

HIPOADRENOCORTICISMO

Parte I

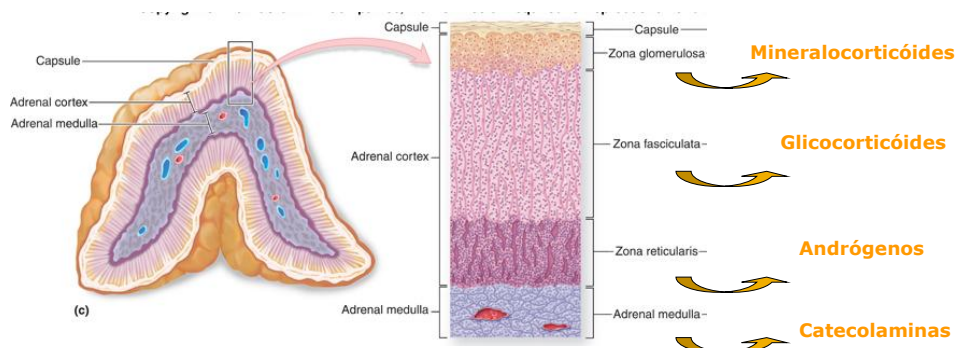
Prof. Dr. Álan Gomes Pöppel

Médico Veterinário - UFRGS
 Residência em Clínica e Cirurgia de Pequenos Animais - HCV/UFRGS
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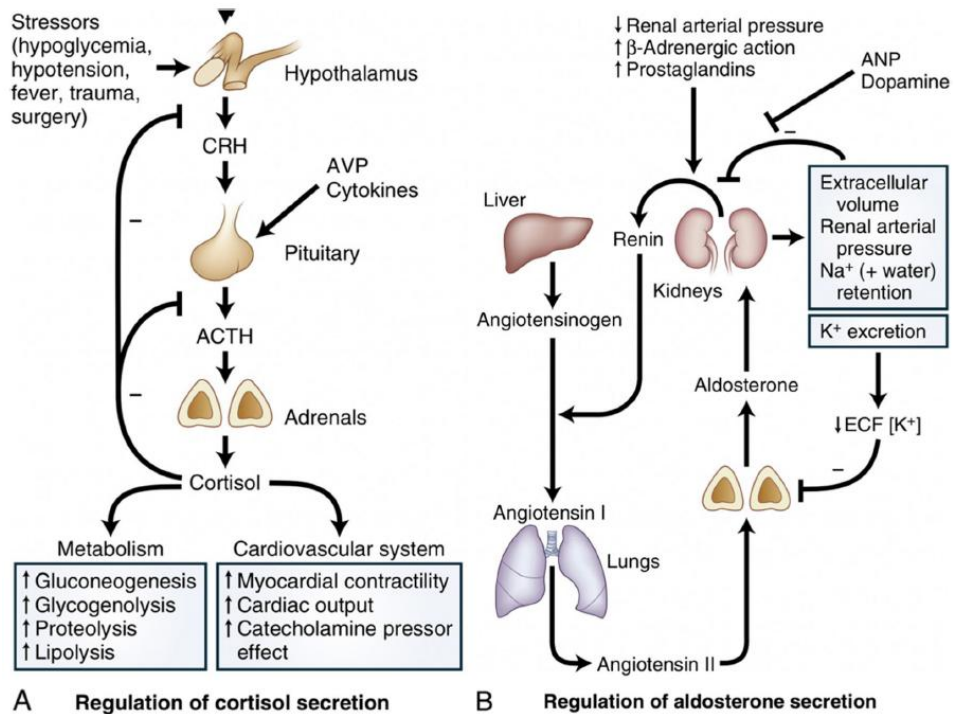


1

Histologia da Glândula Adrenal

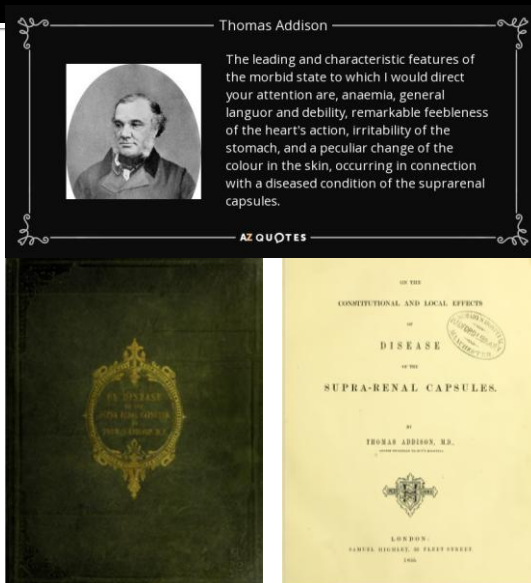
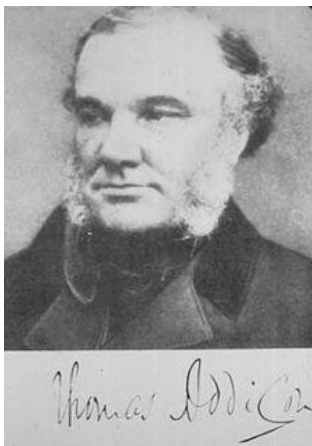


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3

Em 1855 Addison descreve pacientes com anorexia, anemia, estômago irritável e alterações na cor da pele associado a atrofia ou necrose das adrenais

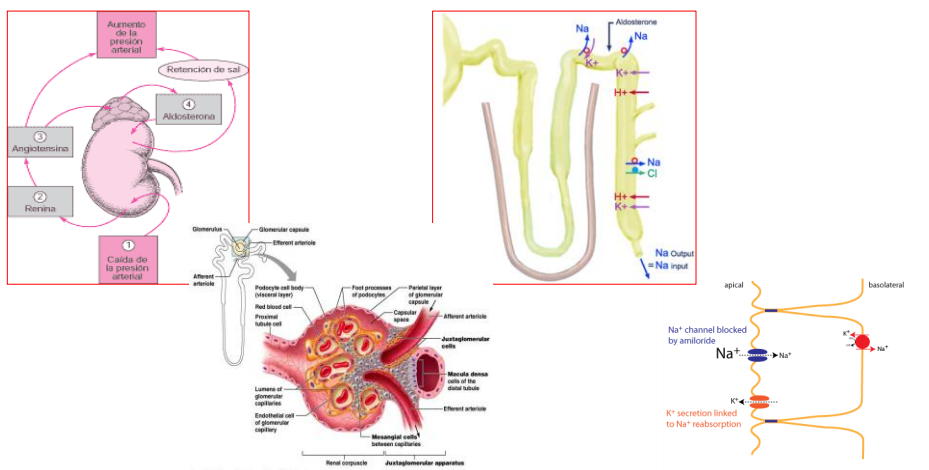


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HIPOADRENOCORTICISMO

“Síndrome de Addison”

- Deficiência de glicocorticoides e mineralocorticoides.



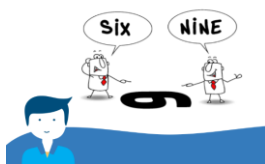
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“Alguns” Efeitos dos glicocorticoides

- Metabolismo intermediário:** Estímulo a gliconeogênese, lipólise periférica e acúmulo gordura central, proteólise
- Sangue:** Supressão do sistema imune humoral e celular, linfocitólise, sequestro eosinófilos, redução diapedese neutrófilos e monócitos, estímulo a eritropoiese e plaquetas
- Cardiovascular:** sensibiliza arteríolas aos efeitos vasoconstritores de catecolaminas e angio-2, mantendo PA basal e atividade do miocárdio. Manutenção do volume sanguíneo e redução na permeabilidade capilar
- SNC:** modulação do humor e do sono, sensação geral de bem estar
- Metabolismo hídrico:** Aumento na TFG, Supressão ADH hipófise e interferência com ação ADH renal
- TGI:** manutenção função mucosa, epitélio em escova e atividade mitocondrial enterócitos. Influência sobre microbioma, digestão e absorção
- Metabolismo Cálcio:** aumenta excreção de cálcio e suprime absorção intestinal

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Projeto ALIVE (Agreing Language in Veterinary Endocrinology) - ESVE

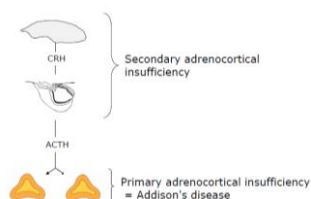


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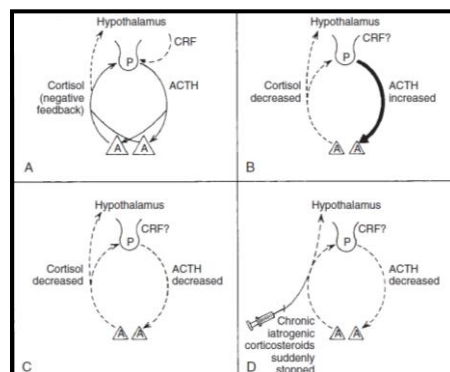
Hipoadrenocorticismo

Termo guarda-chuva para as diferentes causas naturais ou iatrogênicas que levam a redução da função adrenal, causando estado de deficiência de glicó e/ou mineralocorticóides

- **Hipoadrenocorticismo primário**
(destruição adrenal > 95%)
- **Hipoadrenocorticismo secundário**
(Insuficiência hipotálamo-hipofisária)



- **Hipoadrenocorticismo iatrogênico:**
 - parada abrupta tto c/corticóides,
 - uso de progestágenos,
 - secundário ttos p/ síndrome de Cushing (farmacológicos ou cirúrgicos)



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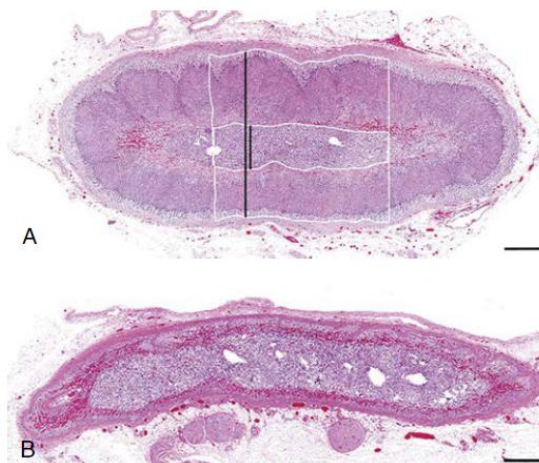
Etiologia Hipoadrenocorticismo Primário ("Doença de Addison" - ALIVE)

- > 95% casos primários destruição autoimune (adrenalite imunomediada)

- **Outras causas:**

- Neoplasias adrenais primárias ou metastáticas
- Infarto hemorrágico
- Abscessos

➔ Normalmente destruição das três zonas!



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Etiologia Hipoadrenocorticismo Primário (Síndrome de Addison)

- 43% cães apresentam Autoanticorpos *Anti-side-chain cleavage enzyme*



RESEARCH ARTICLE

Autoantibodies against Cytochrome P450 Side-Chain Cleavage Enzyme in Dogs (*Canis lupus familiaris*) Affected with Hypoadrenocorticism (Addison's Disease)

Alisdair M. Boag¹, Michael R. Christie^{2,3}, Kerry A. McLaughlin², Harriet M. Syme⁴, Peter Graham⁵, Brian Catchpole^{6,*}

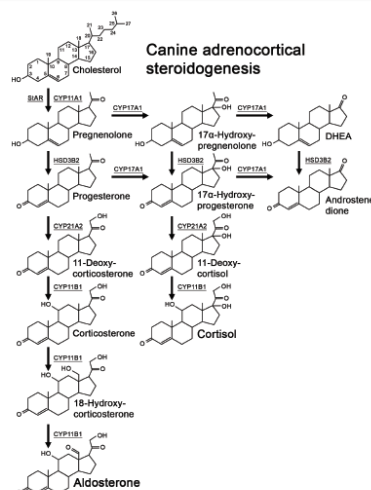


Figure 6 Proposed canine adrenocortical steroidogenesis. StAR, steroidogenic acute regulatory protein; CYP11A1, cytochrome P450 side chain cleavage; HSD3B2, 3 β -hydroxysteroid dehydrogenase 2; CYP17, 17 α -hydroxylase/17,20-lyase; CYP21A2, 21-hydroxylase; CYP11B1, 11 β -hydroxylase; cytochrome P450.

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Etiologia Hipoadrenocorticismo Primário (Síndrome de Addison)

Immunogenetics (2013) 65:291–297
DOI 10.1007/s00251-013-0686-7

ORIGINAL PAPER

MHC class II association study in eight breeds of dog with hypoadrenocorticism

Jonathan Massey · Alisdair Boag · Andrea D. Short ·
Rachel A. Schley · Paulo S. Henriques ·
Meryl P. Littman · Eystein Husebye · Brian Catchpole ·
Niels Pedersen · Cathryn S. Melicni ·
William E. R. Ollier · Lorna J. Kennedy

Published in final edited form as:
Int J Immunogenet. 2006 June; 33(3): 179–184. doi:10.1111/j.1744-313X.2006.00590.x

Understanding the genetics of autoimmune disease: two loci that regulate late onset Addison's disease in Portuguese Water Dogs

K. Chae¹, D. Bargan^{1,5}, K. Miller², E. A. Ostrander¹, and K. G. Lark³

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²Comparative Genetics Section, Cancer Genetics Branch, NCI/NIH, Bethesda, Maryland 20892, USA

³The George Project, Portland, Maine, USA

⁴Center for Veterinary Science, Department of Veterinary Medicine, University of Cambridge, Cambridge, UK

Short Communication

Putative candidate genes for canine hypoadrenocorticism (Addison's disease) in multiple dog breeds

A. D. Short, B. Catchpole, A. M. Boag,
L. J. Kennedy, J. Massey, S. Rothwell,
P. S. Henriques, M. P. Littman, E. Husebye,
B. Ollier

the major locus and others 2007
2011 (and other
and others 2011)
The candidate
genes were found
in the major locus
and others 2007
2011 (and other
and others 2011)
The candidate
genes were found
in the major locus
and others 2007
2011 (and other
and others 2011)

TISSUE ANTIGENS

Tissue Antigens 93:291–297 (2015)

Association of a dog leukocyte antigen class II haplotype with hypoadrenocorticism in Nova Scotia Duck Tolling Retrievers

A. M. Hughes^{1,2}, P. Jokinen^{3,4}, D. L. Breenach⁵, H. Loh² & A. M. Oberbauer¹

¹Department of Animal Science, University of California, Davis, CA, USA

²Department of Basic Veterinary Sciences, Department of Medical Genetics, Program in Molecular Medicine, Institution of Medicine, University of Toronto, Toronto, Canada

³Department of Medicine, University of Helsinki, Helsinki, Finland

⁴School of Veterinary Medicine, Population, Health and Reproduction, University of California, Davis, CA, USA

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Boag et al. *Canine Medicine and Genetics*
<https://doi.org/10.1186/s40575-020-0081-4>

(2020) 7:2

Canine Medicine and
Genetics

RESEARCH

Open Access

Polymorphisms in the *CTLA4* promoter sequence are associated with canine hypoadrenocorticism

Alisdair M. Boag^{1,2*}, Andrea Short³, Lorna J. Kennedy³, Hattie Syme⁴, Peter A. Graham⁵ and Brian Catchpole¹

Abstract

Background: Canine hypoadrenocorticism is an immune-mediated endocrinopathy that shares both clinical and pathophysiological similarities with Addison's disease in humans. Several dog breeds are overrepresented in the disease population, suggesting that a genetic component is involved, although this is likely to be polygenic.

Previous research has implicated *CTLA4* as a potential susceptibility gene. *CTLA4* is an important regulator of T cell function and polymorphisms/mutations in *CTLA4* have been associated with a number of autoimmune phenotypes in both humans and rodent models of autoimmunity. The aim of the current study was to undertake a case-control association study of *CTLA4* promoter polymorphisms in three dog breeds, cocker spaniels, springer spaniels and West Highland white terriers (WHWT).

