

STEROIDS IN THE EMERGENCY SETTING



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INTRODUCTION

- ▶ Glucocorticoid hormones are produced in the adrenal glands
- ▶ These are essential to help regulate:
 - ▶ Glucose metabolism
 - ▶ Protein metabolism
 - ▶ Fat metabolism
- ▶ During high level of stress induced by disease or trauma, glucocorticoids allow the body to respond adequately and promptly.

STEROID USE

- ▶ There are many publications regarding steroid use in
 - ▶ Sepsis
 - ▶ Anaphylaxis
 - ▶ ARDS
 - ▶ Polytrauma
 - ▶ Hemorrhagic shock
 - ▶ Neurologic trauma
- ▶ These publications often contradict each other, therefore definitive conclusions are difficult to draw.

WHAT WE KNOW!

- ▶ There 4 main uses for steroids
 - ▶ Replacement for adrenal insufficiency
 - ▶ As an anti-inflammatory
 - ▶ As an anti-neoplastic
 - ▶ As an immunosuppressant

- ▶ We can list over 25 diseases that will respond to steroids
 - ▶ Asthma
 - ▶ Skin diseases
 - ▶ Immune mediated diseases
 - ▶ Joint/articular diseases
 - ▶ Back injuries

WHAT WE KNOW

- ▶ Glucocorticoids can be divided by the time it suppresses the hypothalamic pituitary adrenal (HPA) axis.
 - ▶ Short acting
 - ▶ Intermediate acting
 - ▶ Long acting
- ▶ Physiologic effects
 - ▶ Anti-inflammatory
 - ▶ Immunosuppressive

Table 1: Glucocorticoid free bases comparison

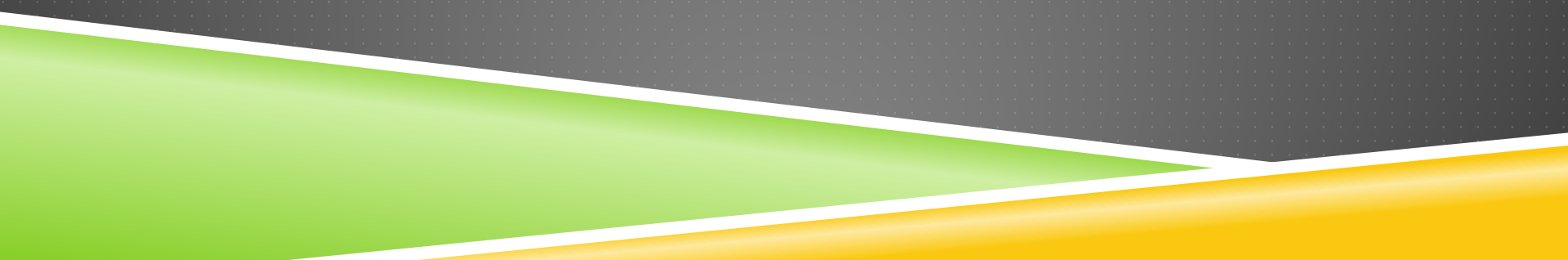
Compound	Relative MC activity	Relative GC and anti-inflammatory potency	Equivalent pharmacologic dose (mg)	Plasma half-life dog (h)	Biologic half-life/ HPA axis suppression (h)
Short acting					
Cortisol	1	1	20	1–1.5	8–12
Hydrocortisone	0.8	1	20	1	8–12
Cortisone	0.8	0.8	25	?	8–12
Intermediate acting					
Prednisone	1	4	5	?	12–36
Prednisolone	1	4	5	1–3	12–36
Methylprednisolone	0	5	4	1.5	12–36
Triamcinolone	0	5	4	?	24–48
Long acting					
Dexamethasone	0	30	0.75	2	35–54
Betamethasone	0	30	0.6	?	>48

GC, glucocorticoid; HPA, hypothalamic pituitary adrenal axis; MC, mineralocorticoid.

