Steroids in ER:
The Good, The Bad, and The Ugly

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MedVet New Orleans

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About Me

- BS Biology: University of Central Florida
- DVM: Ross University
- Internship / Residency: Pittsburgh Veterinary Specialty and Emergency
- Research: High flow nasal oxygen
- Interests: Respiratory failure, extracorporeal therapies, polytrauma, immune mediated disease, sepsis
- Currently: MedVet, New Orleans

Outline

- Physiology
- Pharmacology
- Indications
- Contraindications
- The Controversies

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Steroid Functions

Maintenance of homeostasis

- Regulate glucose, protein and fat metabolism

Component of neurohormonal response

- Adaptive response during disease / acute stress

Endogenous Steroids

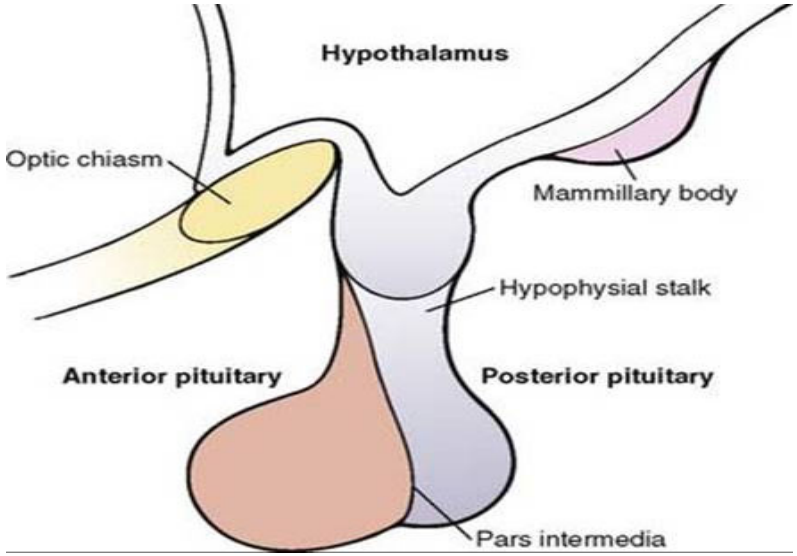
Transported in the blood and mostly protein bound

- AKA Lipophilic hormones
- Less than 10% free
- Inactive while bound
- Acts as fast acting reservoir

Stimulate synthesis of proteins at target cell

- Act as enzymes, transport or structural proteins

Major Player ‘Pituitary Gland’ AKA: Hypophysis



- Anterior pituitary
  - Corticotropes -> Adrenocorticotropin (ACTH)

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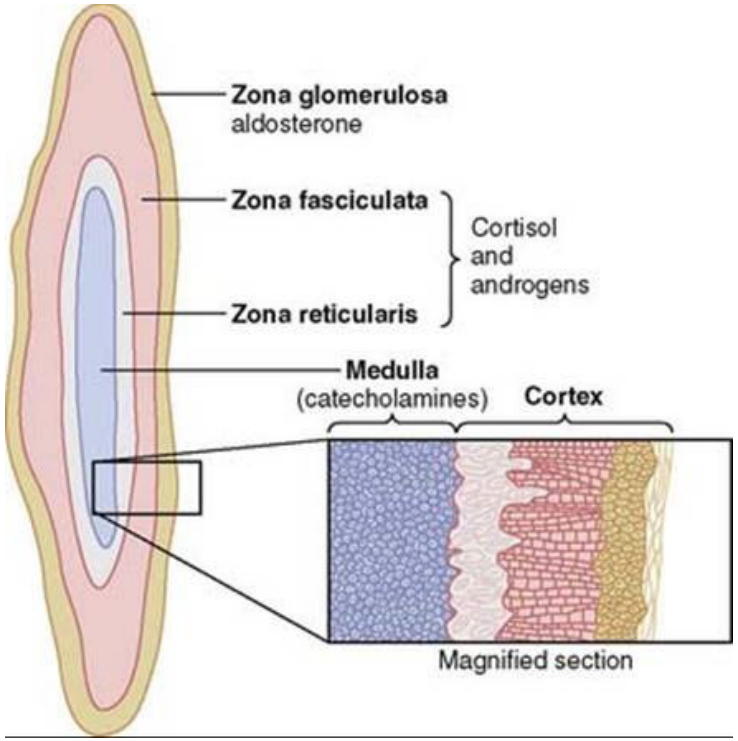
Pituitary Hormones and Their Control by the Hypothalamus - Endocrinology and Reproduction - Guyton and Hall Textbook of Medical Physiology, 12th Ed (doctorlib.info)