Results: Polymorphisms in the *CTLA4* promoter were determined by PCR and sequence-based typing. There were significant associations with three promoter haplotypes in cocker spaniels ($p = 0.003$). A series of SNPs were also associated with hypoadrenocorticism in cocker spaniels and springer spaniels, including polymorphisms in predicted NFAT and SP1 transcription factor binding sites.

Conclusions: This study provides further evidence that *CTLA4* promoter polymorphisms are associated with this complex genetic disease and supports an immune mediated aetio-pathogenesis of canine hypoadrenocorticism.

Keywords: Addison's, Canine, *CTLA-4*, Hypoadrenocorticism, Promoter

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Apesar de alguns padrões autossômicos recessivos descritos, um padrão de herdabilidade mais complexo como o descrito em humanos é mais provável

TABLE 12-2 ESTIMATES OF HERITABILITY, ESTIMATED PREVALENCE OF HYPOADRENOCORTICISM, AND SEX PREDISPOSITION IN BREEDS WITH HERITABLE HYPOADRENOCORTICISM				
BREED	HERITABILITY	MODE OF INHERITANCE	ESTIMATED PREVALENCE	SEX PREDISPOSITION
Standard Poodle	0.75	Autosomal recessive	8.6%	None
Portuguese Water dog	0.49	Autosomal recessive	1.5%	None
Nova Scotia Duck Tolling Retriever	0.98	Autosomal recessive	1.4%	None
Bearded Collie	0.76	Unknown	9.4%	None

From Ettinger SJ, Feldman EC: *Textbook of veterinary internal medicine*, ed 7, St Louis, 2010, Saunders/Elsevier.

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Sundberg et al. BMC Veterinary Research (2016) 12:278
DOI 10.1186/s12917-016-0911-5

BMC Veterinary Research

RESEARCH ARTICLE

Open Access

 CrossMark

Gonadectomy effects on the risk of immune disorders in the dog: a retrospective study

Crystal R. Sundberg¹, Janelle M. Belanger¹, Danika L. Bannasch², Thomas R. Famula³ and Anita M. Oberbauer^{1*}

Abstract

Background: Gonadectomy is one of the most common procedures performed on dogs in the United States. Neutering has been shown to reduce the risk for some diseases although recent reports suggest increased prevalence for structural disorders and some neoplasias. The relation between neuter status and autoimmune diseases has not been explored. This study evaluated the prevalence and risk of atopic dermatitis (ATOP), autoimmune hemolytic anemia (AIHA), canine myasthenia gravis (CMG), colitis (COL), hypoadrenocorticism (ADD), hypothyroidism (HYPO), immune-mediated polyarthritis (IMPA), immune-mediated thrombocytopenia (ITP), inflammatory bowel disease (IBD), lupus erythematosus (LUP), and pemphigus complex (PEMC), for intact females, intact males, neutered females, and neutered males. Pyometra (PYO) was evaluated as a control condition.

Results: Patient records (90,090) from the William R. Pritchard Veterinary Medical Teaching Hospital at the University of California, Davis from 1995 to 2010 were analyzed in order to determine the risk of immune-mediated disease relative to neuter status in dogs. Neutered dogs had a significantly greater risk of ATOP, AIHA, ADD, HYPO, ITP, and IBD than intact dogs with neutered females being at greater risk than neutered males for all but AIHA and ADD. Neutered females, but not males, had a significantly greater risk of LUP than intact females. Pyometra was a greater risk for intact females.

Conclusions: The data underscore the importance of sex steroids on immune function emphasizing a role of these hormones on tissue self-recognition. Neutering is critically important for population control, reduction of reproductive disorders, and offers convenience for owners. Despite these advantages, the analyses of the present study suggest that neutering is associated with increased risk for certain autoimmune disorders and underscore the need for owners to consult with their veterinary practitioner prior to neutering to evaluate possible benefits and risks associated with such a procedure.

Keywords: Neuter, Dog, Immune function, Gonadectomy

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DOI: 10.1111/jvim.16896

STANDARD ARTICLE

Journal of Veterinary Internal Medicine
Open Access
American College of Veterinary Internal Medicine

A case-control survey study of environmental risk factors for primary hypoadrenocorticism in dogs

Amy E. Treeful^{1,2} | Kelly M. Searle³ | Dana M. Carroll⁴ | Kathleen J. Yost⁵ | Anna L. Hedger² | Steven G. Friedenberg²

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted P value
Neutered			
Yes	6.6 (3.2-13.7)	6.0 (2.6-13.9)	$P < .001$
Spayed			
Yes	3.6 (2.1-6.4)	2.5 (1.4-4.5)	$P = .003$

TABLE 2 Multivariable logistic regression analysis.

TABLE 1 Univariate logistic regression analysis.

Variable	Cases (n = 330) n (%)	Controls (n = 2726) n (%)	Odds ratio (95% CI)	P value
Breed				<.001
Portuguese Water Dog	48 (14.6%)	117 (4.3%)	3.8 [2.7-5.4]	
Standard Poodle	282 (85.5%)	2609 (95.7%)	REF	
Neutered				<.001
No	8 (5.5%)	377 (27.8%)	REF	
Yes	138 (94.5%)	981 (72.2%)	6.6 [3.2-13.7]	
Spayed				<.001
No	14 (7.7%)	318 (23.3%)	REF	
Yes	167 (92.3%)	1045 (76.7%)	3.6 [2.1-6.4]	
Other medical conditions				<.001
No	254 (80.6%)	2441 (89.7%)	REF	
Yes	57 (18.1%)	260 (9.6%)	2.1 [1.5-2.9]	
Do not know	4 (1.3%)	20 (0.7%)	OMIT	
Community				<.001
Farm	4 (1.3%)	196 (7.3%)	0.2 [0.1-0.5]	<.001
Rural	71 (23.1%)	687 (2.4%)	0.8 [0.6-1.2]	.27
Suburban	176 (57.3%)	1325 (49.4%)	1 [0.8-1.5]	.82
Urban/city	51 (16.6%)	399 (14.9%)	REF	
Other	5 (1.6%)	65 (2.4%)	OMIT	
Food				
Canned	52 (15.8%)	317 (11.6%)	1.4 [1-2]	.03
Campfires				.02
Never	234 (77.2%)	1779 (67.2%)	REF	
A few times a year	55 (18.2%)	676 (25.5%)	0.6 [0.5-0.8]	.002
A few times a month	8 (2.6%)	98 (3.7%)	0.6 [0.3-1.3]	.2
Monthly	3 (1.0%)	58 (2.2%)	0.4 [0.1-1.3]	.12
Weekly	3 (1.0%)	34 (1.3%)	0.7 [0.2-2.2]	.5
Lawn fertilizer				.05
No	152 (53.7%)	1499 (59.7%)	REF	
Yes	131 (46.3%)	1011 (40.3%)	1.3 [1-1.6]	

Note: Qualified participants were restricted to those with known spay/neuter status ≥ 25 months old at the time of survey (n = 330 dogs with hypoadrenocorticism, n = 2726 controls).
Abbreviations: CI, confidence interval; OMIT, the variable was omitted from evaluation due to low frequency; REF, the variable choice which was set as the reference to which other choices for the same variable were compared.

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DOI: 10.1002/vrc2.426

CASE REPORT

Companion or pet animals

VetRecord
CaseReports

Hypocortisolism in a dog caused by bilateral pheochromocytoma

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²Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands

³Facultad de Ciencias Agrarias y Veterinaria, Universidad del Salvador, Buenos Aires, Argentina

Correspondence

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Abstract

We present a 12-year-old French bulldog with muscle weakness, epigastric pain, weight loss, high systolic blood pressure and cardiac arrhythmias. Physical and laboratory examination revealed no abnormalities. On a computed tomography scan, severely enlarged adrenals were found, and endocrine and biochemical evaluations excluded hypercortisolism and hyperaldosteronism. Urinary metanephrine and normetanephrine/creatinine ratios were elevated, compatible with a diagnosis of pheochromocytoma. Symptomatic treatment with phenoxybenzamine was started and resulted in normalisation of a systolic blood pressure and reduction of arrhythmias. However, the onset of anorexia, vomiting and clinical deterioration prompted exploration of the adrenocortical reserve through an adrenocorticotrophic hormone stimulation test, which confirmed glucocorticoid deficiency. Mineralocorticoid deficiency was ruled out by normal plasma aldosterone concentration and renin activity. Finally, an elevated endogenous plasma adrenocorticotrophic hormone concentration defined the primary origin of the hypocortisolism. Clinical resolution occurred with prednisolone supplementation. This is the first report of hypocortisolism in a dog caused by a bilateral pheochromocytoma.

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Epidemiologia ocorrência natural

- Média de 1 caso para cada 2000 cães, prevalência reportada entre 0,06-0,28% população
- Mais comum em fêmeas (69%) (OR=1,85-2,6)
- Afeta todas as idades (2 meses a 14 anos)
- SRDs, Poodles, West White, Pastor, Rottweiler, Doberman, Cão d'água Português, Airedale, Basset hound, Sheep Dog, Dinamarquês...
- Prognóstico excelente com tratamento,

TABLE 12-3 BREEDS REPORTED TO BE EITHER AT INCREASED OR DECREASED RISK OF HYPOADRENOCORTICISM

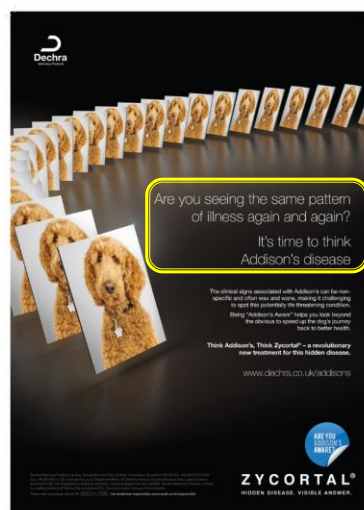
BREED	INCREASED RISK	DECREASED RISK
Airedale Terrier	X	
Basset Hound	X	
Bearded Collie	X	
Boxer		X
Chihuahua		X
Cocker Spaniel		X
Dalmatian		X
Golden Retriever		X
Great Dane	X	
Lhasa Apso		X
Nova Scotia Duck Tolling Retriever	X	
Pit Bull Terrier		X
Pomeranian		X
Portuguese Water Dog	X	
Rottweiler	X	
Saint Bernard	X	
Shetland Sheepdog		X
Shih Tzu		X
Springer Spaniel	X	
Standard Poodle	X	
West Highland White Terrier	X	
Wheaten Terrier	X	
Yorkshire Terrier		X

From Ettinger SJ, Feldman EC: *Textbook of veterinary internal medicine*, ed 7, St Louis, 2010, Saunders/Elsevier.

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Histórico ocorrência natural

- “Doença que vem, passa e volta episodicamente”
- “parece melhorar após tratamentos veterinários com uso de Fluídos / corticoides”
- Há apresentações agudas e crônicas, sendo que nas crônicas, os pacientes podem apresentar períodos sem manifestações de sinais clínicos
- Iatrogênico frequentemente agudo



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Canine hypoadrenocorticism: A retrospective study of 32 cases from 2011 to 2018

Cinthia PERES CAMILO^{1,2}, Mauro José LAHM CARDOSO³, Paula NASSAR DE MARCHI⁴, Rafael FAGNANI¹¹Department of Veterinary Clinics, State University of Londrina, Londrina, Paraná, Brazil²Department of Veterinary Clinics, Faculty of Veterinary Medicine, University of Sorocaba, Sorocaba, São Paulo, Brazil³Department of Preventive Veterinary Medicine, State University of Londrina, Londrina, Paraná, Brazil

Received: 13.08.2020 • Accepted/Published Online: 20.12.2020 • Final Version: 23.02.2021



Figure 1. Relative and absolute frequency of breed and sex of 32 dogs with hypoadrenocorticism*. *Patients attended during the period from 2011 to 2018.

TABLE 12-3 BREEDS REPORTED TO BE EITHER AT INCREASED OR DECREASED RISK OF HYPOADRENOCORTICISM

BREED	INCREASED RISK	DECREASED RISK
Airedale Terrier	X	
Basset Hound	X	
Bearded Collie	X	
Boxer		X
Chihuahua		X
Cocker Spaniel		X
Dalmatian		X
Golden Retriever		X
Great Dane	X	
Lhasa Apso		X
Nova Scotia Duck Tolling Retriever	X	
Pit Bull Terrier		X
Pomeranian		X
Portuguese Water Dog	X	
Rottweiler	X	
Saint Bernard	X	
Shetland Sheepdog		X
Shih Tzu		X
Springer Spaniel	X	
Standard Poodle	X	
West Highland White Terrier	X	
Wheaton Terrier	X	
Yorkshire Terrier		X

From Ettinger SJ, Feldman EC: *Textbook of veterinary internal medicine*, ed 7, St Louis, 2010, Saunders/Elsevier.

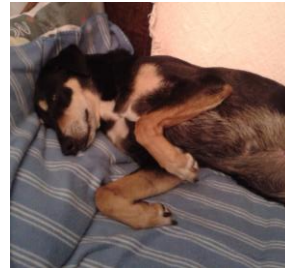
Sinais Clínicos / Anamnese

- Anorexia / apetite fraco
- Letargia / depressão
- Perda de peso
- Vômitos (com ou sem hematêmese) / regurgitação
- Diarreia (com ou sem melena/hematoquesia)
- Poliúria / Polidipsia discreta
- Tremores
- Colapsos
- Dor abdominal

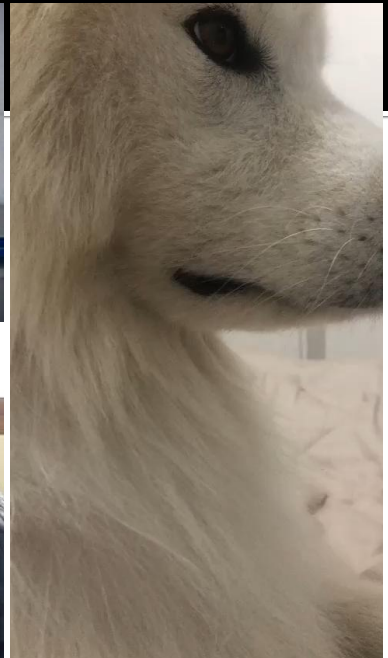


Exame clínico

- Colapso / Postura antálgica
- Desidratação
- Caquexia
- **Bradicardia**
- Pulso fraco
- Hipotensão
- Hipotermia
- Fraqueza/Hipotonia



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Manifestações clínicas

- Nem todos sinais possíveis estarão presentes ao mesmo tempo...
- Inclusão de HipoA entre diagnóstico diferencial para queixas vagas é fundamental

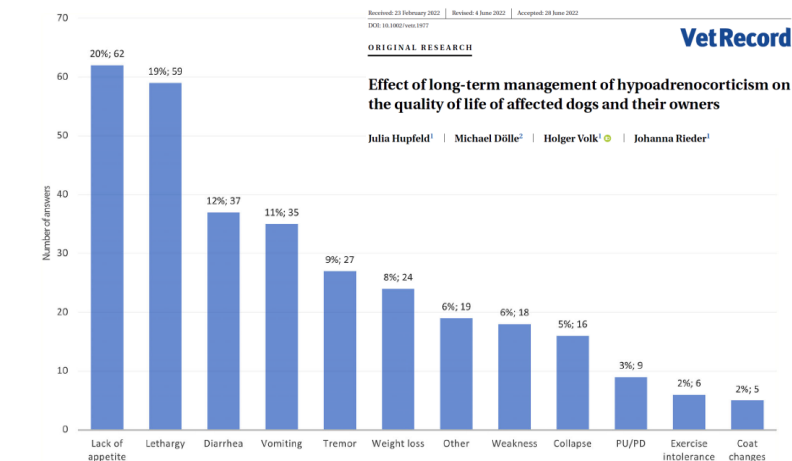


FIGURE 1 Main clinical signs presented (%; n)

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Patologia Clínica / Exames Compl.

- Anemia é comum, porém desidratação pode mascarar devido a hemoconcentração.
- ↑ **URÉIA** e Creatinina
- Hipoglicemia, Hipocolesterolemia, Hipoalbuminemia e hipoproteinemia
- Densidade urinária reduzida (<1.030)
- Eosinofilia absoluta ou relativa, ausência de leucograma de estresse!!!

