

# IVG Newsletter

APRIL 2010 | VOLUME 10, ISSUE 2



## UPCOMING LECTURES

**SUN. APRIL 25**

### Surgery Symposium

LOCATION: Marriott Peabody, MA  
Open to Doctors, Technicians,  
Students, Residents, and Interns.  
Register online: [www.IVGHospitals.com](http://www.IVGHospitals.com)

**WED. MAY 6**

### Thoracic Radiographs: Pointers and Pitfalls

LOCATION: Port City

**WED. MAY 19**

### As the Stools Loosen

LOCATION: Mass Vet

**TUES. JUNE 8**

### Tackling Inter-Dog & Inter-Cat Household Aggression

LOCATION: Mass Vet

## UPCOMING CONTINUING EDUCATION LECTURES FOR DOCTORS

For current list of upcoming CE and for registration, go to [www.IVGHospitals.com](http://www.IVGHospitals.com) and click on CE Lectures.

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We hope you enjoy the new look and feel of the IVG newsletter. As IVG rebrands, you will begin to see a number of changes to our materials. What remains unchanged is our dedication and commitment to providing you, your clients and their pets with the highest standards of veterinary medical care.

*G. Ames Prentiss*  
CEO, IVG

# Solu-Medrol: Friend or Foe?

A critical evaluation of the human & veterinary literature

**ACUTE SPINAL CORD INJURY (SCI)** secondary to external trauma or intervertebral disk disease is a common cause for paresis and ataxia in people and dogs. The annual incidence of SCI in dogs is unknown. In human medicine, there are approximately 12,000 new spinal cord injuries annually. Beyond prevention of injury, surgical decompression, and repair of fractures/luxations, there are few treatments available to treat the spinal cord itself.

## SPINAL CORD PATHOPHYSIOLOGY

Understanding the pathophysiology of SCI is important to developing effective treatments. Primary cell death occurs at the time of injury and is due to a combination of direct biomechanical forces to the vertebral column and the subsequent compression applied to the spinal cord. The goal of surgical intervention in these cases is to prevent further spinal cord injury and to reestablish vertebral stability. However, surgery does not prevent secondary injury, a cascade of biochemical reactions that begins to occur in the spinal cord within minutes of primary injury, and can progress over weeks. Secondary injury is due to a variety of factors, including hypoxia, ischemia, lipid peroxidation, free radical production, release of excitotoxic molecules, prostaglandin production, ionic shifts, neutral protease activation, and programmed cell death. These chemical reactions lead to the death of additional neurons and glial cells that survived the initial primary injury.

Prevention of secondary spinal cord injury is the focus of intense ongoing pharmaceutical research. This newsletter will examine several studies that lead to the widespread use of methylprednisolone sodium succinate (MPSS), the controversy surrounding the data, and the advantages and disadvantages to using MPSS in both human and veterinary medicine.

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## NATIONAL ACUTE SPINAL CORD INJURY STUDIES (NASCIS)

These three studies constitute the primary reason that MPSS is used in traumatic SCI in humans with extrapolation to veterinary medicine.

### NASCIS I (1979)

This study compared a standard dose of MPSS (100mg) to a megadose (1000 mg) given IV once daily for 10 days. There was no difference between treatment groups at all time points for both sensory and motor assessments.

### NASCIS II (1990)

The NASCIS II study (1990) examined 487 patients who arrived to the hospital within 12 hours of injury and were given a megadose of MPSS (30mg/kg IV bolus followed by 5.4mg/kg/hr for 24 hours), naloxone, or a placebo. Motor function was evaluated by testing the power in 14 muscle groups which were given a graded score from 0 to 5 (total score range 0-70). Sensory function was evaluated by pinprick & tactile sensation in 29 dermatomes and given a graded score of 1-3 (total score range 29-87). Post hoc statistical manipulation was performed and the patients were divided into those in which treatment was initiated within eight hours of injury and those in which treatment was started later. The authors reported that patients who received MPSS had a

better outcome at six months compared to placebo, but this effect disappeared at one year. They also reported that patients receiving MPSS within eight hours of injury had a statistically significant improvement in motor scores at both six months and one year.