Hormones To More Hormones



- Anterior pituitary
  - Corticotropes -> Adrenocorticotropin (ACTH)
- Adrenal Cortex
  - Adrenocorticotropin (ACTH) ->
    - Corticosteroids
    - Sex hormones
  - GFR ->
    - Aldosterone, cortisol, androgens
    - Salt, sugar, sex

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Adrenocortical Hormones - Endocrinology and Reproduction - Guyton and Hall Textbook of Medical Physiology, 12th Ed (doctorlib.info)

Classifications

Corticosteroids

- Mineralocorticoids (MC)
- Glucocorticoids (GC)

Sex Hormones

- Androgens
- Estrogens
- Progestogens

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Corticosteroid Functions

- Mineralocorticoids (MC): Mimics aldosterone
  - Increases absorption sodium and secretion potassium
  - Increases hydrogen ion secretion

- Glucocorticoids (GC): Cortisol
  - Resist stress and inflammation
  - Gluconeogenesis & glucose utilization
  - Reduces cellular protein, increased liver and plasma proteins
  - Mobilization of fatty acids

Who is Who ?!

- Mineralocorticoids (MC): Mimics aldosterone
  - Hydrocortisone
  - Prednisone / prednisolone
  - Methylprednisone

- Glucocorticoids (GC): Mimic cortisol
  - Hydrocortisone
  - Prednisone / prednisolone
  - Methylprednisone
  - Dexamethasone

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Half Life

- Biologic effects
- HPA axis suppression

- Short acting: < 12-hours
  - Cortisol
  - Cortisone
  - Hydrocortisone
- Intermediate acting: 12-36 hours
  - Prednisone / Prednisolone
  - Methylprednisone
  - Triamcinolone
- Long acting: > 48 hours
  - Dexamethasone
  - Betamethasone

Daily Dosage Variations

Corticosteroid	Physiologic	Anti-inflammatory	Immunosuppressive
Hydrocortisone	1 mg/kg	2-4 mg/kg	8-16 mg/kg
Prednisone / Prednisolone	0.25 mg/kg	0.5-1 mg/kg	2-4 mg/kg
Methylprednisone	0.2 mg/kg	0.4-0.8 mg/kg	1.6-3.2 mg/kg
Dexamethasone / SP	0.025 mg/kg (0.04 mL/10lbs)	0.05-0.1 mg/kg (0.07-0.14 mL/10 lbs)	0.2-0.4 mg/kg (0.3-0.6 mL/10 lbs)

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Hydrocortisone

- Structurally identical to cortisol
  - MC & GC activity
  - Rapid absorption
  - Short acting
  - Oral, injectable topical
  - Prednisone equivalent: 0.25: 1

Solu-Cortef® (Hydrocortisone Sodium Succinate), Act-O-Vial®, SDV Vial | McGuff Medical Products

HYDROCORTISONE (Generic) Cream 1% for Dogs & Cats, 1-oz - Chewy.com

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Prednisone / Prednisolone

- 4 times as potent as cortisol
- 0.8 times MC activity of cortisol
- Intermediate acting
- Prednisone biologically inactive -> prednisolone

Prednisolone | 1800PetMeds
Prednisolone Acetate Ophthalmic Suspension 1% 10 ml | 1800PetMeds

Methylprednisone

- 5 times potency of cortisol GC
- Half potency MC
- Intermediate activity
- May attenuate secondary injury
  - Inhibits lipid peroxidation after injury
- Prednisone equivalent: 1.25:1

Prednisolone | 1800PetMeds
Pfizer 00009004722 - McKesson Medical-Surgical

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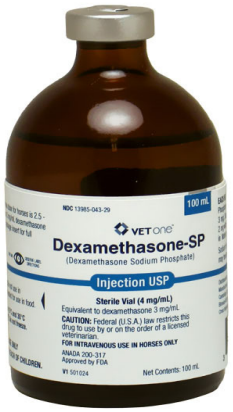

Dexamethasone

- CG potency of 25-30x cortisol
- Virtually no MC
- Long-acting steroid
- Prednisone equivalent: 10:1

What is Dexamethasone? | Moffitt
Dexamethasone-SP (Sodium Phosphate) Inj 4mg (100 ml) | On Sale | EntirelyPets Rx (entirelypetspharmacy.com)

