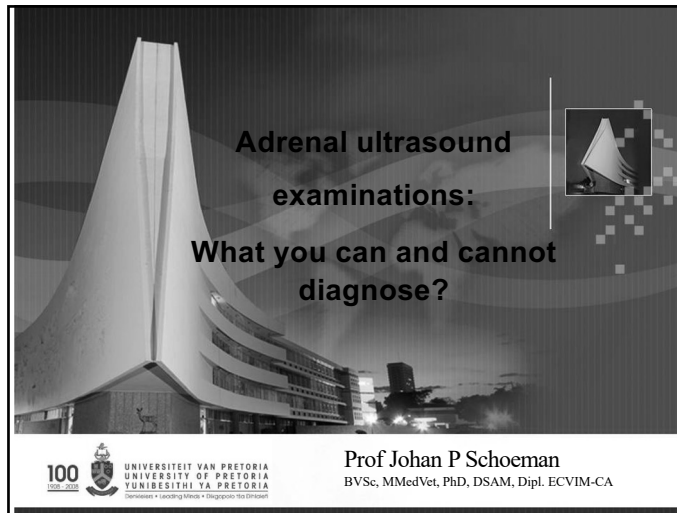




Adrenal ultrasound examinations:
What you can and cannot diagnose?

Prof Johan P Schoeman
BVSc, MMedVet, PhD, DSAM, Dipl. ECVIM-CA

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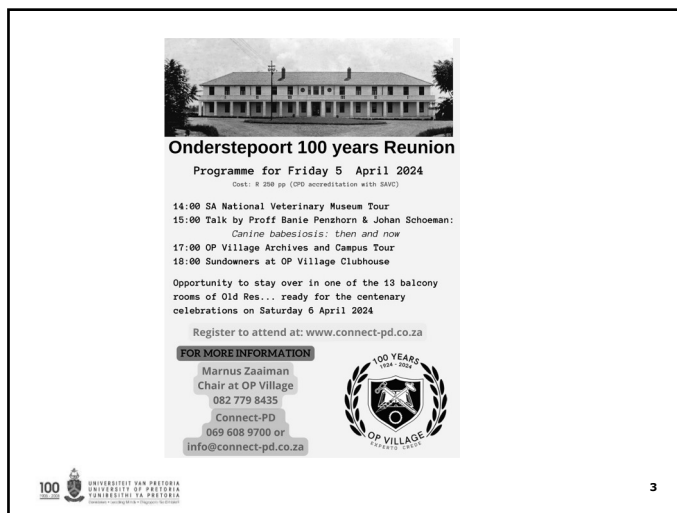
Questionnaire?

- Please fill out the circulating questionnaire on CPD requirements
 - Which ultrasound courses would be most desirable?
 - Free text any topics for 3-5 day CPD courses

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2



Onderstepoort 100 years Reunion
Programme for Friday 5 April 2024
(Cost: R 200 pp (CPD accreditation with SAVC))

14:00 SA National Veterinary Museum Tour
15:00 Talk by Proff Banie Penshorn & Johan Schoeman:
Canine babesiosis: then and now
17:00 OP Village Archives and Campus Tour
18:00 Sundowners at OP Village Clubhouse

Opportunity to stay over in one of the 13 balcony rooms of Old Res... ready for the centenary celebrations on Saturday 6 April 2024

Register to attend at: www.connect-pd.co.za

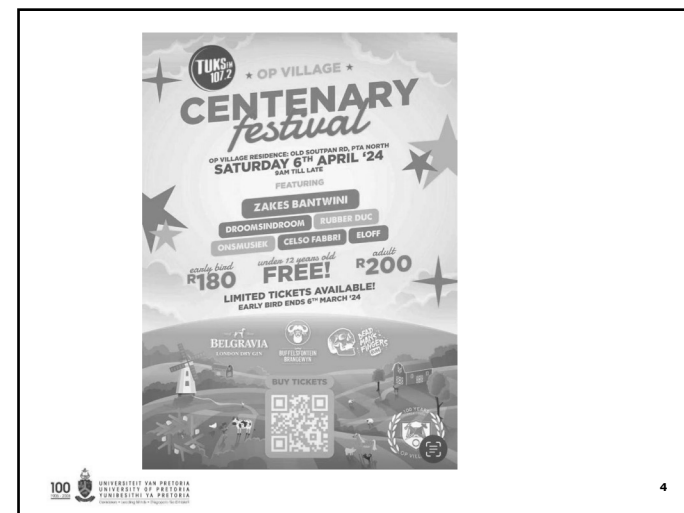
FOR MORE INFORMATION
Marnus Zaaiman
Chair at OP Village
082 779 8435
Connect-PD
069 608 9700 or
info@connect-pd.co.za

100 YEARS 1924-2024
OP VILLAGE 1924-2024

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3

3



TUES 10/2 • OP VILLAGE •
CENTENARY festival
OP VILLAGE RESIDENCE: OLD SOUTHRAN RD, PTA NORTH
SATURDAY 6TH APRIL '24
8AM TILL LATE

FEATURING
ZAKES BANTWINI
DROOMSINDROOM RUBBER PUC
CHUMBAHISEN CELSO FABBRI ELOFF

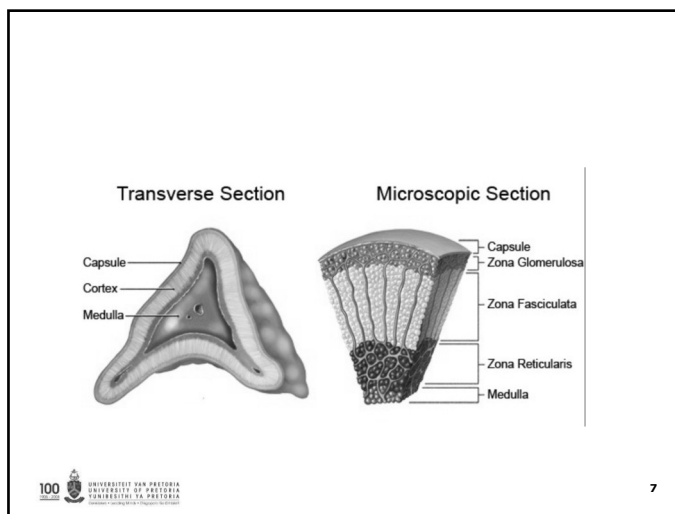
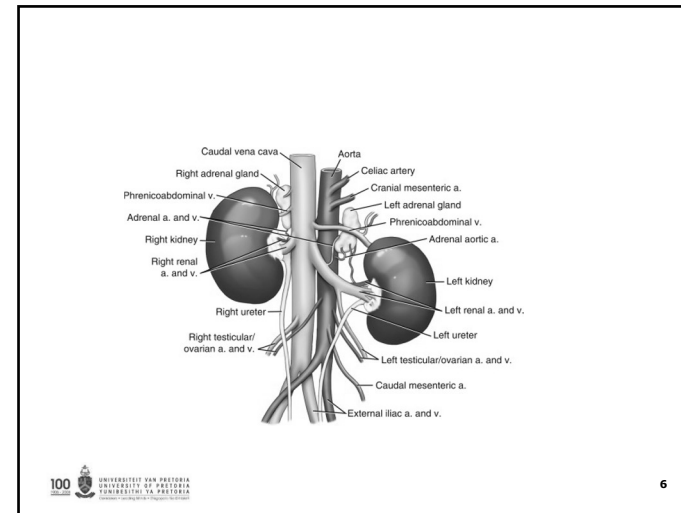
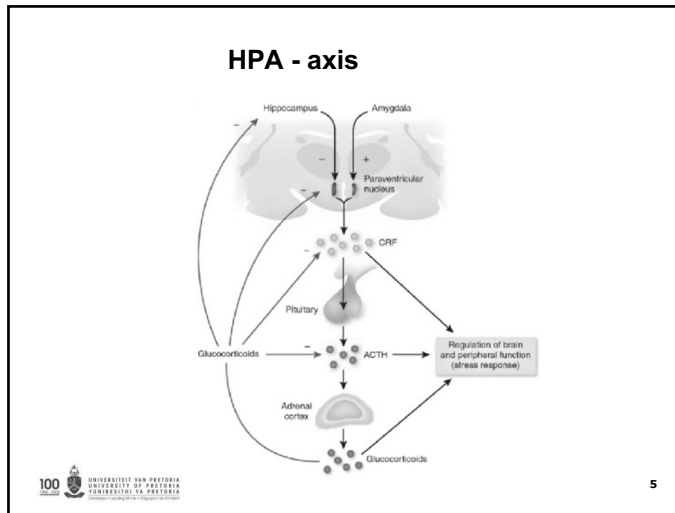
early bird **R180** under 13 years old **FREE!** adults **R200**
LIMITED TICKETS AVAILABLE!
EARLY BIRD ENDS 6TH MARCH '24