Numerous criticisms have been made regarding this study, only some of which will be highlighted here. First, the time point for statistical analysis was changed from 12 hours to 8 hours without logical explanation. This suggests that the authors tested the effects at various times and found the best effect at the eight hour time point which compromises the scientific value of the data. Next, only 62 placebo patients and 65 MPSS patients were analyzed meaning that 70% were excluded! Additionally, there was no consideration given to whether aggressive medical management or surgical intervention may have had an effect on patient outcome. Finally, functional recovery was not tested, so it is unclear if the modest improvements in motor scores lead to improved function.

Two unusual results were reported in this study that suggests that the conclusions may be based on statistical artifacts. First, patients who received a placebo within eight hours of injury had a worse outcome than patients who received a placebo more than eight hours after SCI. Second, the placebo group of patients presenting with incomplete SCI after eight hours from injury had an almost identical outcome to those patients who were treated with MPSS within eight hours. Regardless of whether or not a patient received MPSS or a placebo, one would expect that patients treated within eight hours of injury would have a better outcome than patients who received treatment after eight hours simply because aggressive treatment was begun earlier. These two points suggest that the placebo had the same effect as MPSS!

### NASCIS III (1997)

This study included 499 patients who presented to the hospital within eight hours of SCI. The patients were randomized into three groups:

1. MPSS 30mg/kg IV bolus followed by 5.4 mg/kg/hr for 23 hours,
2. MPSS 30 mg/kg IV bolus followed by 5.4 mg/kg/hr for 47 hours, or
3. MPSS 30 mg/kg IV bolus followed by Tirilizad 2.5 mg/kg q6hr for 48 hours.

Sensory & motor scores were obtained as for the NASCIS II trial, but they also evaluated the patient's functional recovery using the Functional Independence Measure (FIM) which includes "self care, sphincter control, mobility, locomotion, communication, and social cognition." At the six month follow-up there was no significant difference between groups. At this point, the authors performed a statistical bait & switch by dividing patients into those that received MPSS within three hours versus those that received it 3-8 hours after SCI. Following this, the authors identified a statistically significant difference in motor scores at six weeks and six months in patients who received 48 hours of MPSS compared to those that received 24 hours, but this was less apparent at one year ( $P=0.053$ ). Based on these results, the authors concluded that patients seen within three hours should receive 24 hours of MPSS while patients seen between 3-8 hours should receive 48 hours of MPSS.

Again, this study has several major limitations. First, there was no placebo group, presumably because they were included in the NASCIS II trial. Second, more patients with an initial normal motor score were randomized into the 24-hour MPSS group, thus skewing the results toward improved benefit. Third, the authors conclude that MPSS should be administered based on modest improvement in motor scores, but the FIM was similar for all groups, which is perhaps

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## Solu-Medrol: Friend or Foe

most important to the patients. Fourth, the three hour time limit appears arbitrary and it's not clear how this time frame was chosen. Manipulation of this time point post hoc alters the scientific value of the data. As with the NASCIS II trial, the effect of standardized medical or surgical care on the outcome was not analyzed. Finally, there was no minimum motor impairment criterion for patient inclusion, and, as a result, patients with normal motor function were admitted into the study thus skewing the results.

### OTHER CLINICAL STUDIES TESTING MPSS TREATMENT

To date, numerous other studies and meta-analyses of data across multiple studies have been unable to reproduce the results obtained in the NASCIS trials. Admittedly, most are either retrospective, or smaller prospective studies with less statistical power. A recent PUBMED search for methylprednisolone and spinal cord injury yielded 47 results, none of which supported the use of MPSS with the exception of articles written by the original NASCIS authors.

### COMPLICATIONS ASSOCIATED WITH THE USE OF MPSS

There appears to be little controversy regarding potential harmful side effects. The most worrisome study was the CRASH trial in people in which MPSS was randomly given to 10,008 patients with traumatic brain injury (TBI) at doses similar to the NASCIS III 48-hour protocol. The study was terminated prior to reaching the target population of 20,000 patients because interim analyses showed the relative risk of death to be 1.18 for MPSS patients compared to controls (P=0.00001). This suggests that 1 in 30 patients with TBI that are treated with 48-hour MPSS will die because of the drug itself! Thus, the current recommendation is to **NEVER** give steroids to human or veterinary patients with head trauma.