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Emergency Indications

- Hypoadrenocorticism
- Upper airway obstruction
- Allergic airway disease
- Allergic dermatitis
- Immune-mediated disease

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Hypoadrenocorticism

Addisonian Crisis:

- Young female dogs
- Present in cardiovascular collapse
- Frequent GI signs with severe dehydration
- Hyponatremia, hyperkalemia (<27:1)

Anti-inflammatory dexamethasone until diagnosis

- Continue anti-inflammatory dose x 1 week
- Drop to physiologic and add mineralocorticoid

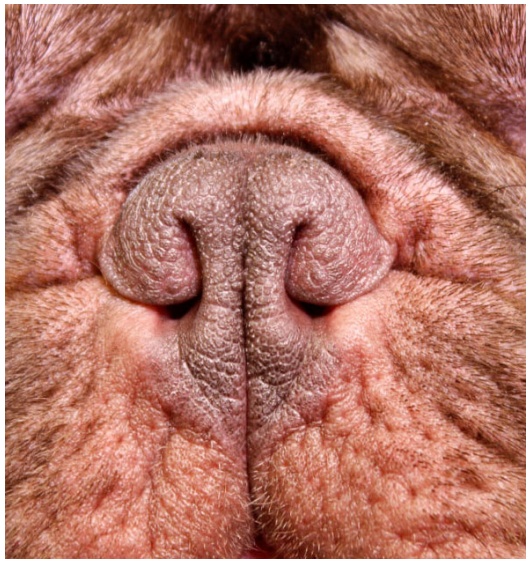
Two AAHA-accredited practice members honored as veterinary heroes

Upper Airway Obstruction

Disease process

- Brachycephalic airway syndrome
- Tracheal collapse
- Laryngeal paralysis
- Allergic swelling

Noisy breathing: stertor / stridor



First things first !

- Calm, cool, resuscitate
- Supplemental oxygen
- Anti-inflammatory corticosteroid
  - Intubate if you need to buy time

https://www.fitzpatrickreferrals.co.uk/soft-tissue-service/brachycephalic-syndrome/

Allergic Airway Disease

Disease Process

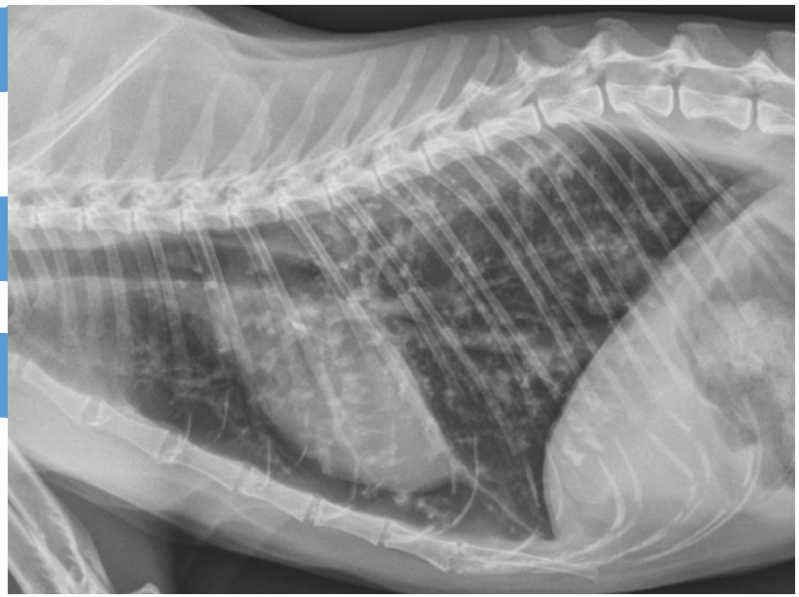
- Feline inflammatory lower airway disease / asthma
- Bronchitis

Breathing pattern: Expiratory push

- Wheezes, coughing, dyspnea

Treatment

- Calm, support with oxygen
- Anti-inflammatory corticosteroids 2-3 weeks
  - Long term goal inhaled fluticasone
- Airway dilators: albuterol, terbutaline, theophylline
- Secondary pathology: bacterial, parasitic