BUY TICKETS
QR CODE

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4

4



- ### Nomenclature “nomen”- name + “calare”- to call
- **Adrenal or supra-renal glands**
 - **Cortex (mesodermal origin)**
 - Z. Glomerulosa – Aldosterone
 - Z. Fasciculata – Cortisol
 - Z. Reticularis – Sex steroids (DHEA & DHEAS)
 - **Medulla (Neural crest origin)**
 - Adrenaline aka Epinephrine “Epi” and “Nephron”
 - Noradrenaline aka Norepinephrine
- 8

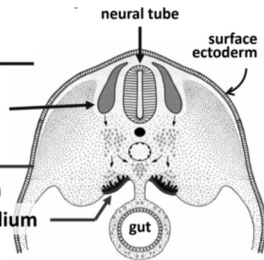
Adrenal gland origin

ADRENAL MEDULLA

- Ectodermal origin
- Neural crest cells

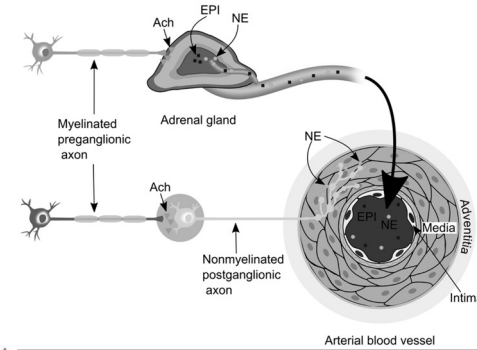
ADRENAL CORTX

- Mesodermal origin
- Coelomic mesothelium



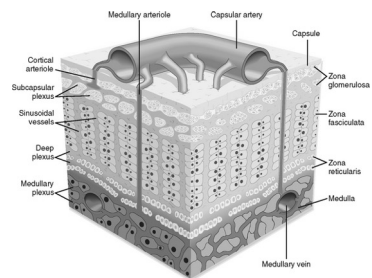
9

The adrenal medulla is a “trapped” ganglion



10

Adrenal blood supply



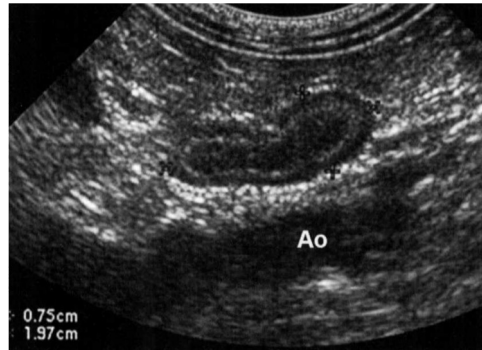
11

Imaging of the adrenal glands

- Small, paired structures located in the craniodorsal abdomen
- Medial to the ipsilateral kidney
- Adjacent to the aorta (Left)
- Adjacent to the caudal vena cava (Right)
- Normal **left** adrenal is hypoechoic to surrounding fat, well-defined with an elongated bilobed shape, resembling a peanut.
- Normal **right** adrenal wedge-shaped in some dogs, but mostly ovoid.
- High resolution reveals a thin hyperechoic line, representing the cortico-medullary junction

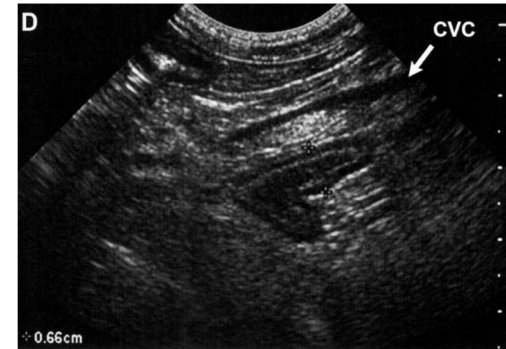
12

Normal left adrenal gland – note the CM junction



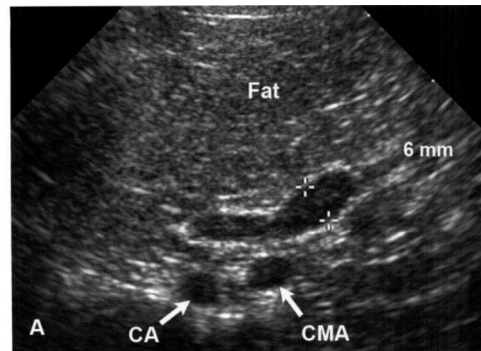
13

Normal right adrenal gland – note the wedged shape



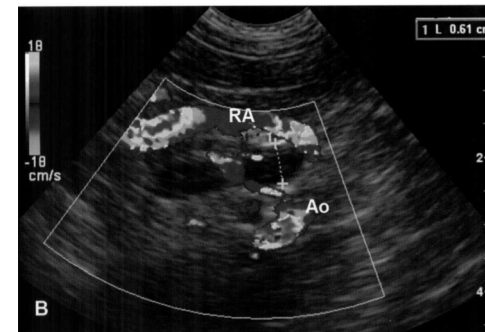
14

Left adrenal



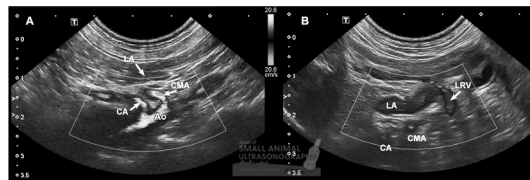
15

Left adrenal with colour Doppler showing
CA, CMA, RA and left phrenico-abdominal artery



16

Vascular landmarks for the left adrenal gland



17

Adrenal ultrasonography



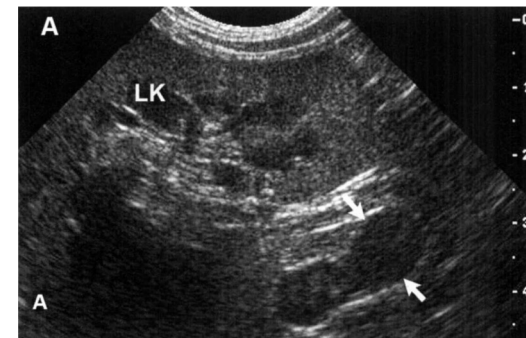
18

Normal adrenal size: Caudal pole width

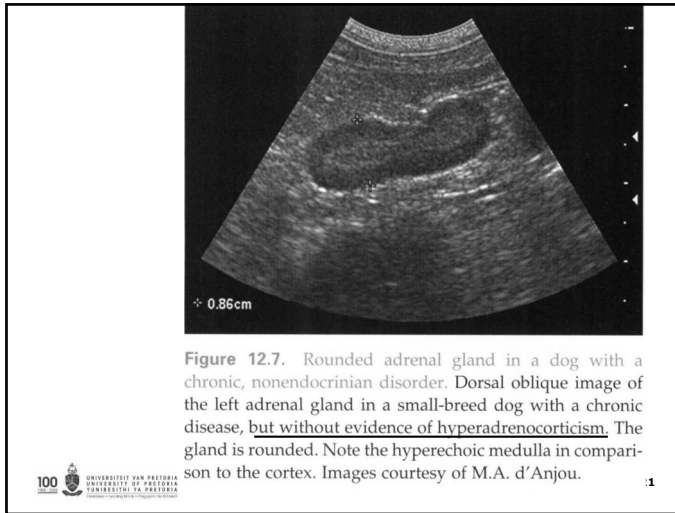
- Dogs
 - < 10 kg: up to 5 mm
 - 10 - 20 kg: up to 6 mm
 - 20 - 30 kg: up to 7 mm
 - > 30 kg: up to 8 mm
- Cats
 - 3 - 4 mm