Returning to SCI trials, a small prospective cohort study by Qian and others showed that high-dose MPSS may cause an acute, rapid myopathy in SCI patients. They suggested that some of the improvement in motor scores may be due to natural recovery from the myopathy rather than protection afforded by MPSS. A veterinary retrospective study by Boag and others compared the incidence of clinically-evident post-operative complications in Dachshunds that were treated surgically for disc extrusion. They found that dogs who were given MPSS ( $\pm$  another corticosteroid) had a significantly higher total hospital charge, increased use of GI protectants, and increased incidence of diarrhea than dogs who received any other steroid.

### CLINICAL STUDIES IN THE VETERINARY LITERATURE

To date, there are no prospective, double-blind, placebo-controlled studies examining the use of MPSS in veterinary patients. Although there are many experimental studies detailing the benefits of MPSS in animals, the method in which SCI is induced is artificial and does not necessarily accurately reflect the consequences of naturally occurring disease. A retrospective study performed by Davis & Brown to determine prognostic indicators for time to ambulation after surgical decompression demonstrated that "there was no difference in time to ambulation between dogs who were treated with any glucocorticoid protocol and dogs not treated with glucocorticoids (P=0.98)." In fact, a recent study by Bush, et. al. (2004), showed that 100% of 51 nonambulatory dogs weighing less than 15 kg body weight with intact pain sensation that **DID NOT** receive MPSS and were treated with hemilaminectomy recovered the ability to walk. A very small study by Coates and others failed to demonstrate a protective effect of MPSS in dogs with experimental SCI. However, only four dogs were given MPSS and the data would only be reliable if the experimental model was extremely

reproducible. Finally, an abstract by Siemering and Vomering in *Veterinary Surgery* described a beneficial effect of using MPSS in dogs undergoing surgery. However, there were no controls included, and the importance of their findings is unknown.

### WHY DO PHYSICIANS USE MPSS IN ACUTE SCI?

Two surveys provide interesting insight into why physicians use MPSS for acute SCI. In the first study, steroids were routinely administered by 98% of all trauma centers in Colorado, but approximately 50% of the medical directors were either uncertain about, or did not believe, the data supporting the use of steroids. In another study of 60 spinal surgeons, only 17% replied that they administer MPSS solely because they found it to be beneficial. Amazingly, 70% of the surgeons prescribed it due to fears of litigation (35%) or due to peer pressure (35%). The remaining surgeons (13%) said they prescribed it for all of the above reasons.

### SHOULD VETERINARIANS USE MPSS IN ACUTE SCI?

Parallels are often drawn between human and veterinary medicine with regard to treatment outcome for many diseases. However, SCI is one area of medicine in which the outcomes we expect are far different. In human medicine, self-sufficiency (e.g., able to eat without assistance, sphincter control) is considered adequate functional recovery. Since dogs and cats are not self-sufficient, our patients have to be able to walk and eliminate voluntarily. Otherwise, euthanasia often is the ultimate outcome.

At this time, there are no conclusive data showing a **CLEAR** and **REPEATABLE** improvement in functional outcome following administration of MPSS in humans. There also is **NO** scientific

proof that MPSS leads to a significant and consistent improvement in functional recovery in veterinary patients with naturally occurring disease. As a result, use of MPSS in veterinary patients remains controversial. However, stay tuned, as there is a multi-institutional, double-blind, placebo-controlled study currently underway being lead by Dr. Natasha Olby at North Carolina State University. This prospective clinical trial will compare MPSS, Polyethylene glycol (PEG), and saline placebo as adjunctive medical therapies to surgical decompression in dogs with acute intervertebral disc herniations.



# I Miss You So Much It Hurts: Canine Separation Anxiety

Separation anxiety is one of the most common behavior problems in dogs, resulting in 20-40% of cases referred to animal behavior practices. It is characterized by excessive vocalization, destructive behavior, inappropriate elimination, vomiting, salivation, diarrhea and self-injurious behavior/self-inflicted trauma in the owner's absence. Separation anxiety is caused by frustration related to a dog's dependency on its owner, not disobedience or boredom, which is a common misconception about the disorder.

## PRESENTATION

The three most common symptoms of separation anxiety in dogs are destructiveness (72%), vocalization (61%), and inappropriate elimination in an otherwise housetrained dog (28%). Dogs with separation anxiety may vocalize to call their owners back to the home or try to remove barriers by chewing and digging at exit points (windows, doors, gates) to join the people they miss. Some affected dogs will engage in even more determined escape attempts and have been known to jump out of windows or break through glass doors. A dog's behavior with separation anxiety is similar to that of a human suffering from panic or phobic disorder. Studies have found a correlation between separation anxiety and noise phobias (such as thunderstorm phobia) in dogs.