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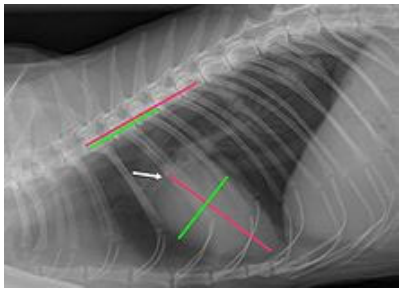

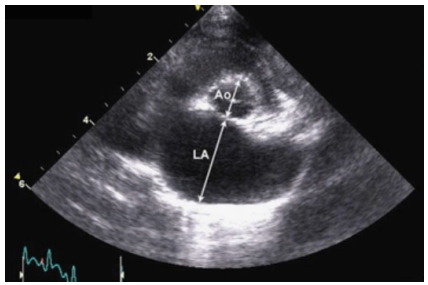

NT-proBNP	Lighter	Equal	Darker
			
Evaluation	Normal	Abnormal	Abnormal
NT-proBNP concentration (pmol/L)	24 (24-31)[a]	162 (100-217)[a]	505 (336-1312)[a]
No of POCT	108	6	25

https://second.wiki/wiki/vertebral_heart_score
https://onlinelibrary.wiley.com/doi/full/10.1111/jvim.15754
https://onlinelibrary.wiley.com/doi/full/10.1111/j.1939-1676.2007.0024.x

Heart vs Lung !?!?

Let's talk about cats ….

- Heart failure cats don't cough
- Breathing pattern:
  - Expiratory asthma / bronchitis
- Vertebral heart score: > 9.3 enlarged for feline
- BNP
- La:Ao – 0.8 to 1.5 considered normal

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Allergic Dermatitis

https://www.thedodo.com/dodowell/dog-skin-allergies

- Disease Processes
  - Secondary to atopy
  - Parasites (fleas)
  - Contact dermatitis
- Primary disease identification and therapy
  - Antibiotics, immunotherapy, avoidance, anti-histamines
- Anti-inflammatory corticosteroids
  - 1-7 day taper to control pain, itch, inflammation
  - Can give with Apoquel short periods

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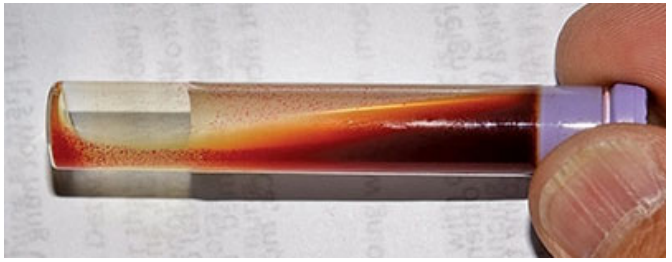
Immune Mediated Disease

Disease Processes

- Immune meditate hemolytic anemia
- Immune mediated thrombocytopenia
- Polyarthritis

Treatment

- Immunosuppressive doses corticosteroids
- 4-6 months
  - 25% taper every 4 weeks IF still in remission !
- Secondary agents ?



https://www.gribblesvets.co.nz/wp-content/uploads/2019/06/How-to-Saline-Agglutination-test.pdf
https://todaysveterinarypractice.com/hematology/diagnosis-of-immune-mediated-hemolytic-anemia/

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https://passtheot.com/quick-reference-to-common-precautions-contraindications/

Contraindications

- Traumatic brain injury (TBI)

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Traumatic Brain Injury

Pathophysiology: Cerebral edema and increased ICP

Pharmacology:

- Reduce tumor-associated vasogenic edema
- Anti-inflammatory

Strong theoretical benefits ?!

CONTRAINDICATED

- Does not help and causes harm
- Increased risk post traumatic seizures
- Promotes hyperglycemia -> worsens outcome in TBI
- Increased risk of death in randomized head injury trial

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The Controversies

https://memegenerator.net/instance/18040326/futurama-fry-not-sure-if-indicated-or-contraindicated

- Acute spinal cord injury
- Anaphylaxis
- Trauma / Hemorrhagic shock
- Critical illness-related corticosteroid insufficiency (CIRCI)
- Acute lung injury (ALI) / Acute respiratory distress syndrome (ARDS)

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Acute Spinal Cord Injury (ASCI)

Primary injury

- Contusion, compression, shearing, laceration, or distension
- Cord or vasculature