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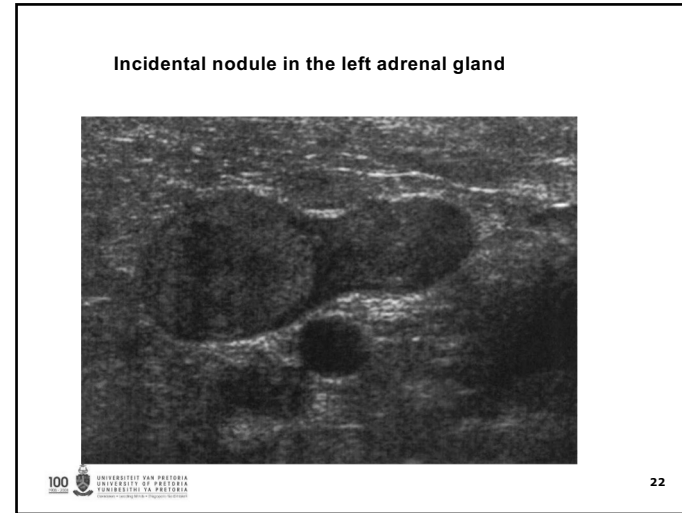
Left adrenal in PDH, measuring 10 mm at the caudal pole



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21



22



23



24

History

- Owner has recently (within the last month) moved house
- Patient stayed with the client's mother for the past 2 weeks
- Became progressively lethargic and depressed
 - thought to be pining for the owner
- Developed acute haemorrhagic diarrhoea and vomiting over night
- Owner woke up at 4 am and rushed her to Outpatients

25

Clinical examination & MDB

- All clinical parameters were within normal limits
- Discomfort on abdominal palpation
- Ht = 0.45 l/l
- TSP = 59 g/dL

26

Serum Lipase concentration

. • CHEMISTRY				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
LIPASE DGGR	21	L U/L	24 - 108	03/31/2022 09:52am

27

Sodium and potassium concentrations

. • BLOOD-GAS & ELECTROLYTES				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
SODIUM	145	mmol/L	142 - 151	03/31/2022 09:52am
POTASSIUM	4.60	mmol/L	3.6 - 5.1	03/31/2022 09:52am

Na/K ratio = 31.6

28

Interim treatment

- Ringer's lactate @ 2 x maintenance
- Cerenia 1ml/10kg = 1.78 ml
- Diomec 5 ml BID
- Omeprazole
- Clopamon @ 0.5 mg/kg

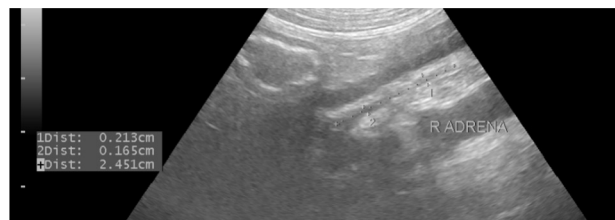
29

Diagnostic imaging (1)



30

Diagnostic imaging (2)



31

Basal cortisol concentration

- ENDOCRINOLOGY				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
CORTISOL BASELINE/SINGLE	<27.6	nmol/L	20 - 200	04/01/2022 02:12pm

Comments:
CORTISOL BASELINE/SIN: Baseline cortisol values can be used to rule out hypoadrenocorticism but are not useful in the diagnosis of hyperadrenocorticism. Values of < 55 nmol/L have an excellent negative predictive value and a sensitivity of 99% (JVM 2016;30:1786-1805) for hypoadrenocorticism. Therefore if a dog has a baseline cortisol above 55 nmol/L, it is unlikely that it has hypoadrenocorticism, but does not completely rule out the diagnosis. If a dog has a baseline cortisol of < 55 nmol/L, it is possible that the dog has hypoadrenocorticism but other diseases are possible as this cut-off value has a specificity of only 67%.

32

Interpretation & treatment over the weekend

- Slowly tapering intravenous fluid therapy
- Prednisolone 1% injections @ 0.2 mg/kg BID
- Awaiting Post-ACTH cortisol on Monday
- What % of dogs with HypoA have basal cortisol concentrations < 55 nmol/l?
 - What is the SENSITIVITY of a basal cortisol @ this cut-off?
 - SENS = positivity in disease; SNOUT
- What % of dogs with chronic gastrointestinal signs have basal cortisol concentrations < 55 nmol/l?
 - What is the SPECIFICITY of a basal cortisol @ this cut-off and in this particular control population?
 - SPEC = negativity in health; SPIN

33

Post-ACTH cortisol concentration

ENDOCRINOLOGY				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
CORTISOL POST 1	<27.6	nmol/L	No Reference Range	04/05/2022 01:20pm
Comments: CORTISOL POST 1 Post-ACTH stimulation cortisol in healthy dogs can reach 450 nmol/L. Values between 450-600 nmol/L are considered a "grey zone". Values >600 nmol are highly suggestive for HAC.				
Containers 8422-30216				

What does prior Glucocorticoid therapy do to a dog's post-ACTH concentrations?

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What is the evidence?

Received: 26 January 2023 | Accepted: 17 October 2023
DOI: 10.1111/jvim.16921

STANDARD ARTICLE

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

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

Antonio Maria Tardo¹ | Francesca Del Baldo¹ | Rodolfo Oliveira Leal^{2,3} |
Giorgia Galiazzo¹ | Marco Pietra¹ | Alba Gaspardo¹ | Federico Fracassi¹

¹Department of Veterinary Medical Sciences,
University of Bologna, Ozzano dell'Emilia,
Bologna, Italy

²CISA - Centre for Interdisciplinary Research
in Animal Health, Faculty of Veterinary

Abstract

Background: Dogs with eunatremic, eukalemic hypoadrenocorticism (EEH) typically show signs of chronic gastrointestinal disease (CGD). Previous glucocorticoid admini-

35

What is the evidence?

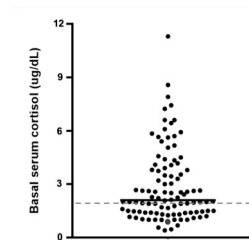
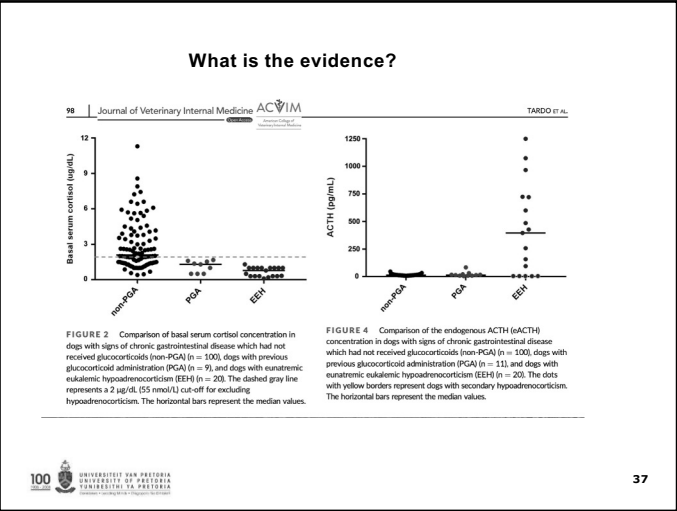
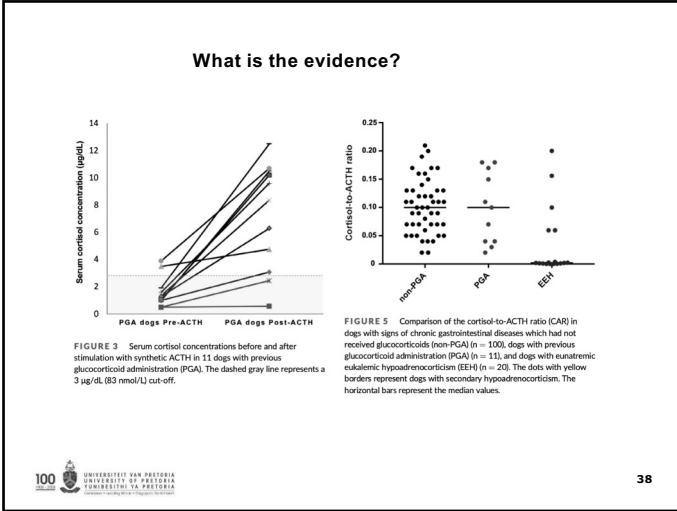