DEXAMETHASONE VS DEX SP

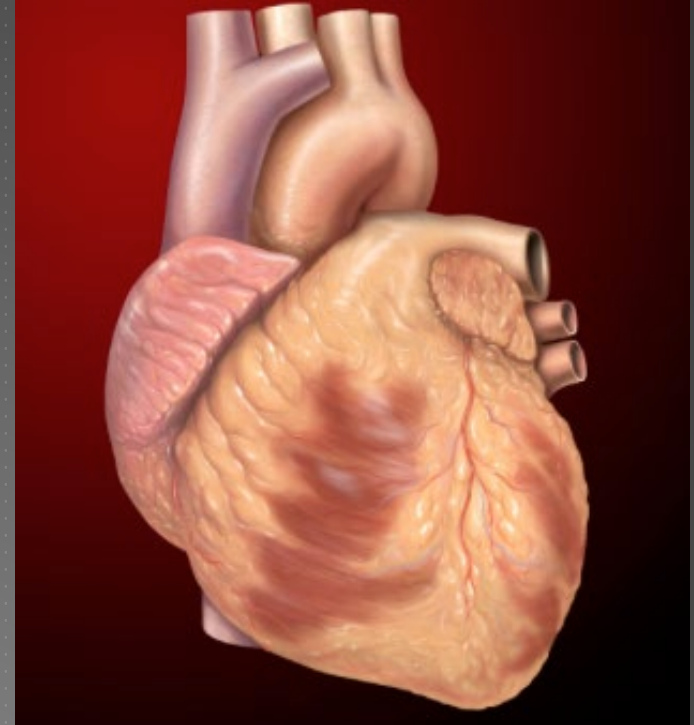
- ▶ Dexamethasone contains propylene glycol.
 - ▶ Prolonged use of dexamethasone can result in RBC oxidative injury and Heinz body anemia.
 - ▶ Dex SP does not
- ▶ Can use either for Addisonian crisis and still perform an ACTH.
 - ▶ ACTH should be collected immediately up to 3 hours post Dex or Dex SP injection
 - ▶ Samples collected > 6 hours post dexamethasone could interfere with HPA axis and affect ACTH.

ORGANS AFFECTED

- ▶ Cardiovascular
 - ▶ Hematopoietic
 - ▶ GI tract
 - ▶ Hepatic
 - ▶ Immune system
- 

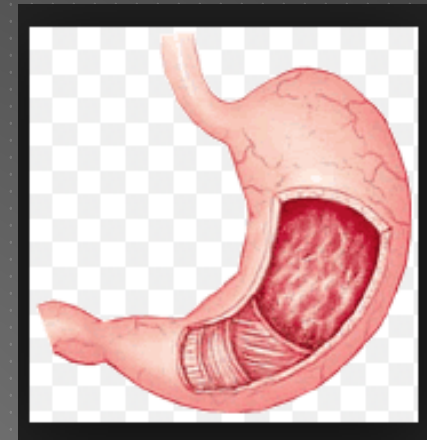
CARDIOVASCULAR SYSTEM

- ▶ Increases blood volume
- ▶ Promotes vasoconstriction
- ▶ Decreases capillary permeability
- ▶ Has no inotropic effects



GASTROINTESTINAL TRACT

- ▶ Increases
 - ▶ Gastric acid
 - ▶ Pepsin
 - ▶ Trypsin
- ▶ Decreases mucosal cell proliferation
- ▶ The end result is gastric inflammation / ulceration



HEMATOPOIETIC EFFECTS

- ▶ Increases the number of RBC, WBC and platelets.
- ▶ Inhibits platelet aggregation.
- ▶ Sequesters eosinophils, monocytes and lymphocytes into spleen and lungs.
- ▶ Reduces release of WBC from bone marrow.

BODY ADAPTATION AND GLUCOCORTICOID EFFECTS

- ▶ Glucocorticoid release into the circulation is increased by 10 folds in the presence of:
 - ▶ Pain
 - ▶ Infection
 - ▶ Trauma
- ▶ These hormones ensure glucose delivery to:
 - ▶ Heart
 - ▶ Brain
- ▶ Catecholamines are also released ensuring an augment in:
 - ▶ Cardiovascular function
 - ▶ Effective circulating volume
 - ▶ Regulation of the inflammatory response to prevent excessive tissue damage.