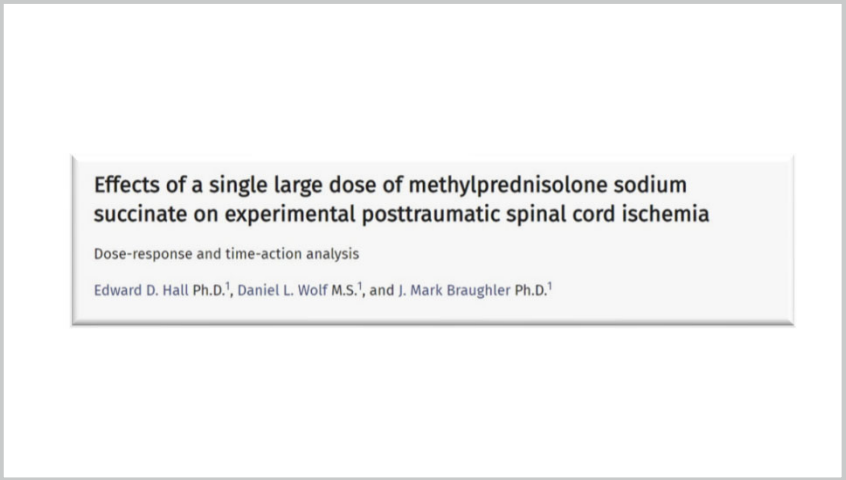
* Secondary injury *

- Ischemia, excitotoxicity, cytotoxic edema, mitochondrial dysfunction
- Activation and production: nitric oxide, eicosanoids and caspases
- Reactive oxygen species -> propagate neuronal cell death

The Evidence…..

- Journal of neurosurgery – 1984
- Feline study
  - MPSS 15,30,60 mg/kg
  - 30 mg/kg found to be optimum WITHIN: 30-90 minutes
- Proposed mechanisms twice more 1992 and 2004

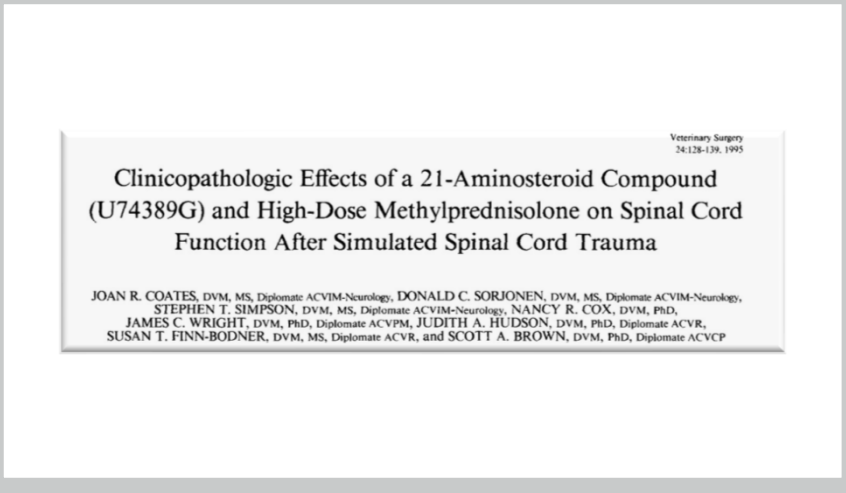
- Veterinary Surgery: 1995
- Simulated IVDD
- Clinical efficacy not established



Effects of a single large dose of methylprednisolone sodium succinate on experimental posttraumatic spinal cord ischemia

Dose-response and time-action analysis

Edward D. Hall Ph.D.[1], Daniel L. Wolf M.S.[1], and J. Mark Braughler Ph.D.[1]



Veterinary Surgery
24:128-139. 1995

Clinicopathologic Effects of a 21-Aminosteroid Compound (U74389G) and High-Dose Methylprednisolone on Spinal Cord Function After Simulated Spinal Cord Trauma

JOAN R. COATES, DVM, MS, Diplomate ACVIM-Neurology, DONALD C. SORJONEN, DVM, MS, Diplomate ACVIM-Neurology, STEPHEN T. SIMPSON, DVM, MS, Diplomate ACVIM-Neurology, NANCY R. COX, DVM, PhD, JAMES C. WRIGHT, DVM, PhD, Diplomate ACVPM, JUDITH A. HUDSON, DVM, PhD, Diplomate ACVR, SUSAN T. FINN-BODNER, DVM, MS, Diplomate ACVR, and SCOTT A. BROWN, DVM, PhD, Diplomate ACVCP