FIGURE 1 Basal serum cortisol concentration in 101 dogs with signs of chronic gastrointestinal disease which had not received glucocorticoids. The dashed gray line represents a 2 ug/dL (55 nmol/L) cut-off for excluding hypoadrenocorticism. The red dot represents the dog with the final diagnosis of eunatremic,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

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37



38

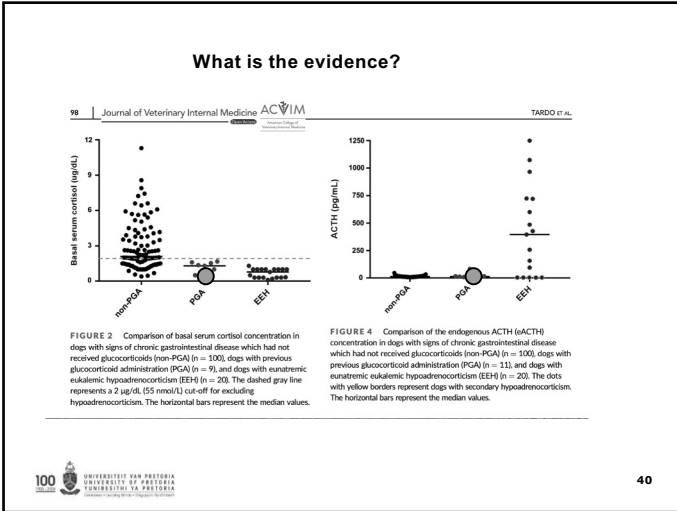
Case 2: Chloe - Pred Rx for past two years?

- Basal eACTH on alternative day without Preds: < 10 pg/ml
- Basal Cortisol: < 27.6 nmol/l (1ug/dl)
- Post ACTH cortisol: 136 nmol/l (5 ug/dl)

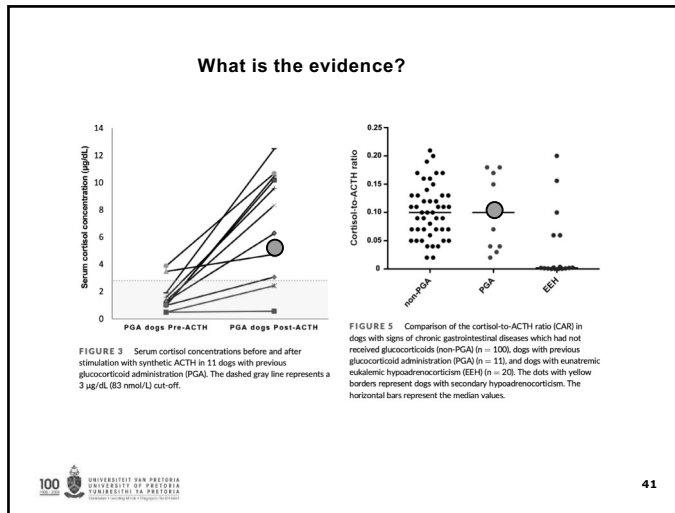
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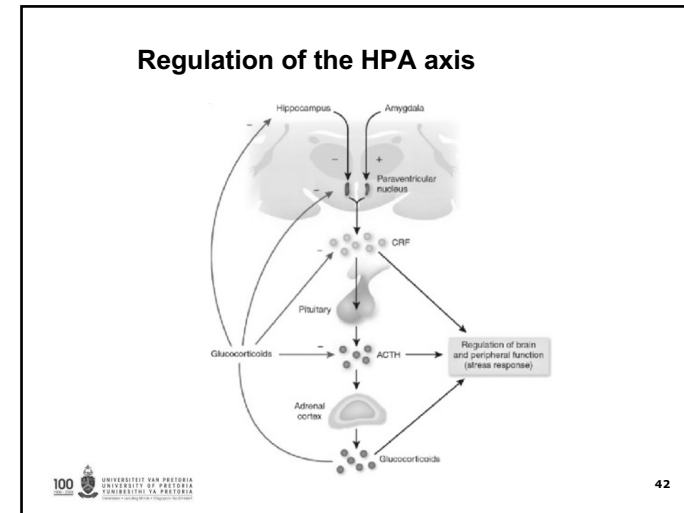
39



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41



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- ### Diagnosis
- Isolated glucocorticoid-deficient primary hypoadrenocorticism
 - A.k.a Eunatremic, Eukalemic Hypadrenocorticism (EEH)
 - In other words, they are "atypical", because their Na/K levels are normal
 - Therefore, their Z. glomerulosas are spared and.....
 - their aldosterone levels are normal – or are they?
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J Vet Intern Med 2014;28:154-159

Evaluation of Aldosterone Concentrations in Dogs with Hypoadrenocorticism

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

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From Baumstark et al....

In 3/70 dogs with HA, both sodium and potassium concentrations were normal and in 1/70 dogs, sodium was normal and potassium decreased. ACTH-stimulated aldosterone concentrations were below the detection limit of the assay in all 4 dogs. In 2 dogs, treatment was initiated with prednisolone. One of them developed hyperkalemia after 6 months, requiring additional mineralocorticoid supplementation. The other dog continued to have normal electrolytes throughout a 2-year observational period. Of the other 2 dogs, treatment of one was initiated and maintained with gluco- and mineralocorticoids and the other was lost to follow-up.

45

Treatment

- Prednisolone @ 0.2 mg/kg BID

Journal of Veterinary Cardiology (2022) 41, 231–235



Case Report

Ventricular systolic dysfunction in dogs diagnosed with hypoadrenocorticism

T. Gunasekaran, BVSc, AH^a, R.A. Sanders, DVM, MS^{b,*}

Journal of
Veterinary
Cardiology
www.elsevier.com/locate/jvc



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Received for peer review last month.....

Journal of Veterinary Internal Medicine
Open Access

Longitudinal Assessment of Thyroid Function in Dogs with Hypoadrenocorticism: Clinical Outcomes and Autoantibody Prevalence

Journal:	Journal of Veterinary Internal Medicine
Manuscript ID:	JVIM-24-030
Wiley - Manuscript type:	Standard Article
Keywords (You can enter any word desired, do not have to use from the list):	Addison's disease, Hypothyroidism < Thyroid gland < Endocrinology, cTSH, polyendocrine, cortisol, ACTH

SCHOLARONE[™]
Manuscripts

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Follow-up two weeks later

CHEMISTRY				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
CREATININE	71	umol/L	40 - 111	04/14/2022 02:13pm

Comments:
CREATININE
The reference interval given on the report is for all body weights combined.
Canine creatinine reference intervals for the CI/ml by body weight cases
dogs <10kg: 38-66 umol/L
10kg-25 kg: 45-110 umol/L
>25 kg: 87-130 umol/L.

