis
  - Giving too much of a dose → equally bad
    - Hepatopathy
    - Cushion symptoms

Glucocorticoid Induced Diabetes

- Glucocorticoids cause hyperglycemia
  - Increased glycolysis
  - Increased gluconeogenesis
- Glucocorticoids suspected in metabolic changes
  - Pancreatic beta cell dysfunction (sensitivity to glucose and ability to release insulin)
  - Insulin resistance in other tissue
    - Glucose unable to enter the cell and be utilized for energy

Common Side Effects of Glucocorticoids

- Some mentioned earlier
  - Retards the body’s immune system
  - Reduces ability to heal
  - Increases risk of GI ulcers
  - Stomach and duodenum high risk
  - Increases thirst (Polydipsia)
  - Increases urination (Polyuria)
  - Increases hunger (Polyphagia)
  - Lethargy