### Some Triggers for separation anxiety include:

- Changes in the owner's schedule
- Coming home after a stay in a kennel
- Moving
- The addition or loss of people or pets in the home
- Health issues in older dogs

Dogs with separation anxiety may engage in persistent following of the owner. Most dogs with separation anxiety show anticipatory distress and anxiety before their owner leaves (becoming anxious at the sound of keys or when owner puts on their coat or shoes). Some also mouth, nip, or bite their owners in attempts

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to foil their departure. When their owner departs, dogs with separation anxiety may become severely agitated resulting in restlessness, pacing, or jumping. Physiological symptoms may be present such as vomiting, salivating, trembling, rapid heart rate, and hyperventilation. Hypersalivation, vomiting, or diarrhea occurs in about 20% of dogs with separation anxiety. Dogs with separation anxiety often destroy furniture or other objects while the owner is away. They may target items containing the owner's scent (personal items, bedding, furniture). While the owners are gone they may appear depressed, accompanied by submissive or fearful postures and expressions, and may display inappetence, lethargy, or social withdrawal. Signs of separation anxiety are generally most intense during first 15 minutes after the dog is left alone. Affected dogs often display exaggerated greeting behavior when the owner returns.

## ETIOLOGY

Individual experience, inborn emotionality, and degree of attachment are factors hypothesized to contribute to the development of separation anxiety. Having a home different than the original owner, having several owners, or having undergone a prolonged period of confinement are also common contributors. Dogs with separation anxiety have lived in multiple homes in 77% of cases. Dogs from shelters and mixed breed dogs are more at risk for developing this issue. Many dogs with separation anxiety show hyperattachment to their owner.

There could be a genetic component predisposing some dogs to separation anxiety. Dogs that are more submissive in temperament, or working breeds that form strong bonds with their owners, such as herding or hunting breeds, may be more susceptible. Dogs over ten years of age are often seen for separation anxiety. Geriatric dogs may be physically uncomfortable or have health issues that cause them to seek out their owners for comfort. Geriatric dogs could also develop separation anxiety due to reduced cognitive capacity or emotional adaptability.

Dogs living in homes with one owner are 2.5 times more likely to have separation anxiety than dogs from multiple owner homes. Sexually intact dogs are 1/3 as likely to have separation anxiety as spayed or neutered dogs.

**Factors not correlated with separation anxiety include:**

- Spoiling the dog (sleeping in owner's bed or feeding from the table)
- Having other dogs or pets in the home
- The sex of the dog
- The age the dog was acquired
- The gender of the owner
- The dog's age at referral
- Early separation from the mother

## TREATMENT

**Medical Rule-Out:** If a dog is showing symptoms of separation anxiety, tests should be run to rule out underlying medical conditions (chemistry profile, CBC, T4, fecal exam and urinalysis).

**Punishment:** Owners should be instructed never to punish their dog for being destructive, barking, house soiling, or other undesirable behavior. Bark collars will make the issue worse. Punishment will make the dog more anxious and uncomfortable, and can worsen the situation.

**Crating is Not a Solution:** Dogs with separation anxiety may injure themselves severely if crated. It is not

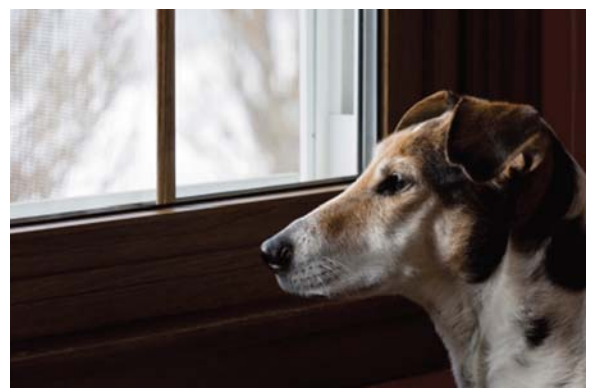
uncommon for them to break teeth or nails, or cut themselves trying to escape. Confining the dog to a room, gated-off area, or exercise pen are better options.