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Eosinofilia “relativa”

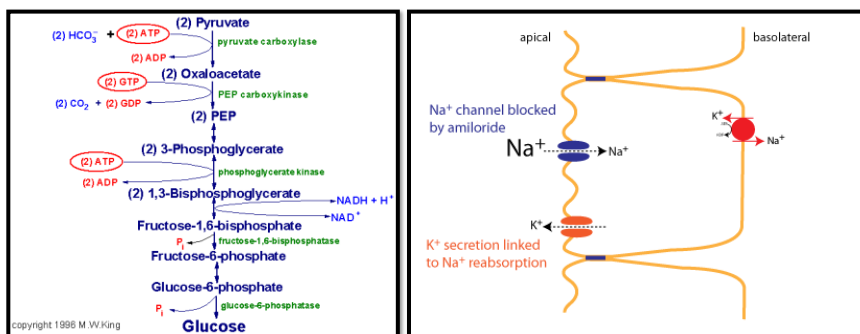
- | | |
|--|---|
| <ul style="list-style-type: none"> ■ Situação 1: ■ Bastonados 2% ■ Segmentados 91% ■ Linfócitos 5% ■ Monócitos 2% ■ Eosinófilos 0% | <ul style="list-style-type: none"> ■ Situação 2: ■ Bastonados 0% ■ Segmentados 75% ■ Linfócitos 17% ■ Monócitos 2% ■ Eosinófilos 6% |
|--|---|



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Patologia Clínica

- | | | |
|---|-----------------------------|--|
| <ul style="list-style-type: none"> ■ Hiponatremia ■ Hipercalemia ■ Hipercalemia/hipocloremia ■ Hipoglicemia ■ Acidose metabólica | RELAÇÃO Na:K < 27 | <ul style="list-style-type: none"> • Na:K < 27 = 94% Espec. • Na:K < 24 = 96% Espec. • Na:K < 20 = 100% Espec. |
|---|-----------------------------|--|



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STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**
Open Access American College of Veterinary Internal Medicine

Prevalence of hypercalcemia in primary hypoadrenocorticism in dogs: Multicenter, retrospective study

Harriet Hall^{1,2} | Daniel Thompson³ | Jessica Florey² |
Mireia Pascual Moreno² | Victoria Black⁴ | Timothy Williams¹ | Barbara Skelly¹

- Estudo multicêntrico com 110 cães com Hipoadrenocorticismo
- Prevalência de Hipercalcemia total ou ionizada de 34%
- HipoA importante diagnóstico diferencial para Hipercalcemia
- Corroborar nos sinais clínicos
 - Pu/Pd, anorexia, depressão, fraqueza, vômitos, constipação, arritmias, convulsões, espasmos
- Mecanismos não são bem esclarecidos...
 - Associação com Azotemia e Hiperalbuminemia
 - Resultado da desidratação e hemoconcentração?
 - Reduzida TFG?
 - Associação com Hipercalemia
 - Resultado da deficiência de Aldosterona?
 - Em casos com Hipoalbuminemia
 - Elevação fração ionizada?
 - Efeito calciúrico dos GCs?
 - Associado a Acidose Metabólica?

27

TABLE 12-4 COMMON CLINICOPATHOLOGIC CHANGES OBSERVED IN DOGS SUFFERING FROM HYPOADRENOCORTICISM

CLINICOPATHOLOGIC CHANGES	PERCENTAGE AFFECTED
Complete Blood Count	
Eosinophilia	20
Lack of stress leukogram	92
Lymphocytosis	10
Neutrophilia	32
Nonregenerative anemia	27
Biochemical Panel	
Azotemia	88
Hypercalcemia	31
Hyperkalemia	95
Hyperphosphatemia	68
Hypoalbuminemia	6 to 39
Hypochloremia	42
Hypocholesterolemia	7
Hypoglycemia	17
Hyponatremia	81
Increased liver enzymes	30 to 50
Metabolic acidosis	40
Urine specific gravity < 1.030	60

From Ettinger SJ, Feldman EC: *Textbook of veterinary internal medicine*, ed 7, St Louis, 2010, Saunders/Elsevier.

Diagnostic efficacy of the leukogram and the chemiluminometric ACTH measurement to diagnose canine hypoadrenocorticism

F. K. Zeugswetter¹, L. Schwandenecker²

¹Department of Companion Animals and Horses, University of Veterinary Medicine Vienna, Vienna, Austria; ²Department of Pathobiology, University of Veterinary Medicine Vienna, Vienna, Austria

- Estudo relações:
- **Neutrófilos: Linfócitos < 2,3**
- **Na:K < 22**

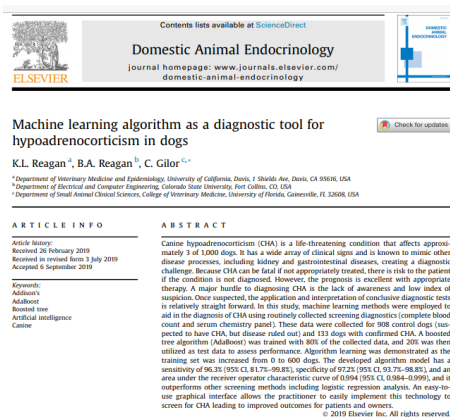


SÓ NO
HIPOADRENOCORTICISMO
PRIMÁRIO CLÁSSICO!

28



TOMMY – Machine Learning Algorithm A Chen Gillor creation



- Algoritmo computador criado baseado em regressão logística de dados de Na/K e contagem de linfócitos
- MLA -1 até +1
- Sensib. e Espec. > 96%
- Próximos passos:
 - Inclusão em relatos de laboratórios
 - Monitoramento tto trilostano

29

Rx

- Microcardia (a-c)
- Vasos pulmonares colabados (a-c)
- Veia cava achatada (a-b)
- Megaesôfago (c)
- Todas alterações são reversíveis com tratamento adequado!

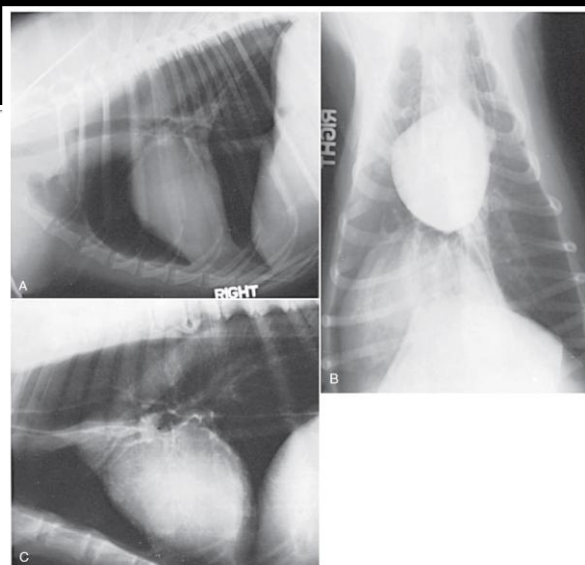
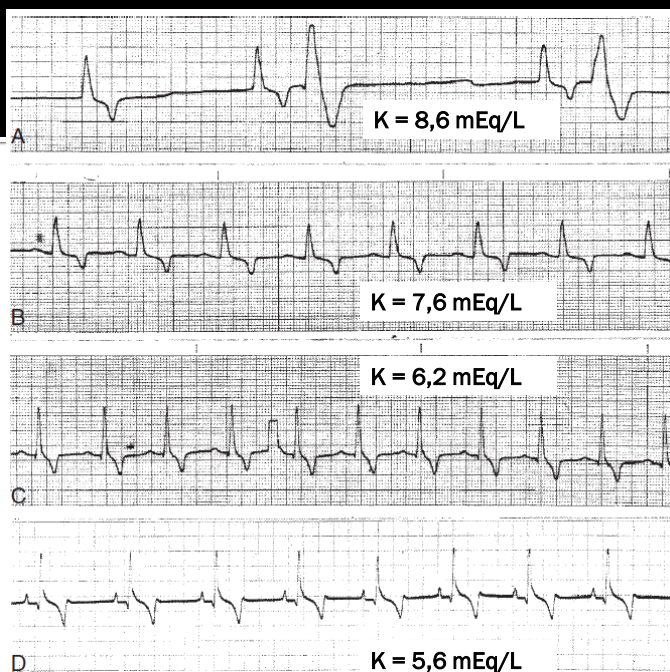


FIGURE 12-8 A and B, Radiographs of a 3-year-old Rhodesian Ridgeback that was brought to the hospital in a shock-like state secondary to hypoadrenocorticism. Note the small heart on both views and the small pulmonary vasculature due to poor cardiac output. C, Lateral thoracic view radiograph of a 5-year-old hypoadrenal dog with microcardia, a flattened caudal vena cava, and a dilated, air-filled esophagus. The esophageal dilation, which is seen occasionally in hypoadrenocorticism, is reversible with appropriate hormonal therapy for the primary disease.

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ECG

1. Aumento amplitude onda T
2. Intervalo Q-T curto
3. Intervalo P-R prolongado
4. Onda P ausente
5. Bradicardia severa
6. Assistolia
7. QRS "Bizarro" e fibrilação
8. PAS ↓ ↓ ↓



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Avaliação Ultrassonográfica Adrenais

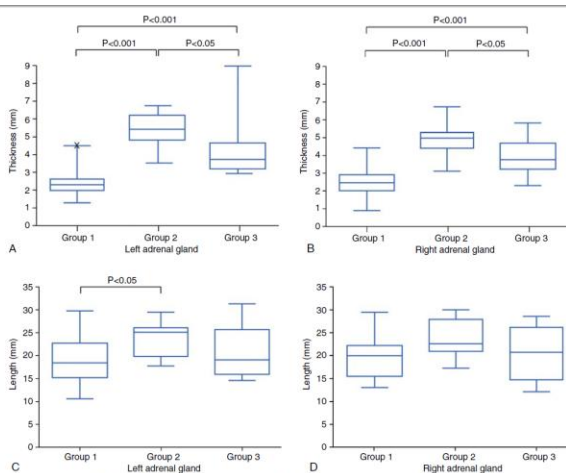


FIGURE 12-9 Measurements of the thickness of the (A) left and (B) right adrenal glands, and the length of the (C) left and (D) right adrenal glands for three groups of dogs. Group 1, dogs with primary hypoadrenocorticism; Group 2, healthy control dogs; Group 3, dogs with diseases mimicking adrenal insufficiency. P values are indicated where differences between groups are significant. Note that in A the overlap between Groups 1 and 2 is limited to one dog indicated by X. (From Wenger M, et al.: Ultrasonographic evaluation of adrenal glands in dogs with primary hypoadrenocorticism and mimicking diseases, *Vet Rec* 167:207, 2010.)



Outros achados:

- Microhepatia
- Microesplenismo
- Hipocogenicidade fígado e baço (hipovolemia)
- Espessamento mucosas TGI
- Fibrose, atrofia, infiltrados nas adrenais...

32

Dia

NÃO SEJAM ENGANADOS
PELO GRANDE
IMPOSTOR

Hipoadrenocorticism
The Great "Pretender"



33

Os Disfarces do Hipoadrenocorticism...



Doenças Renais

- Perda de peso, apetite fraco, vômito / diarreia
- Azotemia, acidose, ↓ albumina, baixa densidade urinária
- Responsivo a administração de fluídos!



Doenças Gastrointestinais

- Perda de peso, apetite fraco, vômito / diarreia
- ↓ Albumina e colesterol
- Parâmetros bioquímicos alterados responsivos à fluídos
- Biópsias gastrointestinais sugestivas de doença inflamatória



Doenças Hepáticas

- Perda de peso, apetite fraco, vômito / diarreia
- ↓ Albumina e colesterol e glicose
- Microhepatia e alterações em biópsias
- Elevação de enzimas hepáticas e testes de função alterados

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HIPOADRENOCORTICISMO "ATÍPICO"

Ausência de alteração Na:K
Deficiência isolada de glicocorticoide?

DEFICIÊNCIA ALDOSTERONA

- Relação Na:K < 27
- Azotemia prerenal
- Hipercalemia
- Acidose Metabólica

DEFICIÊNCIA DE CORTISOL

- Anemia
- Hipoglicemia
- Hipocolesterolemia
- Hipoalbuminemia
- Hipoproteinemia
- Eosinofilia
- Linfocitose (> 6 milhões/ μ L 100% Espec. para Addison)
- Hipercalemia

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ALIVE - ESVE

Hipoadrenocorticismo
hiponatrêmico e/ou
hipercalêmico



HIPOADRENOCORTICISMO
PRIMÁRIO

Hipoadrenocorticismo
eunatrêmico/eucalêmico



HIPOADRENOCORTICISMO
"ATÍPICO" → PODE SER 1º ou 2º

36

Comparison of classic hypoadrenocorticism with glucocorticoid-deficient hypoadrenocorticism in dogs: 46 cases (1985–2005)

Ann L. Thompson, BVSc; J. Catharine Scott-Moncrieff, MA, MS, Vet MB, DACVIM;
Johnna D. Anderson, MS

Table 1—Percentages of dogs with various clinical signs among 46 dogs with MGDH or GDH and *P* values for comparisons of clinical signs between the 2 groups.

Clinical sign	MGDH	GDH	<i>P</i> value
Vomiting	85	54	0.048
Anorexia	82	63	NS
Lethargy	87.5	63.6	NS
Diarrhea	50	63	NS
Weight loss	47	45	NS
Polyuria	17	18	NS
Tremors	15	9	NP
Polydipsia	14	27	NS
Melena	9	0	NP
Urinary incontinence	9	9	NP
Ataxia	9	0	NP
Collapse	9	0	NP
Signs of abdominal pain	9	0	NP
Seizures	6	27	NS
Difficulty breathing	3	9	NP

NS = Not significant. NP = Comparison not performed.

- “Atípicos” mais velhos (7 A vs. 4,4 A)
- Sinais clínicos presentes + tempo antes diagnóstico (4,4 M vs. 1,2 M)
- Raramente desenvolvem choque (1/11 vs. 9/35)
- < risco de óbito (0/11 vs. 3/35)
- < risco de azotemia, hipercalcemia e acidose metabólica
- > risco de anemia, hipoalbuminemia e hipocolesterolemia

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Table 2. Clinical and clinicopathological features of apparent isolated glucocorticoid deficiency

Clinical features	Clinicopathological features
Lethargy	Eosinophilia
Anorexia	Lymphocytosis
Weight loss	Absence of a stress leukogram
Vomiting	Anaemia
Diarrhoea	Hypoalbuminaemia
Regurgitation	Hypocholesterolaemia
Abdominal pain	Hypoglycaemia
Polyuria and polydipsia	Mildly increased liver enzyme activities
Collapse	Hypercalcaemia (rare)

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Guzmán Ramos et al. Canine Medicine and Genetics
https://doi.org/10.1186/s40275-022-00119-4

2022 9:6

Canine Medicine and Genetics

REVIEWOpen Access

Diagnosis of canine spontaneous hypoadrenocorticism

Pedro J. Guzmán Ramos^{1*}, Michael Bennaim², Robert E. Shiel³ and Carmel T. Mooney⁴

Clinical features

Hypoadrenocorticism

"Atypical" hypoadrenocorticism

	No. affected (No. evaluated)	%	No. affected (No. evaluated)	%
Lethargy	495 (585)	84.6	49 (77)	63.6
Anorexia	424 (532)	79.7	37 (77)	48.1
Vomiting	420 (585)	71.8	49 (77)	63.6
Weakness	226 (450)	50.2	20 (66)	30.3
Diarrhoea	222 (532)	41.7	39 (77)	50.6
Hypothermia	94 (267)	35.2	0 (77)	0
Dehydration	174 (468)	37.2	2 (18)	11.1
Weight loss	164 (485)	33.8	21 (77)	27.2
Abdominal pain	44 (223)	19.7	9 (77)	11.7
Polyuria	86 (460)	18.7	9 (77)	11.7
Polydipsia	85 (460)	18.5	10 (77)	12.9
Melaena	50 (355)	14.1	4 (59)	6.8
Haematemesis	12 (278)	4.3	0 (77)	0
Shock/collapse	119 (349)	11.3	3 (29)	10.3
Incontinence	3 (35)	8.5	1 (11)	9.1
Shaking/shivering	108 (475)	22.7	1 (11)	9.1

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STANDARD ARTICLE

Journal of Veterinary Internal Medicine

ACVIM
American College of Veterinary Internal Medicine

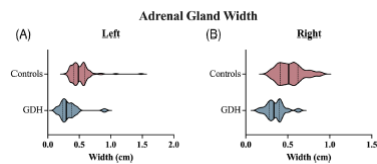
Characterization of clinicopathologic and abdominal ultrasound findings in dogs with glucocorticoid deficient hypoadrenocorticism

Krystle L. Reagan¹ | Ehren McLarty² | Stanley L. Marks¹ | Jamie Sebastian³ | Jennifer McGill³ | Chen Gilor⁴

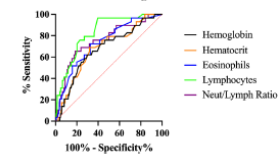
- ❖ 29 cães com HAEE
- ❖ 594 cães com HAEE descartado

❖ SE HIPOADRENO FOR DIFERENCIAL ➔ TESTAR!