BLOOD-GAS & ELECTROLYTES				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
POTASSIUM	4.84	mmol/L	3.8 - 5.1	04/14/2022 02:13pm
SODIUM	145	mmol/L	142 - 151	04/14/2022 02:13pm

Continues
8122-163412
8122-163413
8122-163411

Na/K ratio = 30

48

Lifelong treatment

- Prednisolone @ 0.15 mg/kg OID
- Practically boils done to ½ tablet Prednisolone ONCE daily
- Follow up on 10 May 2022 (4 weeks later). Owner reported that the patient is doing very well
- Warned the owner to double the dose during stressful episodes
- Re-iterated that she should return monthly (for the first 4-6 months) to check electrolyte levels

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Case 3: “Bagheera” German Shorthaired Pointer



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Bagheera: History and clinical findings

- Presented with acute haemorrhagic diarrhoea
- Anaemia; Ht = 21; Coomb's and ISA negative
- Electrolytes normal
- Basal cortisol < 27.6 nmol/l (after 48 hours of Dexamethasone treatment)
- Post ACTH cortisol: 49 nmol/l
- Gastric and pyloric ulcerations on Gastroscopy

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Gastroscopy (1)



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Gastroscopy (2)



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J Vet Intern Med 2016;30:1798-1805

Evaluation of Basal Serum or Plasma Cortisol Concentrations for the Diagnosis of Hypoadrenocorticism in Dogs

A.J. Gold, D.K. Langlois, and K.R. Refsal

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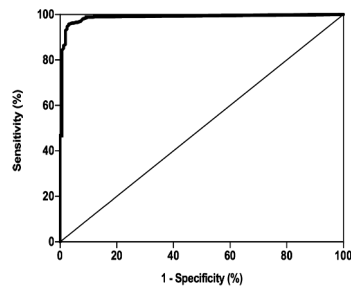


Fig 3. Receiver operating characteristic (ROC) curve (dogs with hypoadrenocorticism versus dogs with nonadrenal illness) for serum or plasma basal cortisol concentrations for the diagnosis of hypoadrenocorticism. The thin diagonal line represents a completely uninformative test, wherein the area under the curve (AUC) is 50%. The area under the ROC curve represented by the thicker line is 98.8% (95% CI, 0.979-0.997). The overall most accurate cut-point identified on the curve was 22 nmol/L, which had a sensitivity and specificity of 96.9 and 95.7%, respectively.

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Basal Cortisol (nmol/L)	Dogs with HA (total n = 163)	Dogs with NAI (total n = 351)	% Sensitivity (95% CI)	% Specificity (95% CI)
≤5.5	133	3	81.6 (74.8-87.2)	99.1 (97.5-99.8)
≤10	144	4	88.3 (82.4-92.8)	98.9 (97.1-99.7)
≤22	158	15	96.9 (93.0-99.0)	95.7 (93.0-97.6)
≤28	160	30	98.2 (94.7-99.6)	91.5 (88.0-94.2)
≤40	162	61	99.4 (96.6-100)	82.6 (78.2-86.4)
≤55	162	116	99.4 (96.6-100)	67.0 (61.8-71.8)

33% of dogs with NAI had BSC < 55 nmol/L

Table 1. Calculated sensitivities and specificities of various serum or plasma basal cortisol concentrations for the diagnosis of hypoadrenocorticism in dogs.

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Greater proportion of dogs (35%) with normal electrolytes have BSC < 55 nmol/l

Table 3. Sensitivities and specificities of various cut-points in 2 subpopulations.

Basal Cortisol (nmol/L)	Normal Electrolyte Profile		Abnormal Electrolyte Profile	
	% Sens (95% CI)	% Spec (95% CI)	% Sens (95% CI)	% Spec (95% CI)
≤5.5	89.3 (71.8–97.7)	98.9 (96.9–99.8)	80.0 (72.3–86.4)	100 (95.3–100)
≤22	96.4 (81.7–99.9)	95.4 (92.5–97.5)	97.0 (92.6–99.2)	96.0 (88.9–99.2)
≤55	100 (87.7–100)	64.7 (58.8–70.3)	99.3 (95.9–100)	75.0 (63.7–84.2)

The sensitivities and specificities (and their respective 95% confidence intervals) of basal cortisol concentrations for the diagnosis of hypoadrenocorticism in dogs with normal and abnormal electrolyte profiles. Sens, sensitivity; Spec, specificity; CI, confidence interval.

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Discussion

- Much debate about this entity called “atypical” hypoadrenocorticism
- Most of these cases actually have low aldosterone levels
- How do they manage to maintain normal electrolyte levels then?

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Table 2. Positive and negative predictive values of various basal cortisol concentrations for the diagnosis of hypoadrenocorticism in dogs.

Basal Cortisol (nmol/L)	Positive Predictive Value (%)			Negative Predictive Value (%)		
	3% Prevalence	15% Prevalence	21% Prevalence	3% Prevalence	15% Prevalence	21% Prevalence
≤5.5	73.7	94.1	96.0	99.4	96.8	95.3
≤22	41.1	79.9	85.7	99.9	99.4	99.1
≤55	8.5	34.7	44.5	100	99.8	99.8

The positive and negative predictive values for 3 basal serum or plasma cortisol concentration cut-points are presented. The predictive values were calculated based on the MSU-VMC prevalence of 21% as well as 2 previously reported prevalence rates.^{10,11}

J Vet Intern Med 2016;30:1798–1805
Evaluation of Basal Serum or Plasma Cortisol Concentrations for the Diagnosis of Hypoadrenocorticism in Dogs
A.J. Gold, D.K. Langlois, and K.R. Refsal

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„Atypical“

- Postulation, in some dogs the destructive process is confined to zona fasciculata/reticularis ➡ isolated glucocorticoid deficiency

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„Atypical“ - However:

- Lack of generally accepted definition
- In most studies limited characterisation of patients, i.e. aldosterone, cACTH not measured
- No histological studies available, confirming intact zona glomerulosa

„It was assumed that aldosterone secretion was normal as sodium and potassium were within reference ranges“ (Mansfield 2000)

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Potential explanation

If sodium intake is sufficient to maintain normal ECF volume and distal tubular flow rate, an animal with hypoadrenocorticism may be able to maintain potassium balance.

DiBartola and Autran de Morais, 2006

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Interesting Case

Possible mechanisms to explain the absence of hyperkalaemia in Addison's disease

Raymonde F. Gagnon¹ and Mitchell L. Halperin²

Renal Divisions, ¹Montreal General Hospital, McGill University, Montreal, Quebec; ²St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

Keywords: adrenal insufficiency; aldosterone; anion gap; cortical collecting duct; hyponatraemia; potassium

absence of aldosterone and to suggest a possible explanation that hinges on an unexpectedly high distal delivery of K⁺ to the cortical collecting duct (CCD).

Introduction

In a patient with Addison's disease, the typical clinical manifestations are due to the absence of mineralocorticoid and glucocorticoid hormones. The combination of hyponatraemia, hyperkalaemia, and hyperchromic metabolic acidosis is a classic triad. Vomiting and anorexia are also common. In the plasma creatinine, BUN, and haematocrit are classical findings [1]. Aldosterone deficiency is confirmed by a low urinary aldosterone to creatinine ratio. In a large series of patients with Addison's disease, hyperkalaemia on admission [2], insufficient data were provided to measure the urinary aldosterone to creatinine ratio and that the urinary aldosterone to creatinine ratio was not abnormally low.

• missed aldosterone peak
• diuretics
• vomiting
• alkalosis
• tubulopathies
• high delivery of K⁺ to CD

A 64-year-old male from India sought medical attention because of orthostatic hypotension 12 days prior to establishing a diagnosis of Addison's disease. His past medical history revealed weakness, fatigue, weight loss over the past 3 months, a 5-pound weight loss, and a distaste of sweet foods that he had enjoyed were also noted. He denied vomiting and the use of laxative agents. On physical examination, his blood pressure was 100/60 mmHg, heart rate was 70 beats per minute, and his temperature was 36.4°C. He had a low jugular venous pressure and poor skin turgor.