**Destructive Behavior:** Plexiglas can be nailed over doors or moldings. "Boundary Spray" or "Bitter Apple" are good deterrents. If the dog is house soiling, use a black light to fluoresce old stains, and eliminate odors with "Zero Odor" ([www.zeroodorstore.com](http://www.zeroodorstore.com)).

**The Hardest Part:** The dog should not be left alone, or at least not for long periods, for the first month while owners implement the behavior modification program. The dog needs to learn in baby steps that they have not been abandoned when their owners leave. Even if the owners are compliant with the rest of the program, leaving their dog alone for long periods will cause a return in the dog's anxiety and fear. A friend, neighbor, family member, pet sitter, or doggie daycare are good options. If owners have to leave the dog without backup, Melatonin or Alprazolam may be given.

**Exercise:** Dogs with separation anxiety are most anxious just after their owners depart so it is ideal if the owners can exercise them prior to leaving.

**Desensitize the Dog to Departure Cues:** Many dogs with separation anxiety become anxious when their



Signs of separation anxiety are generally most intense during first 15 minutes after the dog is left alone.

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## I Miss You So Much It Hurts

owners prepare to leave (put on their shoes or coat, get their keys, grab their purse, walk to the door, etc.) Owners should work on desensitizing their dog to departure cues that make them anxious when the owners are not leaving. For example: pick up a shoe then set it down again, jingle the keys while walking by, or wear a coat in the house.

**Planned Departures:** Owners should habituate their dog to them coming and going. They can start by walking out the door and coming right back in. They will need to build up to leaving the dog for short periods. When the owners come inside they should not greet their dog. If the dog is barking, whining, or showing signs of anxiety when they return, they have proceeded too quickly and should shorten the length of departures. Since most dogs with separation anxiety tend to panic the most during the first 15 minutes after their owners leave, if the owners can leave them for 20 minutes without them getting upset they should be able to leave for longer periods.

**Coming & Going:** For the first 10-15 minutes prior to leaving or returning owners shouldn't soothe their dog or be overly-affectionate in any way. They should ignore their dog but still remain upbeat and calm.

Owners should feed their dog as they are leaving. Putting the dog's meals inside food puzzles (Kong, Buster Cube, Twist-n-Treat) will keep them entertained. Many dogs with separation anxiety don't eat at first but once they get in the habit of expecting food every day when their owners leave they should start eating. High value treats and toys should be given as the owners leave as well, and should be switched out daily for variety. The dog should only have access to these items when left alone and they should be picked up as soon as the owner returns.

It can also help to leave the lights, a radio, or the television on, or the window blinds/curtains open when owners leave the house.

**Another Pet?:** Most dogs with separation anxiety will not show improvement with the addition of another dog or pet.

**Independence Training:** Many dogs with separation anxiety are extremely bonded to family members and shadow their owners. They may vocalize or become destructive when access to their owners is blocked. Owners should give these dogs less social and body contact.

To train their dog to do things on their own, owners can tether their dog on a leash to a nearby object with something fun to do (food puzzle, bone). They should be tethered for a few minutes at first and for longer periods over time. Owners should go about their business and eventually build up to moving in and out of the room or to different areas of the house with the dog tethered.

**Medication:** Fluoxetine (Reconcile) and clomipramine (Clomicalm) are effective drugs for treating separation anxiety. Alprazolam can be prescribed in the short term until they reach therapeutic levels (typically 4-5 weeks). There can be a paradoxical reaction of increased excitement or agitation in some dogs given Alprazolam. Owners can give a half dose to their dog while they are home to see if this occurs. Alprazolam can disinhibit behavior so it is not recommended for aggressive dogs. Separation anxiety dogs administered clomipramine improved three times faster than those given placebo. Improvement was reported in 73% of dogs receiving Reconcile versus 51% of dogs receiving placebo. Medication alone will not resolve this issue but it is a useful adjunct to treatment.



# Hypoadrenal Disorders

**IT WOULD BE SAFE** to declare steroids the world's most important hormone given the role they play in homeostasis and regulation of every organ in the body. Glucocorticoids (GC) are well known to regulate energy metabolism (gluconeogenesis, lipolysis and glycolysis), immune function, wound healing and gastrointestinal health at physiologic doses. Mineralocorticoids (MC) are important actors in the renin-angiotensin-aldosterone axis; aldosterone regulates potassium (K+) closely and by stimulating sodium (Na+) reabsorption, affects water retention in normal metabolism and in hypovolemia as water is reabsorbed closely with Na+.