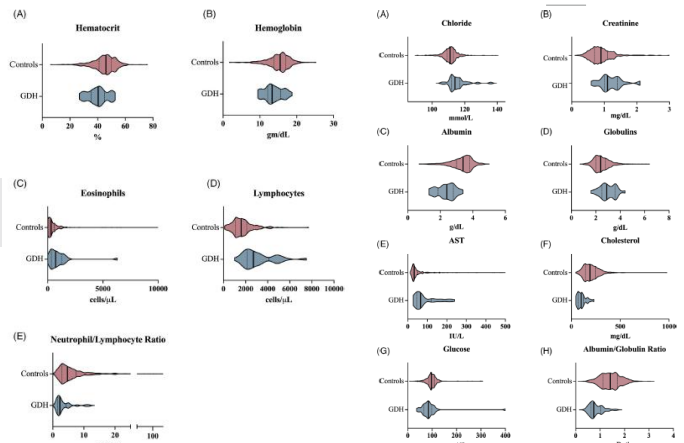
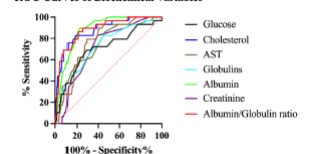
Conclusion and Clinical Importance: No single variable could be used to confidently rule out GDH and obviate the need for cortisol testing in dogs with a clinical presentation consistent with GDH.



ROC Curves of Hematologic Variables



ROC Curves of Biochemical Variables



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Evaluation of Aldosterone Concentrations in Dogs with Hypoadrenocorticism

M.E. Baumstark, N.S. Sieber-Ruckstuhl, C. Müller, M. Wenger, F.S. Boretti, and C.E. Reusch

Background: Some dogs with primary hypoadrenocorticism (HA) have normal sodium and potassium concentrations, a phenomenon called atypical Addison's disease. The assumption that the zona glomerulosa and aldosterone secretion in these dogs are normal seems widely accepted; however, aldosterone measurements are missing in most published cases.

Objectives: To measure aldosterone in dogs with HA with and without electrolyte abnormalities and to determine the time point of aldosterone peak concentrations during ACTH stimulation.

Animals: Seventy dogs with HA, 22 dogs with diseases mimicking HA, and 19 healthy dogs.

Methods: Prospective study. Blood samples were taken before and 60 minutes after injection of 250 µg ACTH in all dogs. Additional blood samples were taken 15, 30, and 45 minutes after ACTH in 7 dogs with HA and in 22 with diseases mimicking HA.

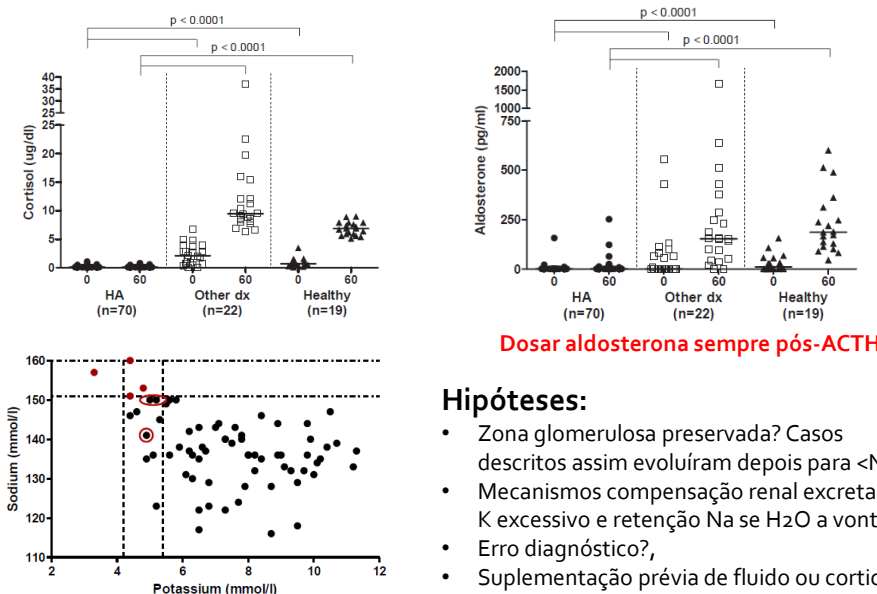
Results: Baseline and ACTH-stimulated aldosterone was significantly lower in dogs with HA than in the other groups. Aldosterone was low or undetectable in 67/70 dogs with HA independently of sodium and potassium levels. In 3 dogs, sodium/potassium concentrations were normal; in 1 dog, sodium was normal and potassium decreased. In all 4, ACTH-stimulated aldosterone concentrations were below the detection limit of the assay. Aldosterone concentrations were not different at 30, 45, or 60 minutes after ACTH administration.

Conclusion and Clinical Importance: Cortisol and aldosterone secretion is compromised in dogs with HA with and without electrolyte abnormalities. The term atypical Addison's disease, used for dogs with primary HA and normal electrolytes, must be reconsidered; other mechanisms allowing normal electrolyte balance without aldosterone should be evaluated in these dogs.

Key words: adrenal insufficiency; canine; mineralocorticoids.

- Um caso "atípico" pode ser monitorado e desenvolveu desequilíbrio Na:K após 6 meses,
- Possibilidade de casos "atípicos" terem HipoA secundário (ACTH baixo)

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Dosar aldosterona sempre pós-ACTH

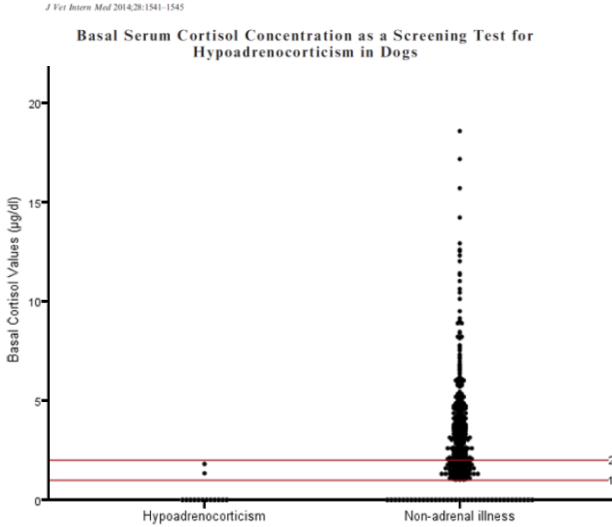
Hipóteses:

- Zona glomerulosa preservada? Casos descritos assim evoluíram depois para <Na:K,
- Mecanismos compensação renal excretando K excessivo e retenção Na se H₂O a vontade,
- Erro diagnóstico?,
- Suplementação prévia de fluido ou corticoide,
- *Upregulation* receptores mineralocorticoides,
- Variabilidade inata dos eletrólitos

- Aldosterona pós-ACTH normal em 3/70, e indetectável em 67/70, incluindo os 4 cães com Na e K normais ●

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Cortisol Basal como Triagem



- Cortisol < 1 mcg/dL ou 10 ng/mL num paciente em crise
 - ALTA CHANCE DE ADDISON
 - Sens. 100%, Espec. 63%
- Cortisol < 2 mcg/dL ou 20 ng/mL num paciente em crise
 - BOA CHANCE DE ADDISON
 - Sens. 85,7%, Espec. 91,8%
- Cortisol > 2 mcg/dL ou 20 ng/mL num paciente em crise → DESCARTADO ADDISON

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DOI: 10.1111/jvim.15921

Journal of Veterinary Internal Medicine ACVIM
STANDARD ARTICLE

Prevalence of eunatremic, eukalemic hypoadrenocorticism in dogs with signs of chronic gastrointestinal disease and risk of misdiagnosis after previous glucocorticoid administration

Antonio María Tardo¹ | Francesca Del Baldo¹ | Rodolfo Oliveira Leal^{2,3} | Giorgia Gallazzo¹ | Marco Pietra¹ | Alba Gaspardo¹ | Federico Fracassi¹

Abstract
Background: Dogs with eunatremic, eukalemic hypoadrenocorticism (EEH) typically show signs of chronic gastrointestinal disease (CGD). Previous glucocorticoid administration (PGA) can give false-positive results on the ACTH stimulation test (ACTHst).
Hypothesis/Objectives: To determine the prevalence of EEH in dogs with signs of CGD, and to identify clinical and clinicopathological features for EEH and PGA.
Animals: One hundred twelve dogs with CGD (101 non-PGA and 11 PGA), 20 dogs with EEH.
Methods: Multicenter prospective cohort study. Basal serum cortisol (BSC) concentration was measured in dogs with signs of CGD. When BSC was <2 µg/dL and in PGA dogs, ACTHst plus measurement of endogenous ACTH (eACTH) were performed. Records of dogs with EEH from 2009 to 2021 were reviewed.
Results: The BSC concentration was <2 µg/dL in 48/101 (47.5%) non-PGA and in 9/11 (82%) PGA dogs. EEH was diagnosed in 1/112 dog (prevalence 0.9%; 95% CI, 0.1%-4.8%); the ACTHst provided false-positive results in 2/11 PGA dogs. PGA dogs showed lower C-reactive protein-to-haptoglobin ratio (median 0.01, range 0.003-0.08; $P = .01$), and higher haptoglobin (140, 26-285 mg/dL; $P = .002$) than non-PGA dogs (0.04, 0.007-1.5; 38.5, 1-246 mg/dL, respectively). eACTH was higher ($P = .03$) in EEH (39.6, 5->1250 pg/mL) than in non-PGA dogs (13.5, 7.3-46.6 pg/mL). Cortisol-to-ACTH ratio was lower ($P < .0001$ and $P = .01$, respectively) in EEH (0.002, 0.0002-0.2) than in non-PGA (0.1, 0.02-0.2) and PGA dogs (0.1, 0.02-0.2).
Conclusions and Clinical Importance: The prevalence of EEH in dogs with signs of CGD was lower than previously reported. The clinical and clinicopathological features herein identified could increase the index of suspicion for EEH or PGA in dogs with an unclear history of glucocorticoid administration.

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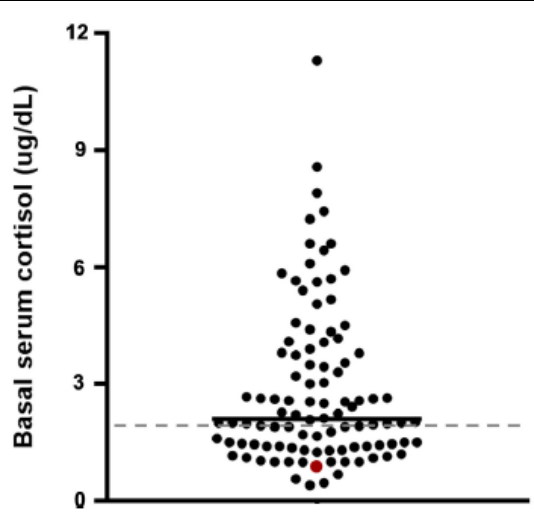


FIGURE 1 Basal serum cortisol concentration in 101 dogs with signs of chronic gastrointestinal disease which had not received glucocorticoids. The dashed gray line represents a 2 µg/dL (55 nmol/L) cut-off for excluding hypoadrenocorticism. The red dot represents the dog with the final diagnosis of eunatremic, eukalemic hypoadrenocorticism.

Comparison of urinary cortisol, urinary cortisol-to-creatinine ratio, and basal serum cortisol as screening tests for hypoadrenocorticism in dogs

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OBJECTIVE

This study investigates whether urinary cortisol (UC) and UC-to-creatinine ratio (UCCR) perform better than basal serum cortisol (BSC) in identifying dogs with hypoadrenocorticism (HA).

METHODS

A retrospective, multicenter study with 120 client-owned dogs included: 20 with HA, 42 healthy, and 60 with diseases mimicking HA. The UC and UCCR were determined on urine samples using a chemiluminescent enzyme immunoassay. The diagnostic performance of the UC and UCCR were assessed based on receiver operating characteristics (ROC) curves.

RESULTS

A cutoff value of UC < 2 µg/dL revealed 100% sensitivity (95% CI, 83.2 to 100) and 90.0% specificity (95% CI, 79.5 to 96.2) in diagnosing HA. A cutoff value of UCCR < 8.5 × 10⁻⁶ revealed 100% sensitivity (95% CI, 83.1 to 100) and 71.7% specificity (95% CI, 58.6 to 82.6) in diagnosing HA. A cutoff value of BSC < 2 µg/dL and < 1 µg/dL revealed 100% sensitivity (95% CI, 83.2 to 100) and 51.7% specificity (95% CI, 38.5 to 64.8) and 100% sensitivity (95% CI, 83.9 to 100) and 90% specificity (95% CI, 79.8 to 95.3) in diagnosing HA, respectively.

CONCLUSIONS

BSC < 1 µg/dL showed the same sensitivity but higher specificity than BSC < 2 µg/dL. The UC < 2 µg/dL showed noninferior performance compared with the BSC < 1 µg/dL.

CLINICAL RELEVANCE

UC should be considered a promising screening test for canine HA.

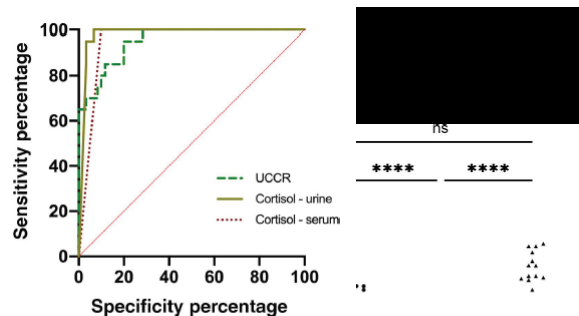


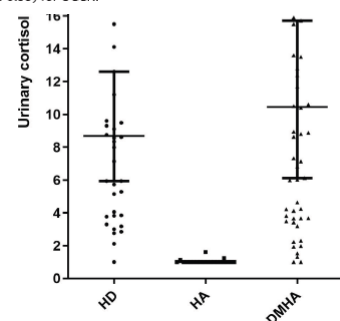
Figure 4—Receiver operating characteristic curves assessing BSC, UC, and UCCR to discriminate dogs with HA from dogs with DMHA. The area under the curve was 0.95 (95% CI, 0.90 to 0.99) for BSC, 0.98 (95% CI, 0.95 to 1.00) for UC, and 0.95 (95% CI, 0.90 to 0.99) for UCCR.

■ Cortisol URINA

■ < 2 mcg/dL

■ 100% Sens.

■ 90% Espec.