BODY ADAPTATION AND GLUCOCORTICOID EFFECTS

- ▶ In the CNS glucocorticoid helps with
 - ▶ Maintenance of cerebral blood flow
 - ▶ Electrolyte concentration for cerebral function
- ▶ In the airways glucocorticoid induce
 - ▶ Bronchodilation by increasing B2 receptor expression
- ▶ In the cardiovascular system
 - ▶ Limits capillary permeability
 - ▶ Maintain vascular tone enhancing response to norepinephrine.
 - ▶ Suppress production of vasodilators.

HYPERSENSITIVITY AND ANAPHYLAXIS

- ▶ Immune-mediated type I hypersensitivity are common emergencies.
 - ▶ Mast cell activation and degranulation
 - ▶ Release of inflammatory mediators (histamine, heparin) into the circulation.
 - ▶ Activation of the arachidonic acid cascade
 - ▶ Platelet activation
 - ▶ Prostaglandins
 - ▶ Leukotrienes
- ▶ End result
 - ▶ Vasodilation
 - ▶ Hypovolemia
 - ▶ Impaired cardiac and respiratory functions



HYPERSENSITIVITY AND ANAPHYLAXIS

- ▶ Glucocorticoids are the most common drugs used during an allergic reaction.
- ▶ Their use has the following effects
 - ▶ Inhibits activation of the inflammatory cascade (TNF, Interlukins)
 - ▶ Suppress the conversion of arachidonic acid into prostaglandins
 - ▶ Inhibit the release of platelet activating factor from mast cells
 - ▶ Inhibits release of histamine.

HYPERSENSITIVITY AND ANAPHYLAXIS

- ▶ A few studies in human and research animals have been performed evaluating the efficacy of steroids in allergic reactions.
- ▶ Results
 - ▶ The anti-inflammatory effects may take 2-24 hours
 - ▶ Improvement in airway inflammation, edema and bronchoconstriction may take 2-6 hours.
 - ▶ Biphasic anaphylactic response (humans)
 - ▶ Improvement x 2-3 days, followed by re-occurrence of clinical signs.
- ▶ In a severely affected anaphylactic shock patient, the treatment of choice is:
 - ▶ Rapid infusion of crystalloids
 - ▶ Epinephrine 0.01 mg/kg
 - ▶ Dex Sp followed by prednisone orally

TRAUMA AND HYPOVOLEMIC SHOCK

- ▶ Pain, infection and trauma stimulate a 10 fold increase in endogenous glucocorticoid release (steroid).
 - ▶ Ensure glucose delivery to:
 - ▶ Brain
 - ▶ Heart
- ▶ Pain and trauma promotes catecholamine release
 - ▶ Augment cardiovascular function
 - ▶ Modulate renal sodium
 - ▶ Regulate the inflammatory response to prevent excessive tissue damage
 - ▶ Maintain vascular tone.
 - ▶ Limits capillary permeability

HYPOVOLEMIC SHOCK

- ▶ Trauma.
 - ▶ Hit by a car
 - ▶ Gun shot wounds
- ▶ Severe fluid losses
 - ▶ Vomiting
 - ▶ Diarrhea
- ▶ Acute abdomen
 - ▶ GDV
 - ▶ Mesenteric torsion
- ▶ Organ failure
 - ▶ Kidney vs Liver vs Heart
- ▶ Blood loss



SHOCK

- ▶ Pale gums
- ▶ Tachycardia
- ▶ Weak pulses
- ▶ Obtunded
- ▶ Hypothermia



APPROACH SHOCK

- ▶ Pale gums
 - ▶ Anemia
 - ▶ Shock
- ▶ IV catheter placement
 - ▶ HCT + TP + BG + Lactate (catheter hub)
- ▶ HCT level
 - ▶ HCT and TP normal = hypovolemic shock
 - ▶ Low HCT and Low TP = blood loss + shock
 - ▶ Normal HCT and low TP = think bleeding

EXCESSIVE STEROIDS IN TRAUMA AND HYPOVOLEMIC SHOCK

- ▶ Suppress Hypothalamic – Pituitary Adrenal (HPA) Axis
- ▶ Blood stasis
- ▶ Hypercoagulability
- ▶ Thromboembolism
- ▶ Increases chances of infection
- ▶ Hyperglycemia
- ▶ Insulin resistance
- ▶ Free water loss
- ▶ Inhibit bone, cartilage and tissue healing
- ▶ GI ulceration

STEROID IN SHOCK

- ▶ Steroids can be considered in shock only when hypotension persists despite
 - ▶ Adequate fluid resuscitation
 - ▶ Vasopressor therapy has failed to improve blood pressure

STATEMENT

- ▶ Given the lack of evidence supporting improved outcome, as well as potential adverse effects, routine use of steroids cannot be recommended in trauma and hypovolemic shock.