National Acute Spinal Cord Injury Study

- NASCIS I,II & III (1997)
- High dose MPSS within 3-8 hours : Improved motor and sensation
- No significant difference: Functional Independence Measure

Cochrane Review - 2012

- Enhanced neurologic recovery
- Unless deficits minimal -> unlikely return to normal

AA of Neurological Surgeons and Congress Neurological Surgeons Joint Guidelines Committee

- 2013
- MPSS is NOT recommended in ASCI

Additional Knowledge Points

- Few newer studies ASCI dogs or cats: most retrospective
- Most information IVDD
- No strong evidence of treatment benefit
- Significant adverse events are well known
  - Diarrhea, melena, hematochezia, hematemesis, anorexia
  - Colonic perforation
  - Urinary tract infection
  - Delayed healing
- JVECC 2017:
  - Recommendations advocating or discouraging use cannot be made …….
  - MPSS 30 mg / kg within 8 hours, 15 mg/kg at 2 & 6 hours
  - No longer listed as acceptable dosage in Plumbs

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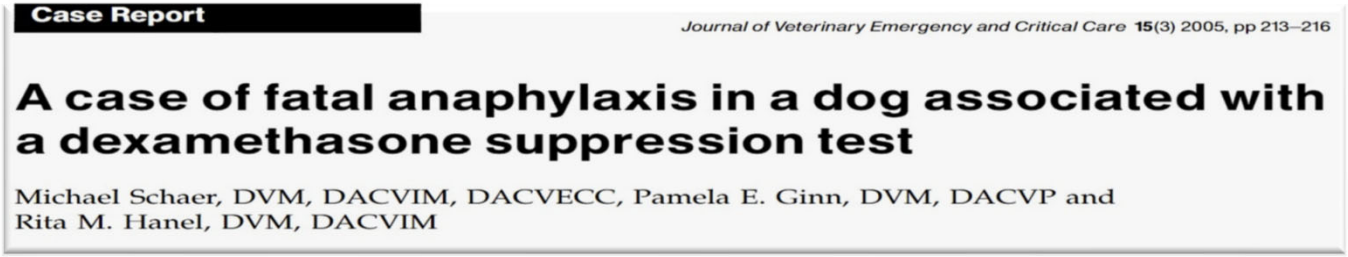
Anaphylaxis

- NEVER should be considered first line drug: EPINEPHRINE
- Onset beneficial effects 4-6 hours
- May be useful in down regulation late phase / biphasic response



Case Report

Journal of Veterinary Emergency and Critical Care **15**(3) 2005, pp 213–216

A case of fatal anaphylaxis in a dog associated with a dexamethasone suppression test

Michael Schaer, DVM, DACVIM, DACVECC, Pamela E. Ginn, DVM, DACVP and Rita M. Hanel, DVM, DACVIM

- Cochrane Review does NOT support use in anaphylaxis
- Pre-treatment does not prevent
  - May blunt physiologic response

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Trauma And Hemorrhagic Shock

- HPA axis activated in shock -> increased cortisol
- Trials in shock and hemorrhage: decades ago
- Recent trails fail to show benefits or survival advantage
- Not Recommended for acute use !
- Maybe CIRCI….. More to come….

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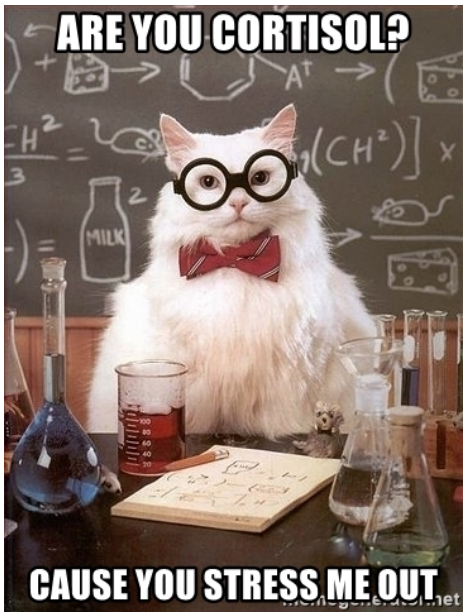
Critical illness-related corticosteroid insufficiency (CIRCI)

- Vasopressor refractory hypotension
  - Demands initial resuscitation
  - Hydrocortisone 4 mg/kg/day
- Inadequate corticosteroid activity
  - Decreased production
  - Resistance at tissues
- CORTICUS, ADRENAL, HYPOLYTE trials
  - No survival difference
  - Faster resolution of shock
  - Quicker discharge from ICU and weaning from ventilation



https://memegenerator.net/instance/75700745/chemistry-cat-are-you-cortisol-cause-you-stress-me-out