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Diagnóstico

Basal normal = 0,5 - 6 µg/dL ou 5 - 60 ng/mL

Pós-ACTH normal = 6 - 17 µg/dL ou 60 - 170 ng/mL



- **Teste de estimulação com ACTH**
- **Maioria tem cortisol basal < 1,0 µg/dL e resposta ausente**
- **Respostas fracas (<6 µg/dL) podem sugerir existência de alguma reserva funcional ainda...**

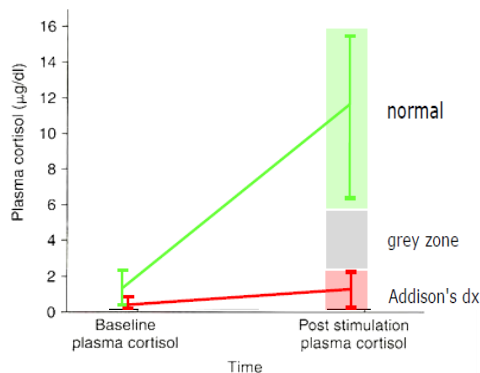
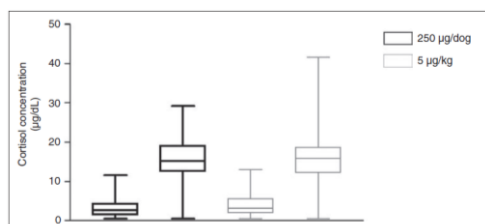


FIGURE 8-8. Radioimmunoassay plasma cortisol concentrations before and after exogenous ACTH stimulation from normal dogs and those with hypoadrenocorticism. The ranges are means ± 2 SD.

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Qual melhor DOSE de ACTH para o teste?



- No passado... 1 ampola inteira
- 2010 - 5 mcg/kg
- 19/9/2018 – 1 mcg/kg

Received: 18 January 2018 | Revised: 27 May 2018 | Accepted: 5 June 2018
DOI: 10.1111/jvim.15254

STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**
American College of Veterinary Internal Medicine

Low-dose ACTH stimulation testing in dogs suspected of hypoadrenocorticism

Annabel Botsford^{1,4} | Ellen N. Behrend¹ | Robert J. Kempainen² | Philippe R. Gaillard³ | Frank Oprandy³ | Hollie P. Lee¹

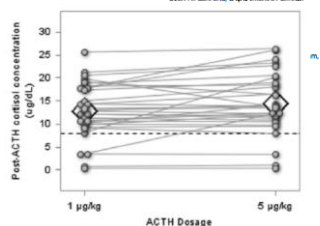
¹Department of Clinical Sciences, Auburn University, Auburn, Alabama

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⁴Atlantic Veterinary Internal Medicine and Oncology, Columbia, Maryland

Correspondence: Ellen N. Behrend, Department of Clinical



Background: Low-dose ACTH stimulation testing would lower cost and may increase sensitivity for identification of partial ACTH deficiency.

Hypothesis: (1) The low-dose ACTH stimulation test will provide comparable results to the standard-dose ACTH stimulation test in dogs suspected of hypoadrenocorticism and (2) partial ACTH deficiency exists in dogs and can result in chronic, intermittent gastrointestinal signs.

Animals: Thirty-one client-owned dogs suspected of having hypoadrenocorticism.

Methods: Prospective study. Dogs suspected of having hypoadrenocorticism received 1 µg/kg cosyntropin IV for the first ACTH stimulation test; the second test was performed 4 h later and dogs received 5 µg/kg cosyntropin IV. Blood samples were obtained pre-ACTH and 1 hour post-ACTH for each dose (4 measurements total). Samples for endogenous ACTH measurement were obtained at the time of initial blood collection.

Results: No significant difference was observed in the basal cortisol concentration before administration of a 1 µg/kg versus before a 5 µg/kg dose of cosyntropin ($P = .544$). For dogs suspected of having hypoadrenocorticism, the ACTH-stimulated cortisol concentrations in response to both doses of ACTH were equivalent (90% confidence interval [CI], 80.5–97.2%; $P = .04$). No cases with partial ACTH deficiency were identified conclusively.

Conclusions and Clinical Importance: A 1 µg/kg dose of cosyntropin is equivalent to a 5 µg/kg dose of cosyntropin for screening dogs suspected of hypoadrenocorticism. The existence of partial ACTH deficiency was not identified in this small group of dogs.

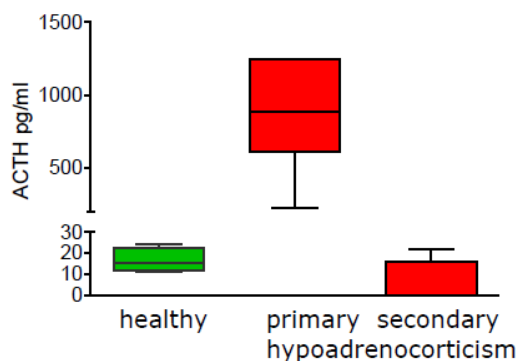
KEYWORDS

Addison's, adrenal, cortisol, cosyntropin

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Mensuração ACTH Endógeno

- Diferencia 1º x 2º x "atípico" (+ Na/K)
- Útil no Dx de pacientes que já iniciaram tratamento



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ENVIO DE AMOSTRAS PARA ACTH ENDÓGENO

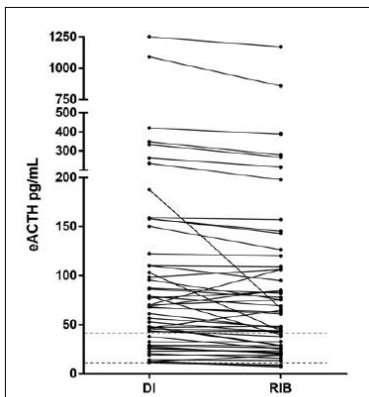


Figure 1 - Individual endogenous adrenocorticotrophic hormone (eACTH) paired samples' results shipped in thermic boxes with dry ice (DI) or recyclable ice bars (RIB). The reference range is represented between dashed lines.

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Razão Cortisol:ACTH

J Vet Intern Med 2014;28:1546-1550

Use of the Cortisol-to-ACTH Ratio for Diagnosis of Primary Hypoadrenocorticism in Dogs

P. Lathan, J.C. Scott-Moncrieff, and R.W. Wills

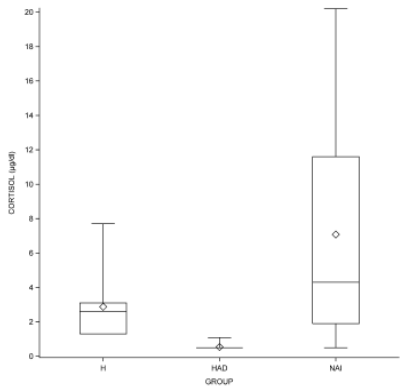


Fig 1. Box and whiskers plot comparing baseline cortisol concentrations among groups (H = healthy, NAI = nonadrenal illness, HAD = hyperadrenocorticism). The box represents the interquartile range from the 25th to 75th percentile, the horizontal bar through the box represents the median, the diamond in the box represents the mean, and the whiskers represent the minimum and maximum values (range).

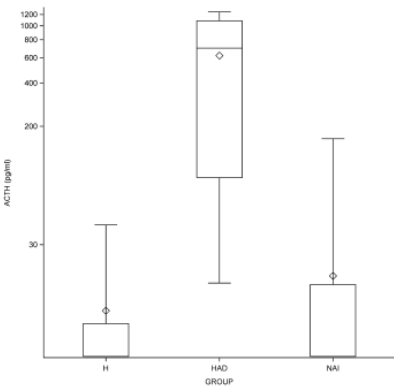


Fig 2. Box and whiskers log scale plot comparing ACTH concentrations among groups (H = healthy, NAI = nonadrenal illness, HAD = hyperadrenocorticism). The box represents the interquartile range from the 25th to 75th percentile, the horizontal bar through the box represents the median, the diamond in the box represents the mean, and the whiskers represent the minimum and maximum values (range).

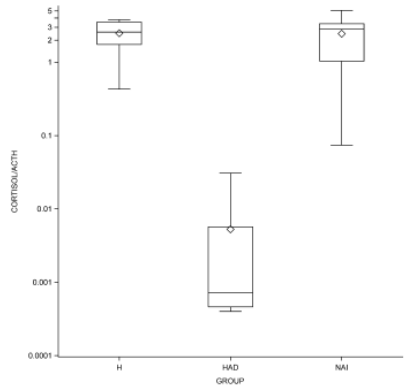


Fig 3. Box and whiskers log scale plot comparing cortisol:ACTH ratio (CAR) among the 3 groups (H = healthy, NAI = nonadrenal illness, HAD = hyperadrenocorticism). The box represents the interquartile range from the 25th to 75th percentile, the horizontal bar through the box represents the median, the diamond in the box represents the mean, and the whiskers represent the minimum and maximum values (range).

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Pacientes Já recebendo corticoides? Como confirmar?

Received: 29 March 2023 | Accepted: 13 December 2023
DOI: 10.1111/jvim.14979

STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**
Open Access American College of Veterinary Internal Medicine

Hypothalamic-pituitary-adrenal axis recovery after intermediate-acting glucocorticoid treatment in client-owned dogs

Francesca Del Baldo¹ | Andrea Corsini² | Antonio Maria Tardo¹ |
Alessandro Tirolo¹ | Ada Sapignoli¹ | Michele Tumbarello¹ |
Kateryna Vasylyeva¹ | Federico Fracassi¹

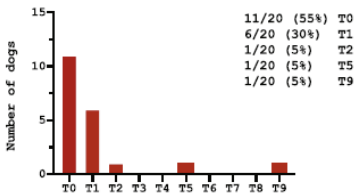
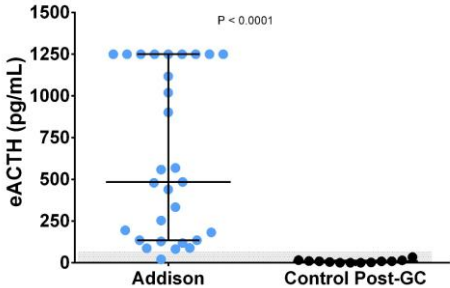


FIGURE 2 Barplot representing the percentage distribution of the population based on time of hypothalamic-pituitary-adrenal axis recovery.

Wodzik et al., 2025 - Endogenous ACTH as an Aid for Primary Hypoadrenocorticism Diagnosis After Glucocorticoid Treatment Beginning – ACVIM FORUM

- ✓ Documentação de ACTHe elevado em pacientes recebendo prednisona sugere HipoA 1º.
- ✓ Medir pré-prednisona...



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Redefining the paradigm of atypical hypoadrenocorticism in dogs

The recognition of apparent isolated glucocorticoid deficiency can be challenging in a clinical setting because of vague clinical signs. The difficulty associated with diagnosis is exacerbated by a lack of standardized terminology and often incomplete investigation and characterization of the disease. Additional testing is usually necessary to confirm the underlying cause, optimize therapy and provide an accurate prognosis. This review suggests a classification system based upon aetiology as well as electrolyte concentrations, and provides an overview of the clinical approach to the diagnosis and treatment of glucocorticoid deficiency in dogs.

Robert E. Shoat MSc PhD PGDipUTL DECVA-CA (Internal Medicine), Carmel F. Mooney MSc MPhil PhD DECVA-CA (Internal Medicine), Section of Small Animal Clinical Studies, School of Veterinary Medicine, University College Dublin, Belfield, Dublin 4, Ireland. robert.shoat@ucd.ie

Key words: atypical hypoadrenocorticism | glucocorticoid deficiency | dogs | cortisol | aldosterone | Addison's disease

Sugestão incluir sempre **ACTHe** e **Aldosterona pós-ACTH** nos testes diagnósticos dos **casos com Na e K normais**

Site				
Primary			Secondary	
Electrolyte changes				
Hyperkalaemia, hyponatraemia or both	Sodium and potassium concentrations within reference interval			
Hormonal changes				
ACTH sufficient			ACTH deficient	
Aldosterone deficient	Aldosterone insufficient		Aldosterone sufficient	
Nomenclature				
Typical primary hypoadrenocorticism (Addison's disease)	Atypical primary hypoadrenocorticism			Secondary Hypoadrenocorticism
ACTH: adrenocorticotrophic hormone				

Figure 2. Expected electrolyte and hormonal abnormalities in dogs with hypoadrenocorticism. Apparent isolated glucocorticoid deficiency (with reference interval electrolyte concentrations) can occur with sufficient, insufficient or completely deficient aldosterone production. In some cases, aldosterone secretory capacity may decrease over time as the disease progresses. In aldosterone deficient animals, electrolyte abnormalities may develop acutely and unpredictably. In secondary hypoadrenocorticism, glucocorticoid deficiency alone is observed.

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 @endocrinohcv_ufrgs
www.ufrgs.br/petendocrine

Obrigado pela
Atenção!



55



HIPOADRENOCORTICISMO

Parte II

Prof. Dr. Álan Gomes Pöppl

Médico Veterinário - UFRGS
 Residência em Clínica e Cirurgia de Pequenos Animais - HCV/UFRGS
 Mestrado em Fisiologia - Laboratório de Metabolismo e Endocrinologia Comparada ICBS/UFRGS
 Doutorado em Ciências Veterinárias - PPGCV/UFRGS
 Atuações na Society for Comparative Endocrinology (SCE) e European Society of Veterinary Endocrinology (ESVE)
 Sócio Fundador e Diretor Executivo da Associação Brasileira de Endocrinologia Veterinária - ABEV
 Fundador e Consultor da Equipe PetEndocrine
 Professor Adjunto, Departamento de Medicina Animal, UFRGS
 Professor do Programa de Pós-Graduação em Ciências Veterinárias FcVet/UFRGS
 Coordenador do Serviço de Endocrinologia e Metabologia, e do Programa de Ações em Endocrinologia Veterinária HCV/UFRGS.



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OBJETIVOS TERAPÊUTICOS NO HIPOADRENOCORTICISMO

CRISE ADRENAL

- Corrigir Sinais Clínicos
- Reverter Hipotensão e Hipovolemia
- Corrigir alterações eletrolíticas, especialmente a hipercalemia
- Corrigir hipoglicemia se presente
- Considerar transfusão em casos de anemia severa
- EVITAR CORREÇÃO RÁPIDA DA HIPONATREMIA PELO RISCO DE INDUZIR MIELINÓLISE OSMÓTICA

CRÔNICO

- Manter paciente sem sinais clínicos
- Manter concentração de eletrólitos dentro do normal, ou próximos ao normal
- EVITAR SUPLEMENTAÇÃO EXCESSIVA DE GLICOCORTICOIDE (Cushing iatrogênico e monitorar marcadores laboratoriais de excesso de GC)
- EVITAR SUPLEMENTAÇÃO EXCESSIVA DE MINERALOCORTICOIDE (Monitorar hipertensão, hipocalemia e/ou hipernatremia)

57

Tratamento da Crise Adrenal (ALIVE) Previamente chamada Crise Addisoniana



- 1) **NaCl 0,9%** ou RL IV (20-30 ml/kg/hora 1^{as} 1 a 2 hs)
- 2) **NaCl 0,9%** ou RL IV (90-120 ml/kg/dia 1 a 2 dias)
 - * Se Na < 120-130 mEq/L escolher solução que tenha no máximo 10 mEq/L Na a mais em relação ao Na do paciente (p.ex. NaCl 0,45, RL).
 - Reposição mais lenta (NaCl 0,45%) para correção de **NÃO MAIS QUE 1 a 2 mmol/L/hora** nas primeiras horas de tto (não mais que 12 mmol/L no primeiro dia)
 - Risco de mielinólise osmótica.... **JAMAIS USAR SALINA HIPERTÔNICA!**

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TABLE 8-3 ELECTROLYTE COMPOSITION OF COMMERCIALLY AVAILABLE FLUIDS

FLUID	NA ⁺ (mEq/L)	CL ⁻ (mEq/L)	K ⁺ (mEq/L)	GLUCOSE (g/L)	BUFFER* (mEq/L)	OSMOLARITY (mOsm/L)
0.9% saline [†]	154	154	0	0	0	308
0.45% saline [†]	77	77	0	0	0	154
Ringer's solution [†]	147	156	4	0	0	310
Lactated Ringer's solution [†]	130	109	4	0	28 (L)	272
Plasma-Lyte 148 [‡]	140	98	5	0	27 (A)	295
Normosol-R [‡]	140	98	5	0	27 (A)	296
Normosol-M [‡]	40	40	13	0	16 (A)	112
Plasma-Lyte 56 [‡]	40	40	13	0	16 (A)	110
5% dextrose in water [‡]	0	0	0	50	0	252

*Buffers used: A, acetate; L, lactate.