TRAUMATIC BRAIN INJURY (TBI)

- ▶ 9 year old Weimeraner
- ▶ Hit by a car
- ▶ Physical exam
 - ▶ Anisocoria
 - ▶ Large wound (head)
 - ▶ Stuporous mentation
 - ▶ Cushing reflex (HR 78 with a BP 210 mmHg)
- ▶ Fluid therapy including crystalloids and hypertonic saline instituted.
- ▶ Mannitol therapy provided once hemodynamic stability was achieved.

TRAUMATIC BRAIN INJURY (TBI)

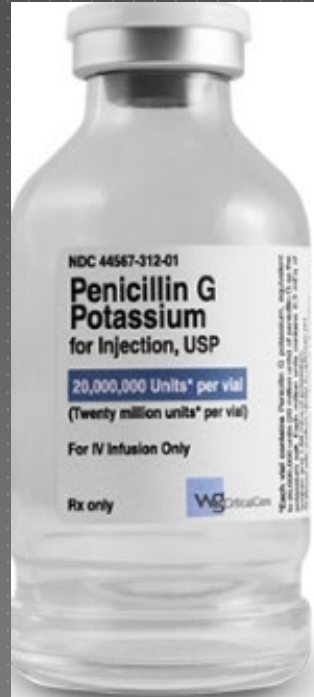
- ▶ During head trauma there is cytotoxic edema of the brain which is accompanied with cell disruption.
- ▶ Many studies have been published regarding the use of steroids in TBI.
- ▶ The benefit expected from steroids in TBI has not been achieved.
- ▶ In fact, steroids are contraindicated in TBI cases.
 - ▶ Increases the risk of post-trauma seizures
 - ▶ Promotes hyperglycemia and insulin resistance
 - ▶ Hyperglycemia exacerbates brain injury
 - ▶ They do not lower intracranial pressure
 - ▶ Increases the risk of death