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Baumstark et al 2014 again..... 70 dogs with HypoA

J Vet Intern Med 2014;28:154-159

Evaluation of Aldosterone Concentrations in Dogs with Hypoadrenocorticism

M.E. Baumstark, N.S. Sieber-Ruckstuhl, C. Müller, M. Wenger, F.S. Boretto, 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.

64

Expected cortisol results after ACTH stimulation

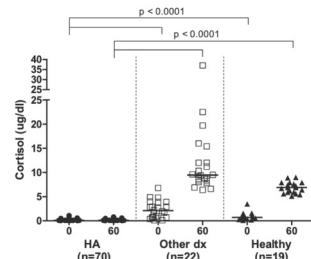


Fig 1. Baseline (0) and ACTH-stimulated (60) serum cortisol concentrations in dogs with HA (HA, n = 70), dogs with diseases mimicking HA (other dx, n = 22), and healthy dogs (healthy, n = 19).

Aldosterone stimulation after ACTH

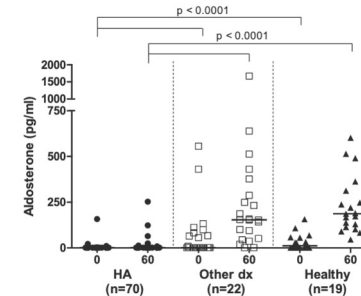


Fig 2. Baseline (0) and ACTH-stimulated (60) serum aldosterone concentrations in dogs with HA (HA, n = 70), dogs with diseases mimicking HA (other dx, n = 22), and healthy dogs (healthy, n = 19).

No "missed" aldosterone peak

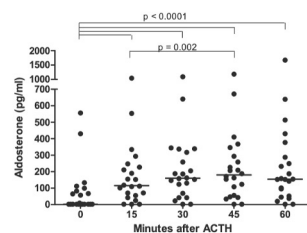


Fig 4. Baseline (0) and ACTH-stimulated (15, 30, 45, 60) serum aldosterone concentrations in dogs with diseases mimicking HA (n = 22).

Dissociation between electrolytes and aldosterone

trations could be followed up. One dog developed sodium and potassium abnormalities after 6 months. The other dog could be followed up for 2 years and was still stable on glucocorticoid therapy only. The observation that most dogs develop electrolyte changes sooner or later led to the assumption that the immune-mediated destruction of the adrenal cortex is first confined to the zona reticularis/fasciculata and in a later phase of disease spreads to the zona glomerulosa. However, aldosterone measurements in our study, as well as in earlier studies, demonstrate that normal electrolytes do not necessarily reflect a normally functioning zona glomerulosa.^{1,2}

In human medicine, normal sodium and potassium concentrations are found in 10% and normal potassium in 25% of patients with primary HA.¹⁹ The

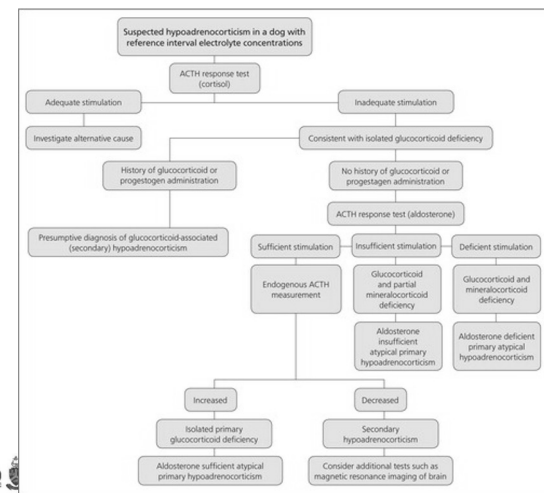
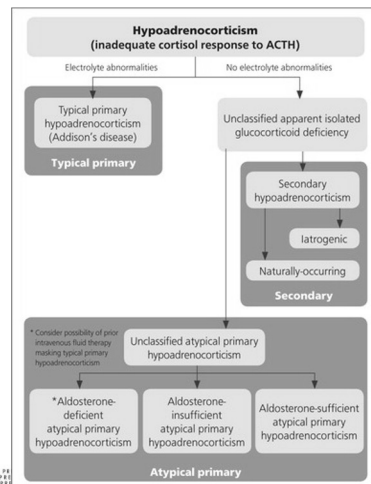
One layer failing at a time.....

degraded. Increased renin concentrations were found in all of those patients, indicating compensation for a failing zona glomerulosa.¹¹ Therefore, in humans, it is currently assumed that a dissociation between zona glomerulosa and fasciculata function occurs very rarely.¹¹ However, segmental sparing of the zona glomerulosa with atrophy of the zona reticularis and fasciculata has been documented in dogs.⁸⁻¹⁰ In addition, a very recent case report documents a dog with hypoaldosteronism preceding hypocortisolemia.²⁰ This demonstrates that failing of 1 layer of the adrenal cortex can occur in dogs. It is most likely that these are rare cases. In future, renin measurements should be included in the work-up of dogs with primary HA and normal electrolyte concentrations, to completely assess the function of the zona glomerulosa.

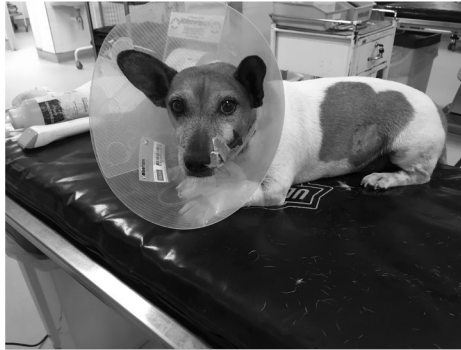
Low/insufficient aldosterone in “atypical” cases

ers should be aware that fluid losses because of vomiting could lead to an acute deterioration of their dog's condition and that a modification in therapy might be necessary in the later course of the disease. In future, determination of the plasma renin activity in these dogs should be intended to better classify their hormonal need.

In summary, aldosterone concentrations in dogs with HA seem to be compromised independent of their electrolyte concentrations. Therefore, normal sodium and potassium concentrations in dogs with HA may not reflect a normal function of the zona glomerulosa.



Case 4: Twit Strydom 14 February 2024 - JRT



73

Twit Strydom



74

Twit Strydom



75

Twit Strydom



76

Case 5: 28/04/2022



77

Signalment

- 15 year old
- Spayed female
- Burmese
- She is fed on a raw diet
- Primary complaint of uncomfortable urination (slight red discolouration), constipation, ataxia and weakness

78

History

- In 2019, she was diagnosed with chronic renal failure
- She had mild azotaemia
- Increased SDMA (value not specified)
- Marked hypokalaemia

79

Minimum data base

- Clinical examination
 - HR = 132; T = 37; RR = 32
 - Distended, gas-filled intestines
 - Painful on palpation of the right hind

80

81

81

82

100
1930-2020
UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
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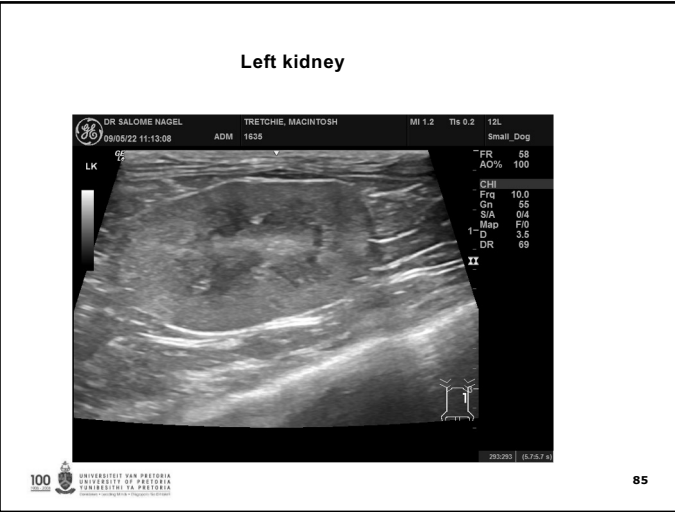
82