[†]Baxter Healthcare Corp., Deerfield, IL.[‡]Abbott Laboratories, Chicago, IL.

VETERINARY PRACTICE GUIDELINES

2024 AAHA Fluid Therapy Guidelines for Dogs and Cats

Mariana Pardo, BVSc, MV, DACVECC¹, Erin Spencer, MEd, CVT, VTS (ECOT)²,
 Adresda Odunayo, DVM, MS, DACVECC, Mary L. Ramirez, DVM, DABVP (Canine and Feline),
 Elise Rudloff, DVM, DACVECC, cHMA, Heidi Shafford, DVM, PhD, DACVAA, Ann Weil, DVM, MS, DACVAA,
 Ewan Wolff, DVM, PhD, DACVIM (Small Animal Internal Medicine)

- 5-10mL/kg em 15-30 min → Hipovolemia
- Reidratação → Peso x % desidratação em 24h
- Manutenção → mínimo 40 mL/kg/dia (considerar perdas...)
- Volume total em 24h pode chegar a > 90mL/kg/dia

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Mielinólise osmótica

Tradicionalmente referida como Mielinólise Pontina Central no HipoAdr



Fig. 2 Brain MRI coronal T1 weighted image (post contrast) revealing enhancement in paracentral pontine lesions

Lauro et al. BMC Res Notes (2018) 11:307
<https://doi.org/10.1186/s13104-018-3814-5>

BMC Research Notes

RESEARCH NOTE

Open Access

Sequential MRI in pontine and extrapontine myelinolysis following rapid correction of hyponatremia

Robert Lauro^{1,2}, Guillaume Lauro^{1,2} and Alexander S. Mark^{1,3}

- Frente a hiponatremia, neurógia perde osmólitos intracelulares para evitar um edema celular
- Rápida correção hiponatremia pode levar a desidratação e mielinólise, uma vez que a neuroglia precisa de tempo de adaptação
- Sinais neurológicos em 2-6 dias
- Alteração nível de alerta, ataxia, tetraparesia, estupor...
- Maior predisposição substância branca pontina?

60



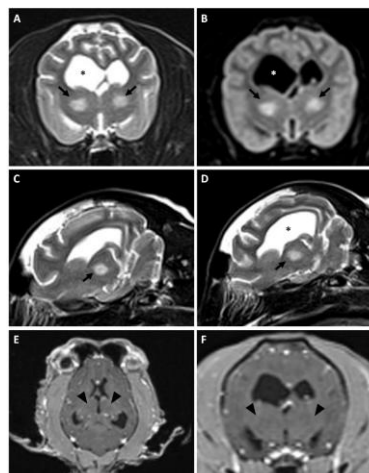
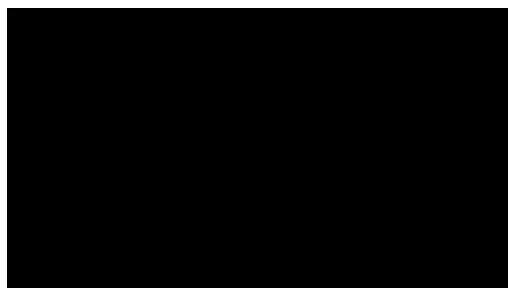
Acta Scientiarum Veterinariae, 2021, 49(Suppl 1): 682.

CASE REPORT
Pub. 682

ISSN 1678-8216

Osmotic Demyelination Syndrome after Primary Hypoadrenocorticism Crisis Management

Alan Gomes Pöppel^{1,2}, Érico Haas Pires³, Claudia Ruga Barbieri⁴ & Lucas Marques Colomé⁴



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Tratamento - Crise

- PROTOCOLO REPOSIÇÃO DE GLICOCORTICOIDES
 - Succinato Prednisolona 1 a 2 mg/kg IV
 - Hidrocortisona 2-5 mg/kg tid ou 0,5 mg/kg/hr IV
 - Dexametasona 0,05-0,1 mg/kg bolus IV + 0,05-0,1 mg/kg na fluido
- *Terapia da Hipercalemia indicada somente se após fluido persistir com K >8 mEq/L e bradicardia importante:*
- Gluconato de cálcio 1 mL/kg ao longo de 10 minutos com monitoramento pelo ECG
- Administração glicose em bolus 1mL/kg glicose 25%
- Insulina + glicose (Cuidado em Pacientes Addisonianos)
 - 0,2 u/kg INS Regular + glicose 1 a 2 g / U insulina

**1 dos três
protocolos**

62

Clinical Significance: Intravenous hydrocortisone is well-tolerated and safe, but no clear additional benefit over traditional glucocorticoid replacement could be identified. Also, it might result in longer hospitalisation time and more intensive monitoring.

Comparison of Hydrocortisone Continuous Rate Infusion and Prednisolone or Dexamethasone Administration for Treatment of Acute Hypoadrenocortical (Addisonian) Crisis in Dogs

OPEN ACCESS

Edited by:
Torrey Fries,
West Bengal University of Animal and
Fisheries Sciences, India

Athanasia Mitropoulou¹, Mia-Katharina Hilse², Hendrik Lehmann² and
Katarina Hazuchova²

¹Department of Veterinary Clinical Sciences, Small Animal Clinic, Justus Liebig University Gießen, Giessen, Germany

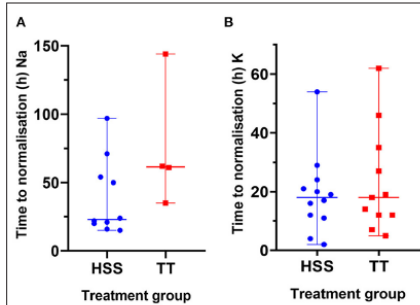


FIGURE 2 | Comparison of time to normalisation of sodium (A) and potassium (B) concentration between the HSS (blue dots) and TT group (red rectangles). Horizontal line represents median, whiskers represent range.

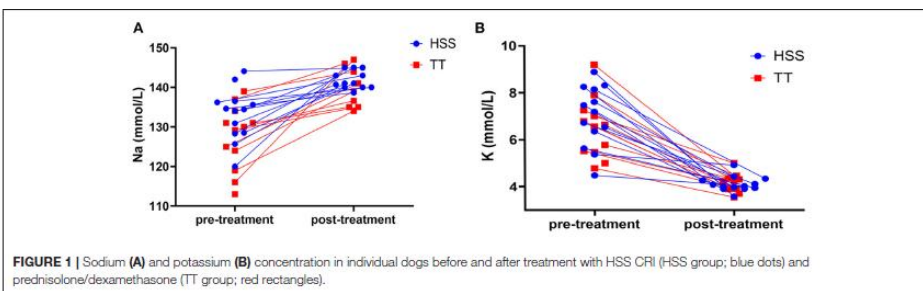


FIGURE 1 | Sodium (A) and potassium (B) concentration in individual dogs before and after treatment with HSS CRI (HSS group; blue dots) and prednisolone/dexamethasone (TT group; red rectangles).

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Check for updates

OPEN ACCESS

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RECEIVED 13 December 2024
ACCEPTED 17 March 2025
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Comparison of prednisolone and alternative glucocorticoid dosing protocols for canine hypoadrenocorticism: insights from a survey-based study

Christin Emming^{1*}, Anna Karoline Gekis¹,
Sajedeh Sajadihezaveh², Thomas Rieker³, Johannes Brutsche⁴,
Holger Andreas Volk¹ and Johanna Rieder^{1*}

¹Department for Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Hannover, Germany; ²AVICURA Small Animal Specialists Augsburg GmbH, Augsburg, Germany;

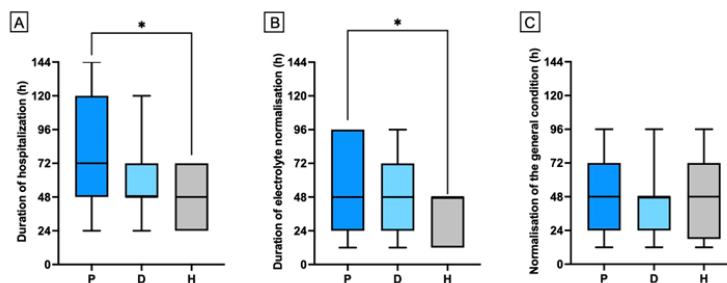


FIGURE 1 | Comparison of hospitalization period (A), time to normalization of electrolytes (B) and time to normalization of general condition (C) among dogs receiving either prednisolone derivative (P; n = 5), dexamethasone (D; n = 26), or hydrocortisone (H; n = 10). Data are presented as bar graphs showing the mean and standard deviation (Mean ± SD). Asterisks (*) indicate statistically significant differences between groups (p ≤ 0.05).

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Tratamento – “long term”

- Pivalato de desoxicorticosterona (DOCP) 1,1-2,2 mg/kg SC mensal + Prednisona/prednisolona 0,2 mg/kg/dia cf necessidade e ir reduzindo;

OU

- Acetato de Fludrocortisona 0,01 mg/kg BID + Prednisona /prednisolona 0,2 mg/kg/dia cf necessidade e ir reduzindo;



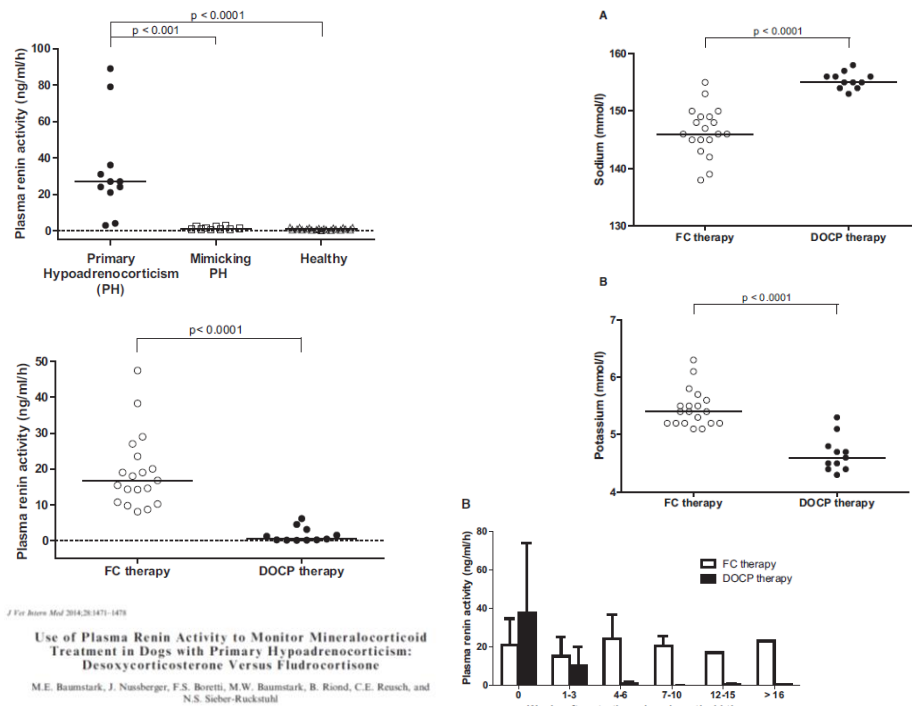
65

Fármaco de Eleição!

- Mineralocorticoide depósito “Puro”
- Metabolizado a DOC por esterases → Potente Mineralo s/ atividade GC
- DOC pode sofrer metabolização pela 11β-HSD e gerar corticosterona
 - Efeito GC e redução de 10x no efeito MC



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Esquema Terapêutico Inicial

Dia 0

- Primeira dose
1,5 a 2,2 mg/kg

Dia 10

- Reavaliação Clínica e reavaliar Na e K

Dia 25-28

- Reavaliação Clínica e reavaliar Na e K

Ajustes doses subsequentes de acordo com relação Na/K no dia 10

Na/K Dia 10	Ajuste dose na reaplicação
> 34	< para 2 mg/kg
32 – 34	< 2,1 mg/kg
27 – 32	Manter dose
24 – 27	> Para 2,3 mg/kg
< 24	> Para 2,4 mg/kg

✓ Avaliar Na e K de forma independente é mais lógico, pois tem mecanismos de controle distintos e são afetados por fatores múltiplos

✓ Valores de ref para Na e de K sugerem que relação Na/K poderia flutuar de 26 a 41!

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Desoxycorticosterone Pivalate Duration of Action and Individualized Dosing Intervals in Dogs with Primary Hypoadrenocorticism

J.A. Jaffey , P. Nurre, A.B. Cannon, and A.E. DeClue**Background:** Clinicians alter dosing for desoxycorticosterone pivalate (DOCP) to mitigate costs, but this practice has not been critically evaluated in a prospective clinical trial.**Hypothesis/Objectives:** The duration of action of DOCP is longer than 30 days in dogs with primary hypoadrenocorticism (PH).**Animals:** A total of 53 client-owned dogs with PH. Twenty-four dogs with newly diagnosed PH (Group 1) and 29 dogs with treated PH (Group 2).**Methods:** Prospective, multicenter, clinical trial. For phase I, DOCP was administered and plasma sodium and potassium concentrations were measured until the dog developed hyponatremia or hyperkalemia at a planned evaluation, or displayed clinical signs with plasma electrolyte concentrations outside of the reference interval independent of a planned evaluation, thus defining DOCP duration of action. Plasma electrolyte concentrations then were assessed at the end of the individualized dosing interval (IDI; i.e., DOCP duration of action minus 7 days, phase II and at least 3 months after concluding phase II, phase III).**Results:** The duration of action of DOCP in dogs in phase I with naïve PH (n = 24) ranged from 32 to 94 days (median, 62 days; 95% confidence interval [CI], 57, 65) and previously treated PH (n = 29) from 41 to 124 days (median, 67 days; CI, 56, 72). Overall, the final DOCP dosing interval for all dogs that completed phase II (n = 36) ranged from 38 days to 90 days (median, 58 days; CI, 53, 61). No dog that completed phase III (n = 15) required reduction in the IDI. The DOCP duration of action, independent of group, was not significantly associated with several baseline variables. The median drug cost reduction using IDI was approximately 57.5% per year.**Conclusion and Clinical Importance:** The duration of action of DOCP in dogs with PH is >30 days, and plasma sodium and potassium concentrations can be maintained with an IDI >30 days long term.**Key words:** Addison's; desoxycorticosterone pivalate; mineralocorticoid.