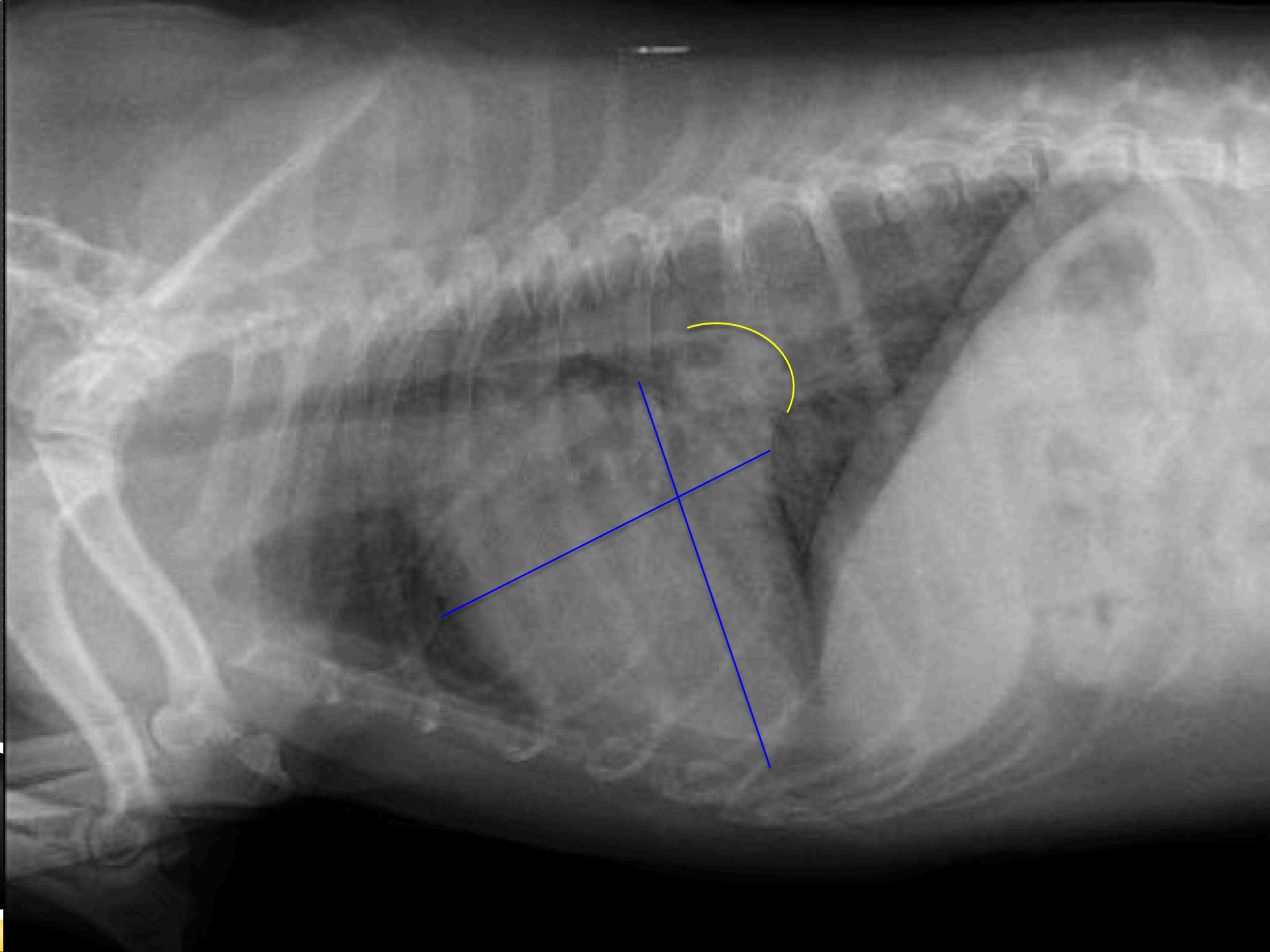


STERIOD IN CONGESTIVE HEART FAILURE

- ▶ 13 year old Shih Tzu
- ▶ History of coughing and decreased activity
- ▶ Presentation and exam
 - ▶ Muddy mucous membranes (CRT 3 sec)
 - ▶ Labor breathing (RR 88)
 - ▶ Heart murmur 4/6 systolic
 - ▶ Weak femoral pulses
 - ▶ Crackles bilaterally

STAT TRIAGE









STEROID USE IN CARDIOGENIC SHOCK

- ▶ Not recommended
- ▶ Steroids will increase intravascular volume.
- ▶ Exacerbate vasoconstriction
- ▶ Increases afterload
- ▶ Exacerbates pulmonary edema

ACUTE SPINAL CORD INJURY

- ▶ Key word “ACUTE” – Trauma to spinal cord
- ▶ Usually seen with
 - ▶ Contusion
 - ▶ Compression
 - ▶ Shearing
 - ▶ Laceration
- ▶ The primary injury begin within minutes and last days after the inciting trauma

ACUTE SPINAL CORD INJURY

- ▶ Trauma leads to inflammation and reactive oxygen species (ROS)
- ▶ Approach
 - ▶ Treat shock first
 - ▶ Stabilize heart rate with IV fluids and pain medication
 - ▶ Make sure blood pressure and vitals are stable
 - ▶ Start GI protectants (Omeprazole vs Famotidine)
- ▶ Workup
 - ▶ Blood work
 - ▶ Thoracic, abdominal, pelvic and spinal radiographs (depending on case)
 - ▶ AFAST
 - ▶ CT ideally

RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ Better neurologic outcome was noticed in Beagles with spinal cord injury treated with decompression and methylprednisolone than with decompression alone.
- ▶ Another study revealed that lactate accumulation within the spinal cord, along with neuronal death and further oxidative injury was noticed in patients that received glucocorticoids.
- ▶ One study show that sensory and motor function improvement was noticed when steroids were given within 8 hours of trauma.
 - ▶ Despite the improvement mentioned above there was no statistical difference between people treated with or without steroid.