83

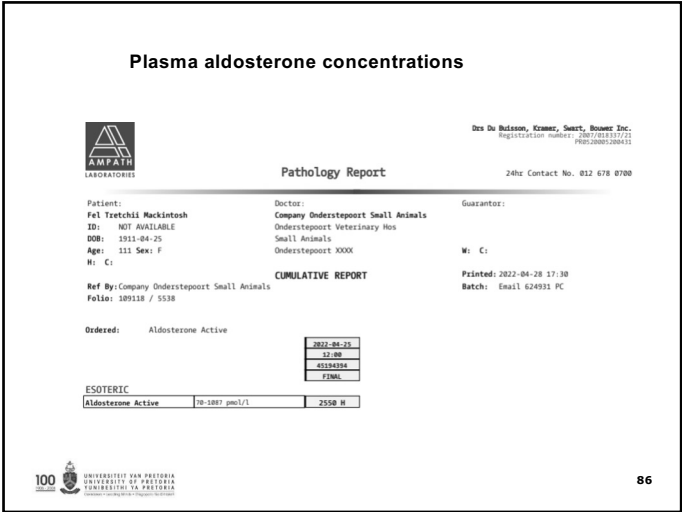
- 83

84

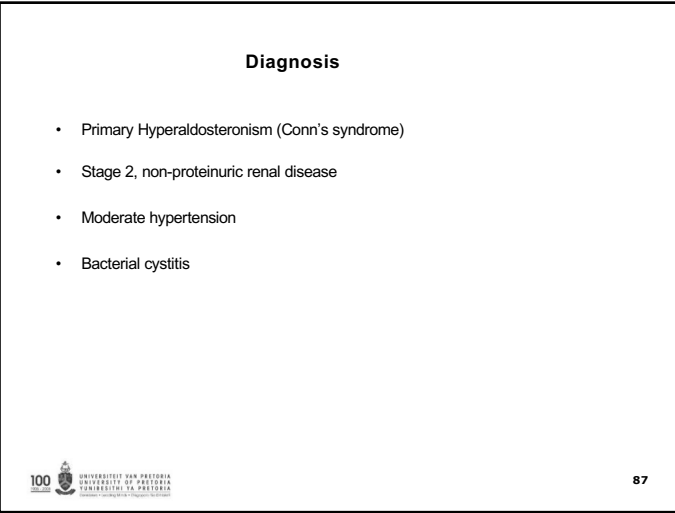




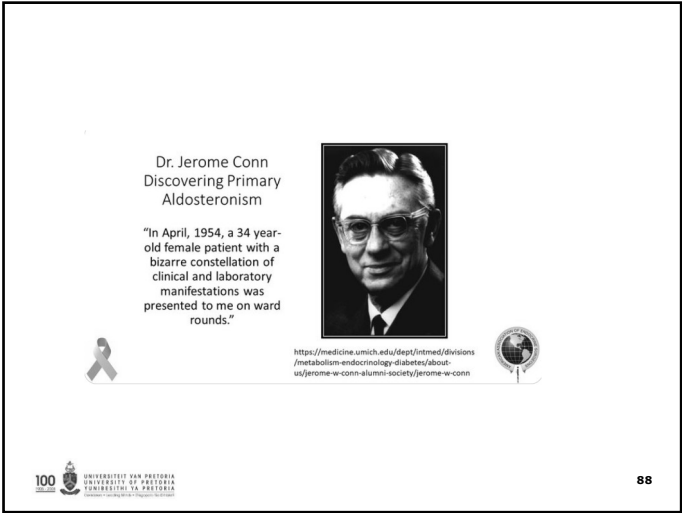
85



86



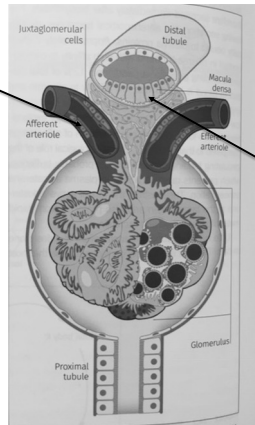
87



88

A bit of pathophysiology.....(1)

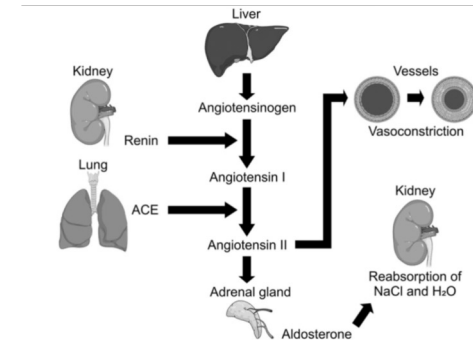
Vascular baroreceptors in the afferent arteriole stimulate renin secretion in response to reduced renal perfusion pressure



The macula densa in the distal tubule, adjacent to the afferent arteriole, senses low distal tubular Na^+ & Cl^- delivery, resulting in renin release

89

A bit of pathophysiology(2)



90

Treatment

- Spironolactone 2mg/kg; ¼ tablet (6 mg) OID
- Semintra (dose)? OID
- Lacson 2 ml BID
- Enrofloxacin 1 tablet (50 mg) OID for 10 days

91

Follow-up visit

-- CHEMISTRY			
TEST	RESULT	UNITS	REF RANGE
CREATININE	181	H $\mu\text{mol/L}$	57 - 138
UREA NITROGEN	23.8	H mmol/L	4.1 - 12.9
Comments:			
CREATININE	Sample condition	Slight Lipemia	
-- BLOOD-GAS & ELECTROLYTES			
TEST	RESULT	UNITS	REF RANGE
POTASSIUM	5.16	mmol/L	3.8 - 5.1
SODIUM	151	mmol/L	144 - 156

92

Treatment decisions

- Aetiology of Hyperaldosteronism
 - Adrenal tumour (much higher aldosterone)
 - Nodular hyperplasia
- Concomitant chronic renal disease
 - ACE inhibitor; ARB?; Ca-channel blocker?

93

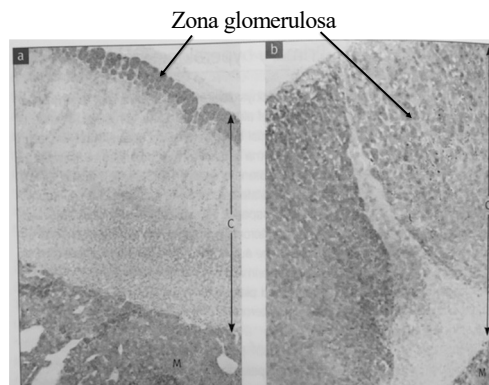
Discussion

- Primary Hyperaldosteronism is the most common adrenocortical disorder in cats
- However, the disease is largely underdiagnosed, because hypertension and hypokalaemia are usually attributed to CRF
- Yet, the CRF may be a consequence of primary hyperaldosteronism
- Moreover, BP is not routinely measured
- Lastly, adrenals are not routinely examined by ultrasound

94

94

Disease manifestations (1)

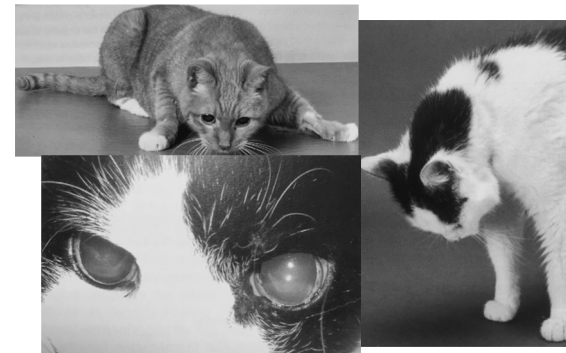


Histology of adrenals stained with neuron-specific enolase (NSE)