- Quanto > cão > chance de controlar com doses menores de até 1,1 mg/kg
- Necessidade de reaplicação a cada 28 dias variável,
- Documentação de "efeito" por até 90 dias
- Recomendado começar com 2,2 mg/kg e reduzir 10-20% dose a cada mês se Na e K normais no 28º dia de aplicação
- K↑ e/ou Na↓ → ↑ dose 10-20%
- K↓ e/ou Na↑ → ↓ dose 10-20%

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Received 20 December 2020 | Accepted 27 May 2021
DOI: 10.1111/jvim.15395

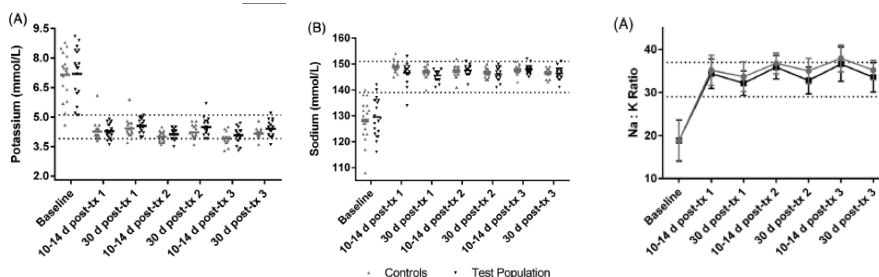
STANDARD ARTICLE

Journal of Veterinary Internal Medicine 

Low-dose desoxycorticosterone pivalate treatment of hypoadrenocorticism in dogs: A randomized controlled clinical trial

Alysha M. Vincent¹ | Linda K. Okonkowski¹ | Jean M. Brudvig² | Kent R. Refsal³ | Nora Berghoff² | N. Bari Olivier¹ | Daniel K. Langlois¹ 

- 2,2 mg/kg x 1,1 mg/kg com intervalo de doses 30/30 dias
- Dose bula associada a pressão alta em alguns casos e cão com aspecto "triste" potencialmente por dor de cabeça 2ª hipertensão (Ransley, ACVIM 2023)



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Development of mass spectrometric methods for determination of desoxycorticosterone pivalate and its esterase product in canine serum

A. F. Lehner^a, Justin Zyskowski^a, J. P. Buchweitz^{a,b} and D. K. Langlois^c

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^bDepartment of Pathobiology and Diagnostic Investigation, College of Veterinary Medicine, Michigan State University, East Lansing, MI, USA;

^cDepartment of Small Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI, USA

ABSTRACT

Hypoadrenocorticism is a serious condition in dogs that results from autoimmune adrenalitis and depletion of mineralocorticoids and glucocorticoids. Affected dogs respond well to glucocorticoid supplementation and treatment with the synthetic mineralocorticoid desoxycorticosterone pivalate

ARTICLE HISTORY

Received 2 January 2025

Revised 28 March 2025

Accepted 29 March 2025

Responses Over Time

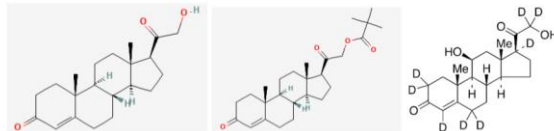
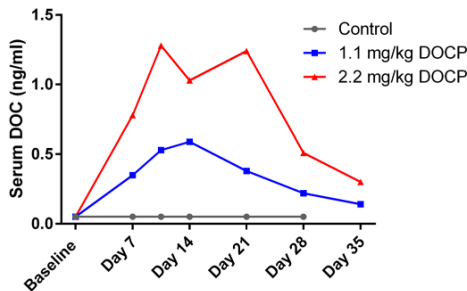


Figure 1. Structures of DOC (left), DOCP (middle) and corticosterone-d8 internal standard (right); configuration as +H⁺ pseudomolecular ions would involve proton coordination on the 3- or 20-ketone functionalities for ESI-MS/MS detectability. Corresponding [M+H]⁺ molecular ion m/z are predicted as 331, 415, and 355, respectively. DOC, DOCP images from <https://pubchem.ncbi.nlm.nih.gov/>, corticosterone-d8 image from <https://www.lgcstandards.com/US/en/Corticosterone-d8-major-1p78C-C695702>.

- ❖ DOCP é 100% convertida em DOC (pré-fármaco)
- ❖ Monitoramento nível sérico de DOC pode ser útil!

71

Received: 5 September 2020 | Revised: 10 December 2020 | Accepted: 15 February 2021

DOI: 10.1080/vet2021

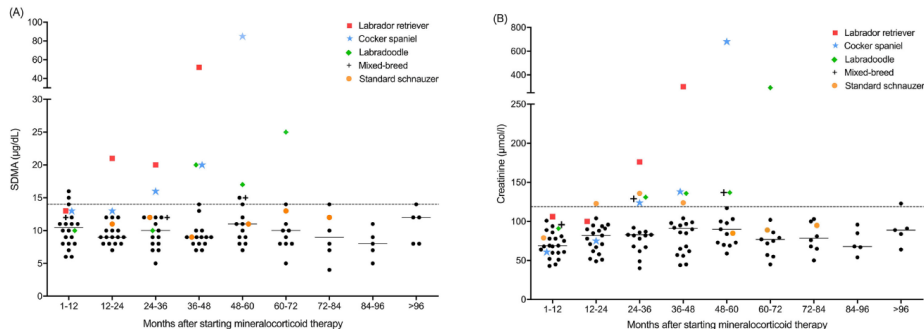
ORIGINAL RESEARCH

VetRecord

Evaluation of symmetric dimethylarginine and creatinine in dogs with primary hypoadrenocorticism receiving long-term mineralocorticoid replacement therapy

Jose L. Casado Díaz¹ | Nadja S. Sieber-Ruckstuhl¹ | Felicitas S. Boretz¹ | Federico Fracassi² | Claudia E. Reusch¹

- Evitar suplementação excessiva de MC
- > risco de DRC associada a uso crônico de MC



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Tratamento – “long term” – Iatrogenico

- Prednisona 0,2-0,5 mg/kg/dia com redução gradual ao longo de dias ou semanas dependendo da intensidade dos sinais
- Intervalo de cerca de 2 semanas após retirada total e novo teste com ACTH para definir retomada do mitotano ou trilostano, ou definição da cura após adrenalectomia
- **SE HOUVER DISTÚRPIO ELETROLÍTICO:**
 ➔ Terapia idem Hipoadrenocorticism clássico...
- Frequentemente irreversível (ADRENALECTOMIA QUÍMICA)

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Tratamento – “Atípico”



Falta de consenso na literatura sobre necessidade de MC x uso isolado de GC...



Como monitorar terapia MC se Na:K normais?



Monitoramento pela atividade da renina seria o ideal...



Preferível suplementar somente GC e seguir monitorando Na/K

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Received: 23 February 2022 | Revised: 4 June 2022 | Accepted: 28 June 2022
DOI: 10.1002/vet.1977

ORIGINAL RESEARCH

VetRecord

Effect of long-term management of hypoadrenocorticism on the quality of life of affected dogs and their owners

Julia Hupfeld¹ | Michael Döller² | Holger Volk¹ | Johanna Rieder¹

■ Orientação adequada dos tutores no monitoramento é fundamental!

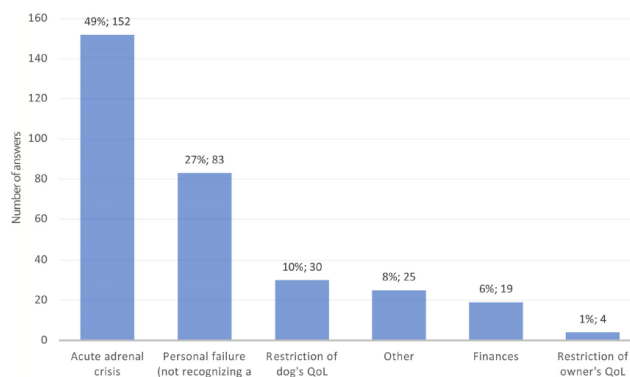


FIGURE 2 Owners' greatest fears about their dog's adrenal insufficiency (%; n). QoL, quality of life

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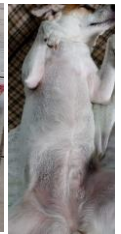
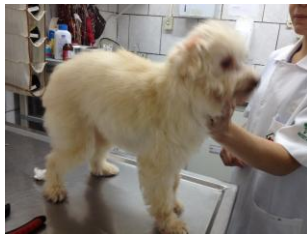
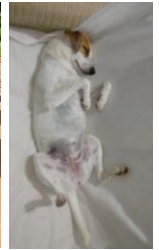
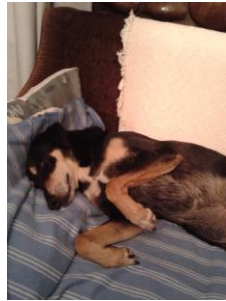
Dicas Monitoramento

- Checar periodicamente até estabilização do quadro eletrolítico e retomada da atividade.
- Reduzir GC até menor dose necessária (p.ex. 0,03 – 0,1 mg/kg)
- Revisão cada 3 a 6 meses
- Aumentar GC em momentos estressantes (100-300%)
- Aumento GC 50% se letargia e/ou sinais TGI
- Redução GC 25% se Pu/Pd ou demora p/ crescer pelo pós-trico
- Redução GC se patologia clínica *Cushing-like*
 - Leucograma Estresse, hiperglicemia, dislipidemias, AUMENTO FA...
- Frequente necessidade de aumentos de fludrocortisona ➔ tolerância e sinais de Cushing

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Hipertricose (Hirsutismo pós-tratamento)

- ✓ Supressão anterior do ciclo folicular pela deficiência de cortisol?
- ✓ Efeito positivo no ciclo folicular dos GC em doses de reposição?
- ✓ Influência direta da melhora geral no metabolismo do paciente?
- ✓ Manutenção de anágeno prolongado como documentado em equinos com Cushing?



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ORIGINAL ARTICLE

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Clinical characteristics, treatment, and outcomes of hypoadrenocorticism in dogs

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OBJECTIVES: To determine the long-term survival of dogs with hypoadrenocorticism during the period that desoxycorticosterone pivalate has become widely used. Secondary goals were to compare age at diagnosis, median survival times, and age at death for dogs with hyponatraemic and/or hyperkalaemic hypoadrenocorticism and eunatraemic eukalaemic hypoadrenocorticism, and to determine the frequency of glucocorticoid-related side effects in these dogs.

MATERIALS AND METHODS: Retrospective cohort study with data collected from medical records and from a questionnaire sent to owners of affected dogs.

RESULTS: 141 cases were identified; 125 had spontaneous hypoadrenocorticism and 16 had iatrogenic hypoadrenocorticism secondary to treatment of hyperadrenocorticism. Dogs with spontaneous hyponatraemic and/or hyperkalaemic hypoadrenocorticism were significantly younger at the time of diagnosis (median age: 5.1, range: 0.8 to 14.1 years, $n=97$) compared to dogs with spontaneous eunatraemic eukalaemic hypoadrenocorticism (median age: 8.3, range: 3.0 to 12.7 years, $n=26$). Sixty-six dogs were included in the survival analysis. For dogs with spontaneous hyponatraemic and/or hyperkalaemic hypoadrenocorticism, all of which were managed with desoxycorticosterone pivalate, median survival time was 5.7 years (95% CI: 4.0 to 7.2 years; $n=47$) and median age at death was 11.0 years (range: 4.0 to 17.0 years; $n=30$). For dogs with spontaneous eunatraemic eukalaemic hypoadrenocorticism, median survival time was 5.6 years (95% CI: 4.1–N/A years; $n=9$) and median age at death was 11.8 years (range: 11.0 to 13.0 years; $n=4$). The majority of owners that completed the questionnaire reported side effects commonly associated with glucocorticoid therapy.

CLINICAL SIGNIFICANCE: Hypoadrenocorticism carries an excellent prognosis. Desoxycorticosterone pivalate was the most frequently used mineralocorticoid therapy in this group of dogs.

Casos de Doença de Addison mais jovens que HipoA Eunatremicos/Eucalêmicos

- HHH = 5,1 anos (0,8 - 14,1)
- HEE = 8,3 anos (3 - 12,7)

DOCP foi empregado em 100% casos HHH

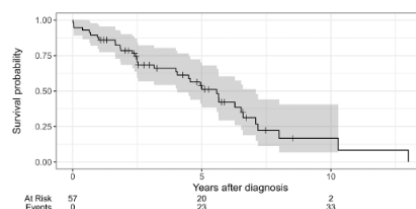
- Dose Inicial média 2,11 mg/kg (1,02 - 2,38)
- Dose final média 1,88 mg/kg (0,2 - 2,44)

Pred

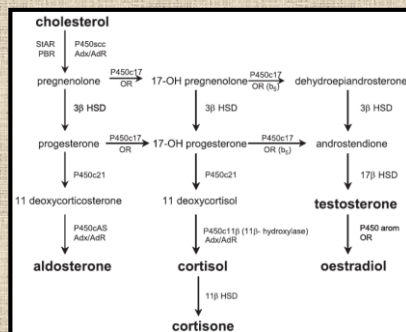
- Dose Inicial média 0,27 mg/kg (0,04 - 0,82)
- Dose final média 0,17 mg/kg (0,03 - 0,86)

Não houve diferença sobrevida dos pacientes

- HHH Sobrevida 5,7 anos (idade ao óbito 4 - 17 anos)
- HEE Sobrevida 5,6 anos (idade ao óbito 11 - 13 anos)



- ✖ Considerar interrupção do uso do Trilostano em pacientes com Hiperadrenocorticism 24h antes de procedimentos cirúrgicos, ou durante internamentos em situações críticas!!!



Hipoadrenocorticismo Felino



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Menos de 100 casos descritos no mundo Doença rara ou subdiagnosticada?

Review Article



Hypoadrenocorticism in cats: a 40-year update

Magdalena J Glebocka and Alisdair Boag

Journal of Feline Medicine and Surgery
1-7
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Abstract

Practical relevance Addison's disease is a very rare condition in cats, with only approximately 40 cases documented in the past 40 years since it was first described in 1983.

Clinical challenges While canine hypoadrenocorticism is a well-recognised disorder with clear diagnostic and treatment guidelines, feline hypoadrenocorticism remains a challenge because of its rarity and waxing and waning clinical signs. Furthermore, empirical treatment with corticosteroids, resulting in clinical improvement, contributes to delays in achieving the diagnosis and initiating treatment. Feline hypoadrenocorticism is diagnosed with an adrenocorticotrophic hormone (ACTH) stimulation test; a low resting cortisol concentration with an inadequate or absent response to synthetic ACTH is diagnostic. Various ACTH stimulation-testing protocols are reported in published cases, with the majority using three time-limited blood samples. This can be limiting clinically, depending on cats' clinical presentation and behaviour at the veterinary practice and tolerance for procedures. Long-term treatment, similar to canine hypoadrenocorticism, consists of oral corticosteroids, with several formulations licensed in the UK, and mineralocorticoids (desoxycorticosterone pivalate), of which the only available formulation (Zycortal; Dechra) is licensed for dogs and its safety has not been assessed in cats.

Global importance Feline hypoadrenocorticism occurs worldwide. Although no breed, sex or age association has been reported, cats aged <6 years are overrepresented.

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STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**
Open Access American College of Veterinary Internal Medicine

Clinical findings, treatment, and outcomes in cats with naturally occurring hypoadrenocorticism: 41 cases

Emma Roberts¹ | Ian K. Ramsey² | Ruth Gostelow³ | Anna Latysheva⁴ |
Luca Battaglia⁵ | Paolo Silvestrini⁶ | Ghita Benckroun⁷ | Karen Brenner⁸ |
Bérénice Conversy⁹ | Riccardo Ferriani¹⁰ | Andre Kortum¹¹ |
Lisa Stammelée¹² | Nele Van den Steen¹³ | Flavia Tavares¹⁴ | Julia Lieser¹⁵ |
Angie Hibbert¹⁶ | Antoine Dudos¹⁷ | Troy Bunn¹⁸ | Alisdair M Boag¹⁹ |
Carolina Arenas²⁰ | Kirsty Roe²¹ | Florian K. Zeugswetter²² | Yi Cui²³ |
Imogen Schofield²⁴ | Federico Fracassi²⁵

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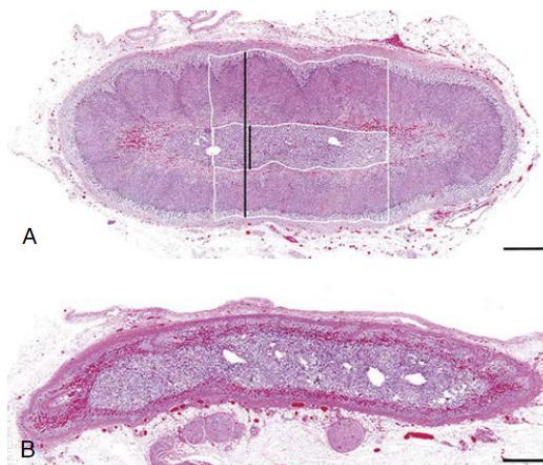
Perfil população descrita

- **Glebocla e Goeb 2024**
 - Média idade 4 anos (7 meses a 14 anos)
 - 20/38 Machos
- **Roberts et al., 2024**
 - Média idade 5,7 anos (3 meses a 13,8 anos)
 - 23/41 Machos
- **Raças Descritas**
 - SRDs >60% casos,
 - British Short Hair, Siamês, Bengal, Charteux, Maine Coon, Norueguês, Ragdoll, Tonquinese, Birmanês

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Etiologia Hipoadrenocorticismo Primário ("Doença de Addison" - ALIVE)

- **Destruição autoimune mais provável como causa principal**
 - Infiltração linfocítica
 - Atrofia e fibrose bilateral (sem inflamação)
 - **Outras causas:**
 - Destruição e infiltração adrenais por linfoma
 - Induzido por trauma
 - Infiltração neutrófilos/macrófagos
- ➔ Normalmente destruição das três zonas!