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CIRCI – Veterinary Literature

Critical illness-related corticosteroid insufficiency in a dog with septic shock

Jamie L. Peyton DVM, Jamie M. Burkitt DVM, DACVECC

First published: 08 June 2009 | https://doi.org/10.1111/j.1476-4431.2009.00407.x | Citations: 26

- JVECC
- First case report
- 5 hours lack of response to pressors (dopamine)
- 2 hours after hydrocortisone: normotension and 8 hours dc dopamine

Retrospective evaluation of the use of hydrocortisone for treatment of suspected critical illness–related corticosteroid insufficiency (CIRCI) in dogs with septic shock (2010–2017): 47 cases

April M. Summers DVM, PhD, Christine Culler DVM, MS, DACVECC, Page E. Yaxley DVM, DACVECC, Julien Guillaumin DVM, DACVECC, DECVECC ... See fewer authors

First published: 17 February 2021 | https://doi.org/10.1111/vec.13037

- JVECC
- HC group: higher risk mortality
- Sicker at initiation of therapy

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ARDS / ALI

- Syndromes of severe pulmonary inflammation and edema
- Few veterinary reports
- GC not studied in dogs or cats
- In humans low dose GC (anti-inflammatory) may benefit
- Two recent trials
  - ARDS Network Trial & MPSS Infusion in early Severe ARDS
  - Suggest early low dose MPSS may have clinical benefit

ARDS – The Berlin Criteria
Symptom begin within 1 week of insult, or new/worsening symptoms in last 1 week
Bilateral opacities on chest imaging*
$PaO_2/FiO_2 \leq 300$ while on PEEP ≥ 5 cm H_2O
Not fully attributed to cardiac failure and/or volume overload

https://www.tamingthesru.com/blog/air-care-series/acute-respiratory-distress-syndrome

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Summary

- Physiologic effects integral to cellular and organ function
- Know your doses: more is NOT better !
- Do you need GC, MC or both ?
- Benefits > Side effects

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Current Indications

- Addison's
- Upper airway obstruction
- Inflammatory lower airway disease
- Allergic dermatitis
- Immune mediated disease
- CIRCI
- ALI / ARDS
- +/- Late / biphasic anaphylaxis

https://memegenerator.net/instance/82053442/skeptical-3rd-world-kid-so-you-saying-you-might-change-your-mind-again

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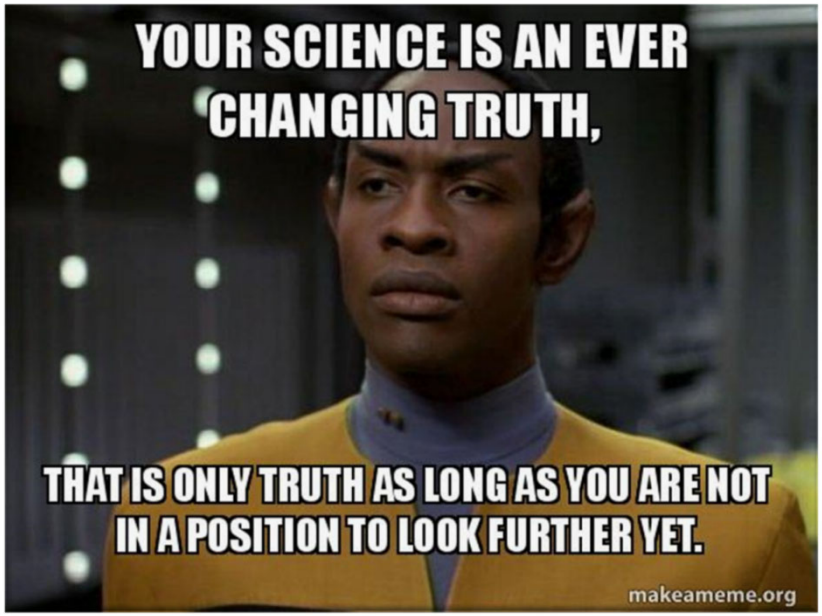
Current Contraindications



https://makeameme.org/meme/your-science-is

- Head / brain injury
- Acute trauma / hemorrhage
- Acute shock
- ASCI unless within 4 hours ?

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