It is these effects of steroids that allow us to diagnose a "typical" hypoadrenal (or Addisonian) crisis with ease (see Fig. 1). Recently, we have started to note a number of hypoadrenal patients with "atypical" presentations. Atypical hypoadrenal animals may not have aldosterone insufficiency and maintain normal Na/K ratios. Identifying these animals is made easier when your level of suspicion is high. Atypical hypoadrenal animals may present with chronic GI signs or seem sicker from a simple disease than could be predicted. A lack of a stress leukogram can be another sign that should not be ignored when your patient is clearly sick.

What is less well known is the important role of steroids in maintaining cardiac function and blood pressure. Both GC and MC have direct chronotropic and inotropic effects. By maintaining heart rate and contractility, steroids maintain cardiac output. Steroids are also extremely important in maintaining systemic blood vessel tone and blocking increased vascular permeability. By supporting cardiac output and systemic vascular resistance, blood pressure is maintained. Steroids are also necessary for blood vessels and the heart to respond maximally to catecholamines (epinephrine, norepinephrine) and will increase  $\beta$ -adrenergic receptor density and synthesis. Steroids also inhibit inducible nitric oxide synthase (iNOS) and therefore

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Clinical Signs	Typical	Atypical
Na/K ratio < 27	Yes	No
Hyperkalemia	Yes	No
Azotemia	Yes	Yes/Maybe
Isothermuria	Yes	Yes/Maybe
GI Signs	Maybe	Maybe
Anemia	Maybe	Maybe
Stress Leukogram	Maybe	Maybe
Hypocholesterolemia	Maybe	Maybe

Fig 1: Diagnosing a Hypoadrenal or Addisonian crisis

**Q:** How atypical is atypical Addisons?

**A:** Maybe not so atypical; literature estimates are from 4-45% of all adrenal disease.

maintain blood vessel tone by countering inflammatory-driven vasodilation.

It is precisely this important facet of physiologic steroids that has led to a resurgence in the investigation of GC steroids in various diseases. A deficiency in MC hormones is less common but can occur concurrently. Research has shown that critically ill humans and animals may have temporary hypoadrenal disorders that occur by three mechanisms related to the hypothalamic-pituitary-adrenal-target cell axis: lack of cortisol production, lack of cortisol effects or lack of cortisol/adrenal reserve.

## Hypoadrenal Disorders

### More specifically:

- 1) hypocortisolemia can occur secondary to interrupted function of the brain or adrenal glands;
- 2) changes in steroid receptor expression and function can manifest as adrenal insufficiency in the face of sufficient cortisol;
- 3) some patients may also have limited adrenal hormone reserves or capacity to respond to further stress.

Hypoadrenal illness in humans is currently called critical-illness related corticosteroid insufficiency or CIRCI, but had recently also been termed relative adrenal insufficiency (RAI.) CIRCI occurs relatively infrequently in the general population but is common in sepsis, traumatic brain injury, and other critically ill patient populations. Diagnosing CIRCI is challenging but relies on basal cortisol, ACTH stimulation testing and sometimes [ACTH]. Studies in dogs have shown that the basal cortisol level in itself may not be helpful.

More important may be the change in cortisol levels due to the stimulation test, also termed the delta cortisol ( $\Delta$  cortisol). A  $\Delta$  cortisol that is too small indicates a lack of adrenal reserve or complete cessation of function. The lower dose ACTH stimulation test may be more sensitive in picking up patients with low adrenal reserves than the high dose test. (The high dose (supraphysiologic) ACTH stimulation test maximally stimulates cortisol release and can override some patient's limited reserve function.) Mortality rates in septic humans are closely tied to the basal cortisol and  $\Delta$  cortisol. One study showed that if the basal cortisol was  $< 34$  ug/dL and  $\Delta$  cortisol was  $> 9$  ug/dL, the mortality rate of that group was 28%. However, if your basal cortisol was the opposite ( $> 34$  ug/dL and  $\Delta$  cortisol was  $< 9$  ug/dL), the mortality rate increased to 82%. A huge difference!