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Achados Clínicos / Laboratoriais

	Sinais Clínicos	Achados Laboratoriais
FREQUENTES (>40% casos)	Apatia/letargia Anorexia Vômito Perda de peso Pulso fraco Colapso / Choque Hipotermia	Hipercalcemia Hiponatremia Hipoalbuminemia Azotemia pré-renal Anemia não-regenerativa Ausência leucograma de estresse DEU < 1.030
INFREQUENTES (<40% casos)	Diarreia Pu/Pd Tremores Regurgitação Convulsões Náusea Hematoquesia Bradycardia	Hipercalcemia Hipoglicemia Neutropenia Linfocitose Eosinofilia Hipocolesterolemia DEU < 1.020

Primary Hypoadrenocorticism in Ten Cats

Mark E. Peterson, DVM, Deborah S. Greco, DVM, and David N. OVM, MS

Primary hypoadrenocorticism was diagnosed in ten young to middle-aged cats of mixed breeding. Five of the cats were male, and five were female. History signs included lethargy (n = 10), anorexia (n = 10), weight loss (n = 9), vomiting (n = 4), and polyuria (n = 3). Dehydration (n = 9), hypothermia (n = 9), prolonged capillary refill time (n = 7), weak pulse (n = 7), collapse (n = 5), and other findings (n = 3) were based on physical examination. Results of basic laboratory tests revealed azotemia (n = 7), elevated lipoproteins (n = 7), decreased electrolytes (n = 4), and anemia and hypoproteins (n = 10). Serum electrolyte changes included hyponatremia (n = 10), hypokalemia (n = 9), hypocalcemia (n = 7), and hypoglycemia (n = 1). The diagnosis of primary hypoadrenocorticism was confirmed on the basis of results of adrenocorticotropic hormone (ACTH) stimulation tests (n = 10) and subsequent plasma ACTH stimulation (n = 7). Initial therapy for hypoadrenocorticism included intravenous administration of 0.9% saline and dexamethasone and intramuscular administration of desoxycorticosterone acetate. These cats were euthanized shortly after diagnosis because of poor clinical response. Results of necropsy examinations were unremarkable for specific findings of adrenal cortex. Some cats were treated clinically with oral prednisone or intramuscular hydrocortisone during the observational period and/or with oral desoxycorticosterone or intramuscular fludrocortisone during the observational period for subclinical hypoadrenocorticism. One cat died after 47 days of therapy from unknown causes; the other nine cats are still alive and well after 1 to 18 months of treatment. (Journal of Veterinary Internal Medicine 1999; 15:55-56)

TABLE 1. Clinical Findings in Ten Cats With Primary Hypoadrenocorticism

	No. of Cats (%)
Historic owner complaints	
Lethargy/depression	10 (100)
Anorexia	10 (100)
Weight loss	9 (90)
Vomiting	4 (40)
Waxing-waning course of illness	4 (40)
Previous response to therapy	3 (30)
Polyuria/polydipsia	3 (30)
Physical examination findings	
Depression	10 (100)
Weakness	9 (90)
Dehydration	9 (90)
Hypothermia	8 (80)
Slow capillary refill time	5 (50)
Weak pulse	5 (50)
Collapse/unable to rise	3 (30)
Bradycardia	2 (20)
Painful abdomen	1 (10)

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Casos de Hipoadreno Eunatremicos-Eucalêmicos já reconhecidas em Felinos

4 of 12 | Journal of Veterinary Internal Medicine ACVIM
Robertson et al.

TABLE 2 The clinical signs reported in all included cases (all cats), based on the assessment of both the clinical history from the PCP and RC (listed from most common to least common) and then further divided into cats classified as hyponatremic and hyperkalemic (HH) and cats classified as nonhyponatremic and nonhyperkalemic (NHNH).

Clinical sign	All cats (n = 41) (n, %)	HH cats (n = 36) (n, %)	NHNH cats (n = 5) (n, %)
Lethargy	36; 87.8%	32; 88.9%	4; 80.0%
Anorexia/hyporexia	32; 78.0%	29; 80.6%	3; 60.0%
Weakness	25; 61.0%	24; 66.7%	1; 20.0%
Weight loss	20; 48.8%	18; 50.0%	2; 40.0%
Vomiting	16; 39%	11; 30.6%*	5; 100%* (P = .01)
Diarrhea	11; 26.8%	9; 25.0%	2; 40.0%
Collapse	10; 24.4%	8; 22.2%	2; 40.0%
Nausea	9; 22.0%	8; 22.2%	1; 20.0%
Seizures/tremors	6; 14.6%	6; 16.7%	0; 0%
Hypodipsia	6; 14.6%	5; 13.9%	1; 20.0%
Constipation	4; 9.8%	4; 11.1%	0; 0%
Polydipsia	4; 9.8%	4; 11.1%	0; 0%
Difficulty swallowing	3; 7.3%	3; 8.3%	0; 0%
Polyphagia	2; 4.9%	0; 0%	2; 40.0%
Polyuria	2; 4.9%	2; 5.6%	0; 0%
Weight gain	2; 4.9%	2; 5.6%	0; 0%
Hematochezia	1; 2.4%	0; 0%	1; 20.0%
Other	Smaller than littermate (1; 2.4%), aggression (1; 2.4%), sneezing whilst eating (1; 2.4%)	Aggression (1; 2.8%), sneezing whilst eating (1; 2.8%)	Smaller than littermate (1; 20.0%)

Note: Data are presented as number and frequency. Significant differences (P < .05) between the HH and NHNH groups are shown as *.

■ Ausência de alteração eletrolítica não exclui...

Relação Na:K baixa em gatos é comum a diversas doenças...

Decreased sodium:potassium ratios in cats: 49 cases

Rory Bell, DVM, J. Miller, Ian Ramsey, Cass Kroemer

Background: Hypoadrenocorticism (HAC) in cats can often present in subtle biochemical events, although the importance of the measurement has not been investigated. **Objective:** The aims of this study were to document the range of other disease states associated with a decreased Na:K ratio, to determine the prevalence of this biochemical abnormality in a general feline population, and to identify any particular disease that was more likely to have a decreased Na:K ratio. **Methods:** A group of 49 cats with decreased Na:K ratios was compared with a group of 95 cats with normal Na:K ratios that were randomly selected from the same hospital population. **Results:** Twelve of the 49 cats (24.5%) had gastrointestinal disease, 10 (20.4%) had urinary disease, 6 (12.2%) had endocrine disease, and 1 (2.0%) had cardiovascular disease. In 15 (30.6%) cats, the Na:K ratio was significantly lower than the normal range (P < .001). In 10 (20.4%) cats, the Na:K ratio was significantly higher than the normal range (P < .001). In 24 (48.8%) cats, the Na:K ratio was within the normal range. In 10 (20.4%) cats, the Na:K ratio was significantly higher than the normal range (P < .001), but there was no significant difference in mean sodium concentrations between the 2 groups. **Conclusions:** Decreased Na:K ratios frequently occur in cats with disease other than hypoadrenocorticism, including cats with chronic renal failure. These findings should be considered when evaluating cats with biochemical abnormalities. (J Am Vet Med Assoc 2001; 168:111-115)

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Diagnóstico

Basal normal = 0,5 - 6 µg/dL ou 5 - 60 ng/mL

Pós-ACTH normal = 6 - 17 µg/dL ou 60 - 170 ng/mL

- Teste de estimulação com ACTH
- Aplicar 125 mcg/gato!
- Maioria tem cortisol basal < 1,0 µg/dL e resposta ausente
- Respostas fracas (<6 µg/dL) podem sugerir existência de alguma reserva funcional ainda...

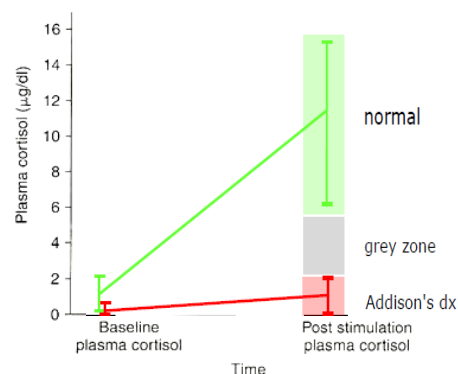
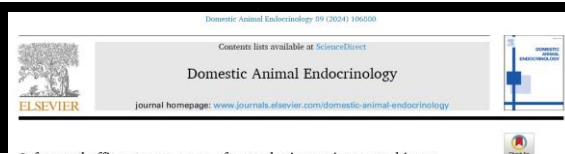


FIGURE 8-8. Radioimmunoassay plasma cortisol concentrations before and after exogenous ACTH stimulation from normal dogs and those with hypoadrenocorticism. The ranges are means $\pm$ 2 SD.

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Safety and efficacy assessment of a synthetic porcine recombinant corticotrophin for the ACTH stimulation test in healthy cats

Daniela J. Lopes^{a,1}, Luciana De Jesus^a, Barbara B. Rivas^a, Milena C. De Oliveira^a, Priscila V. Furtado^a, Debora Cattaruzzi^a, Alan G. Poppi^{a,c,d}

^a Veterinary Sciences Post-Graduation Program (PPGCV), Veterinary Faculty, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil
^b Hormone Laboratory, Petvet - Medicina Veterinária Diagnostic, São Paulo, Brazil
^c Animal Medicine Department, Veterinary Faculty, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil

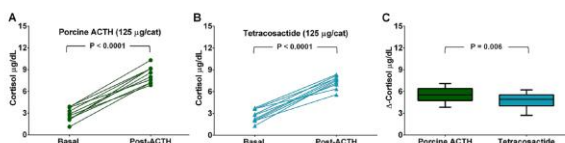
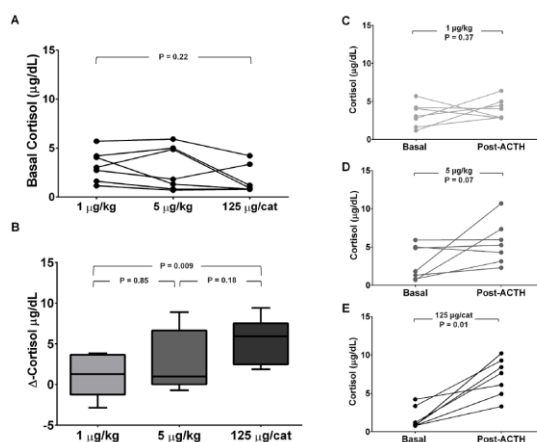


Fig. 4. Comparison of ACTH stimulation test in a population of ten healthy cats with a 15-day interval between tests. A) Basal and post-ACTH cortisol after intravenous 125 µg/cat of a recombinant porcine ACTH. B) Basal and post-ACTH cortisol after intravenous 125 µg/cat of tetracosactide. C) Δ-cortisol in response to the ACTH tested in the study.



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Tratamento – “long term”

- Pivalato de desoxicorticosterona 2,2 mg/kg SC mensal + Prednisolona 0,5 mg/kg/dia cf necessidade e ir reduzindo;
- OU Acetato de Fludrocortisona 0,01 mg/kg BID + Prednisolona 0,5 mg/kg/dia cf necessidade e ir reduzindo;

Problemas Florinefe (Administração diária, Perda dose pode causar crise)

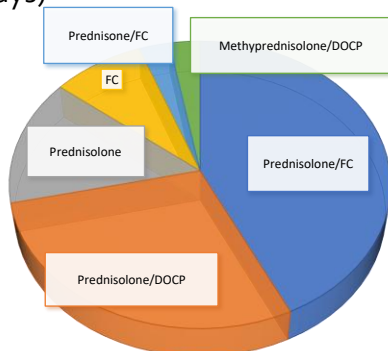


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Treatment of feline hypoAC

Ramsey, apresentação Adrenais 360, ABEV 2023

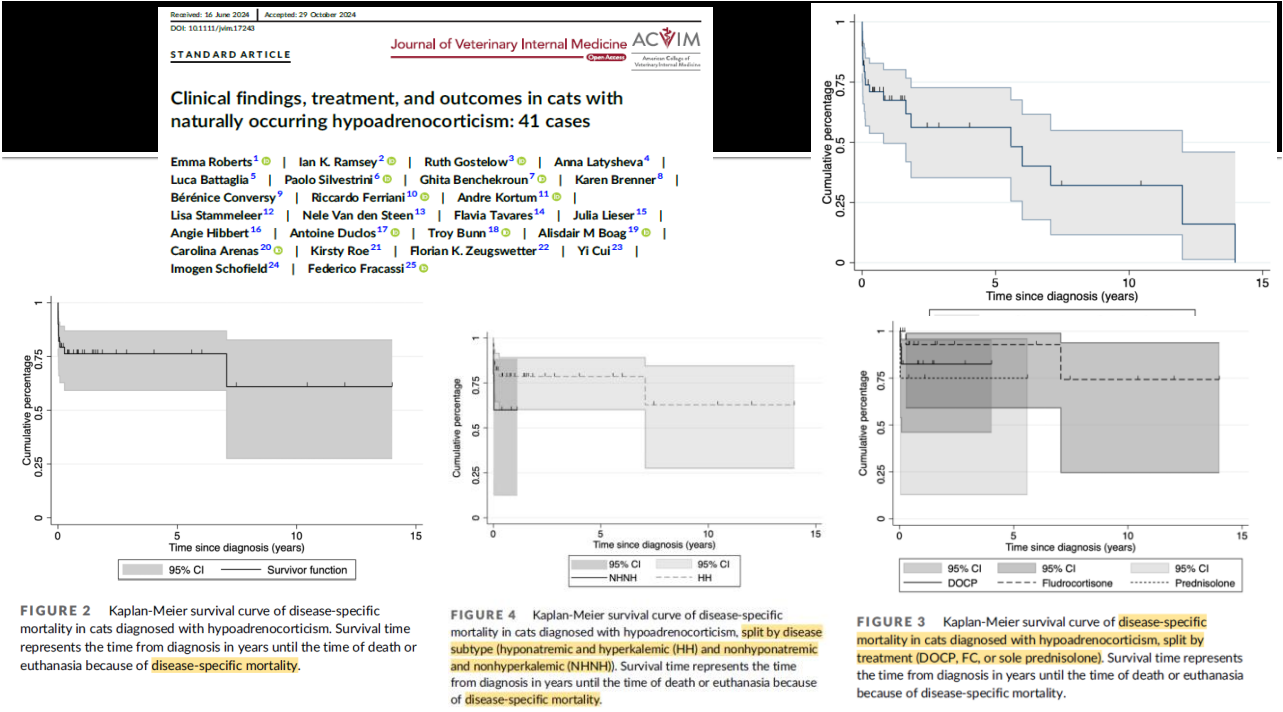
- 35/41 (85.4%) cases survived to discharge
- Median follow-up time: 287 days (range 0-5103 days)



Treatment

- FC
 - Start: 0.02 mg/kg/day (range 0.01 to 0.14)
 - End: 0.03 mg/kg/day (range 0.01 to 0.05)
 - Change to DOCP (n=1)
- DOCP
 - Start: 2.2 mg/kg (range 1.2 to 3.1 mg/kg)
 - End: 2.2 mg/kg (range 1.3 to 3 mg/kg)
 - Frequency
 - Monthly (n=8)
 - 21-25 days (n=4)
- Prednisolone
 - Start: 0.5 mg/kg/day (range 0.2 to 2.2 mg/kg)
 - End: 0.33 mg/kg/day (range 0.02 to 2 mg/kg/day)

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