HUMAN RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ Steroid use in acute spinal cord injury is controversial
- ▶ Cochrane study 2012 concluded that MPSS enhances neurologic recovery, however unless the initial deficits are minimal, it is unlikely to bring a return to normal.
- ▶ Cochrane recommends that injury within 8 hours should be treated with
 - ▶ MPSS bolus (30 mg/kg) followed by a CRI 5.4 mg./kg/hr x 24
 - ▶ 2 injections of 15 mg/kg at 2 and 6 hours.

HUMAN RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ American Association of Neurological Surgeons and Congress of Neurological Surgeons 2013 Statement.
 - ▶ “MPSS is not recommended for the treatment of acute spinal cord injury”.
- ▶ Favorable neurologic outcome still questionable in patients with IVDD.
- ▶ Two separate studies did not find a significant difference in:
 - ▶ Ambulation recovery rates
 - ▶ Length of time till ambulation was achieved

VETERINARY RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ Another study of 105 dogs with neurological injury treated with high dose of MPSS revealed that:
 - ▶ 35% of dogs developed complications such as
 - ▶ Diarrhea, melena and hematochezia
 - ▶ Vomiting and hematoemesis
- ▶ Neiger et al performed an endoscopic evaluation of gastric mucosa of dogs that received dexamethosone injection for spinal cord injury prior to surgery.
 - ▶ 76% of dogs had gastric mucosa ulceration despite of antiulcer treatment.

VETERINARY RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ Boag et al revealed that Dachshund that received 3 doses of MPSS were more likely to develop severe GI signs and required prolonged hospitalization than dog that received a single dose of Dex Sp.
- ▶ Also Boag et al revealed that there was no difference in neurologic outcome between groups.

VETERINARY RESEARCH OF STEROIDS IN ACUTE SPINAL CORD INJURY

- ▶ Levine et al demonstrated that dogs that received steroids had an 11.4 fold increase of urinary tract infection and 3.5 fold increase to develop diarrhea. Neurologic function at discharge or at recheck did not differ between groups.
- ▶ Levine et al also demonstrated that glucocorticoid were not associated with successful medical management or improved quality of life in dogs with presumptive cervical IVDD. Also was associated with a lower quality of life and decreased odds for successful outcome in dogs with presumptive T3-L3 IVDD.

- ▶ There is no universal report that says “steroid therapy improves”
 - ▶ Morbidity
 - ▶ Mortality
 - ▶ Quality of life
- ▶ Also major side effects have been reported
 - ▶ GI ulceration
 - ▶ Colonic perforation
 - ▶ Urinary tract infections

ACUTE SPINAL CORD INJURY

- ▶ Patients with acute spinal injury, that are ambulatory can be approached medically
- ▶ Normally I will use NSAIDs.
- ▶ If patient is severely affected and finances don't allow for CT and surgery, then
 - ▶ Methylprednisolone Sodium Succinate – Solu – Medrol
 - ▶ 30 mg/kg IV once
 - ▶ 15 mg/kg every 6 hours x 3 doses.
 - ▶ This protocol reduces inflammation and attenuates lipid peroxidation
- ▶ If the patient worsens or is not improving, then CT/Myelogram followed by surgery is strongly recommended.

TAKE HOME

- ▶ The use of steroid therapy should be avoided at all cost in cases with:
 - ▶ Head trauma (traumatic brain injury)
 - ▶ Hypovolemic, hemorrhagic shock
 - ▶ Cardiogenic shock
- ▶ The use of steroid should be reserved for conditions that their use is beneficial
 - ▶ Anaphylactic shock
 - ▶ Feline asthma
 - ▶ Hypoadrenocorticism
- ▶ A definitive answer about the use of steroid in spinal cord injury is controversial, use your best judgement.
- ▶ An accurate diagnosis is extremely important in differentiating disease processes that will or will not require steroid therapy.
- ▶ The misuse of steroid will increase the risk of morbidity and mortality.



“But my breeder said...”