**Q:** Will my atypical Addisonians eventually develop abnormal electrolytes?

**A:** Likely not. A small percentage of atypical Addisonion dogs in the literature became typical (MC deficient).

**Q:** What steroid can I give a suspected Addisonian in crisis so I don't affect the ACTH Stim test?

**A:** Only Dexamethasone (NaP) because it doesn't interfere with the measurement of cortisol in assay.

**Q:** What steroid do I give in shock? And what dose?

**A:** No steroids for shock; only in Addisonian crisis are steroids indicated. Human studies show **INCREASED MORTALITY** using high dose steroids for shock.

Unfortunately, in real practice, guidelines for lab tests and diagnosis of CIRCI do not always fit every case; clinicians also have to factor in other clinical testing. Hypotension that is unresponsive to vasopressors is also an indication to consider CIRCI. Some doctors also suggest a clinical trial of hydrocortisone in patients with clinical signs that fit CIRCI. Hydrocortisone doses to treat CIRCI are remarkably small: 2 mg/kg/day, compared to "shock" doses of 50 mg/kg. The high doses will not give you more of a "good thing." Only the low dose effectively treats hypotension and other clinical effects of hypocortisolemia. Hydrocortisone is also the steroid of choice for dogs given its chemical similarity to endogenous cortisol; but, I have used prednisone injectable for cases of CIRCI at a dose of 0.5 mg/kg/day with success. CIRCI is a temporary disease and supplementation with steroids is only necessary for short periods (1-7 days possibly).

### How often do I think CIRCI occurs in dogs and cats?

That's a difficult question. Two studies have looked at hypoadrenal symptoms and CIRCI lab testing in dogs. Sepsis is the clear number one disorder that canine CIRCI is associated with, but some other dogs with trauma and GDV have also been studied. In cats the associated disease states may be more diverse, but there is literature evidence for an association with neoplasia, specifically lymphoma. There was also a case report of a CIRCI cat with polytrauma.

### How often do I document CIRCI?

Potentially, only once a month at most.

Another confounding factor can be dogs with atypical Addison's disease who become clinical for a second disorder (trauma, sepsis, rickettsial disease). These dogs are permanently hypoadrenal and cannot respond to illness appropriately. As clinicians, we can get fooled by the primary illness and fail to notice the hyperkalemia or low Na/K ratio, eosinophilia, lack of stress leukogram, profound weakness despite aggressive fluid therapy, peripheral vasoconstriction and poor perfusion (extremely cool feet with normal core body temperature). These small "blips on the radar" should alert the clinician to look for something else; there's more to the story. Remember to avoid using any steroid other than dexamethasone in any animal that you might consider testing with an ACTH stimulation test. Other steroids (methylpred, pred, depomedrol) are chemically similar to cortisol and interfere with measurement of cortisol levels at the lab.

In summary, hypoadrenal disorders can come in many varieties: typical, atypical, permanent, and temporary. A small population of critically ill dogs and cats may be hypoadrenal, and the usual manifestation of that insufficiency is hypotension. The ACTH stimulation test is the gold standard at this time but a much lower dose can be used. Treatment of hypoadrenal disorders is with

extremely low doses of steroids, because high doses of steroids will increase mortality and will not help blood pressure.



## LITERATURE SNAPSHOTS

### Parvo puppies

Schoeman JP et al. Serum cortisol and thyroxine concentrations as predictors of death in critically ill puppies with parvoviral diarrhea. *JAVMA* 2007;231:1534-1539

- Basal cortisol measured 48 hours into hospitalization reliably predicted mortality.
  - If [cortisol] > 8.06 ug/dL, mortality 100%.

### Lower dose Cortrosyn for ACTH stimulation test

Martin LG et al. Effect of low doses of cosyntropin on serum cortisol concentrations in clinically normal dogs. *Am J Vet Res* 2007;68:555-560

- The usual ACTH stimulation test uses a supraphysiologic dose of cosyntropin (Cortrosyn) 5 mcg/kg IV.
- In this study a much lower dose (0.5 mcg/kg) induced maximal stimulation.
- Savings on Cortrosyn would make ACTH stim testing more economical.

IVG is dedicated to providing referring veterinarians and their clients with an unparalleled range of emergency and specialty services.



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**NEUROLOGY**  
Mass Vet – Woburn, MA

**OPHTHALMOLOGY**  
Bulger – N. Andover, MA  
Mass Vet – Woburn, MA  
Port City – Portsmouth, NH

**PHYSICAL THERAPY & REHABILITATION**  
Mass Vet – Woburn, MA  
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**SURGERY**  
Bulger – N. Andover, MA  
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