95

95

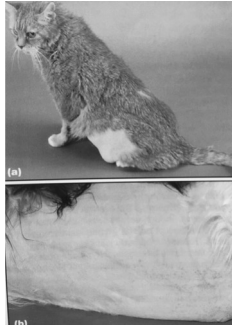
Disease manifestations (2)



96

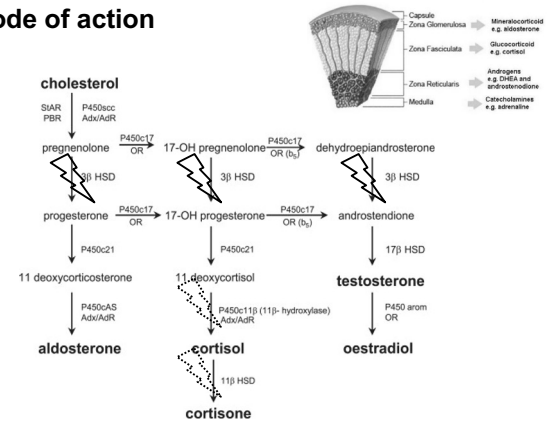
96

Disease manifestations (3)



Both cats were diagnosed with concurrent hyperaldosteronism and hyperprogesteronism. Cat (a) developed diabetes mellitus. Cat (b) demonstrates the very thin skin and prominent blood vessels commonly seen in cases with high progesterone and cortisol.

Mode of action



Case 6: Munkee, 13-year-old DLH cat



Serum Aldosterone

Patient: Fel Munkee Dengler
ID: NOT AVAILABLE
DOB: 1911-06-10
Age: 11 Sex: F
M: C

Doctor: Company Onderstepoort Small Animals
Onderstepoort Veterinary Hos
Small Animals
Onderstepoort XXXX

Guarantor: W: C

Ref By: Company Onderstepoort Small Animals
Folio: 110445 / 49540

Specimen: 8610-AL01464R
PT Loc: 09400

Collected: 2022-06-10 08:00
Received: 2022-06-10 13:04
Printed: 2022-06-13 15:30
Batch: APR STD

Ordered: Aldosterone Active
Sample: E03 EDTA Active (2)

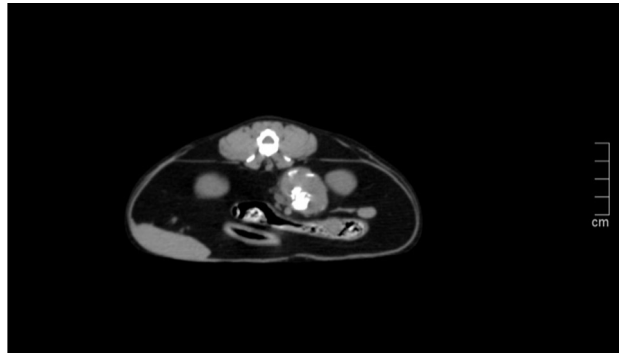
Test: ESOTERIC

Test	ABN	Result	Reference Range	Unit	1/1
Aldosterone Active	*H	6040	70-1087	pmol/L	

DISCLAIMER:
Specimen received was collected from a cat.
Analysis was performed by means of chemiluminescent immunoassay methodology from supplier Diasorin Liaison.
The reference range above is applicable to humans only.

4:03 pm

Right adrenal tumour



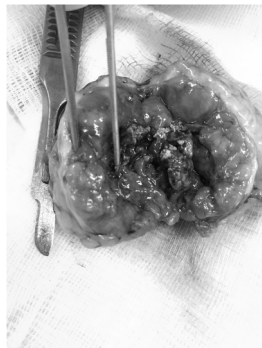
101

Post-adrenalectomy



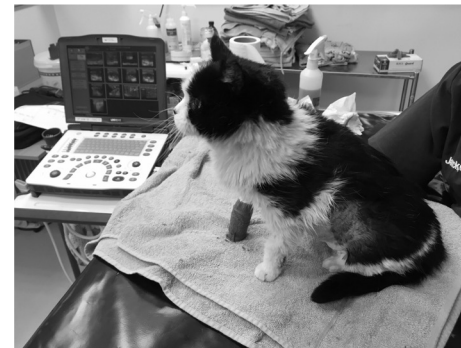
102

Excised tumour



103

Post-operative picture



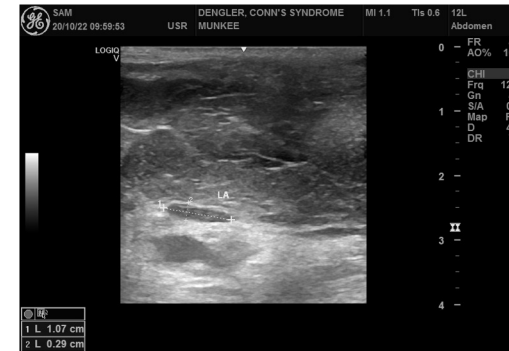
104

Pupils are constricting



105

Contra-lateral adrenal 1 week post operation



106

Case 7: one year old Cat
Anorexic, listless



107

History of Depo-Medrol Rx over the past 6 months

Comments: Status: 09/19/2022 12:45pm

-- ENDOCRINOLOGY				
TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
CORTISOL BASELINE/SINGLE	<27.6	nmol/L	30 - 390	09/19/2022 12:45pm
CORTISOL POST 1	<27.6	nmol/L	No Reference Range	09/19/2022 12:45pm

Comments:
CORTISOL BASELINE/SIN Baseline cortisol values can be used to rule out hypoadrenocorticism but are not useful in the diagnosis of hyperadrenocorticism. Values of > 55 nmol/L have an excellent negative predictive value and a sensitivity of 99% (JVM 2016;30:1788-1805) for hypoadrenocorticism. Therefore if a dog has a baseline cortisol above 55 nmol/L, it is unlikely that it has hypoadrenocorticism, but does not completely rule out the diagnosis. If a dog has a baseline cortisol of < 55 nmol/L, it is possible that the dog has hypoadrenocorticism but other diseases are possible as this cut-off value has a specificity of only 67%.

CORTISOL POST 1 Post-ACTH stimulation cortisol in healthy dogs can reach 450 nmol/L. Values between 450-600 nmol/L are considered a "grey zone". Values >600 nmol are highly suggestive for HAC.

108

Aldosterone pre- and post ACTH stimulation

Ordered: Aldosterone Active

2022-09-16	2022-09-16
15:20	16:44
47510482	47510481
FINAL	FINAL

ESOTERIC

Aldosterone Active	78.1087 pmol/l	2768 H	3570 *H
--------------------	----------------	--------	---------

Specimen Comments: 47510481 on 2022-09-16 16:44:00

Post Synacthen
Dr R Watson
Breed: Feline Domestic Shorthair

Test Comments: Req no: 47510481 on 2022-09-16 16:44

Aldosterone Active

This result has been confirmed with dilution.

pg/ml to
pmol/l x 2.77

109

Case 8: Lexi Mouton – 6 year old Yorkshire Terrier



110

History

- Signalment: Lexi is an approx. 6 year old female spayed Yorkshire Terrier with a weight of 8.5 kg.
- Presenting complaint: Lexi presented for a Cushing's workup.
- History: Lexi was diagnosed with hyperadrenocorticism in July 2020. Owners noticed a severe increase in weight, potbellied appearance and polyphagia. They also noticed polyuria and polydipsia. A low dose dexamethasone suppression test was performed and the following results were obtained:
 - Basal cortisol: 353 nmol/L,
 - 4 hours post: 139 nmol/L,
 - 8 hours post: 263 nmol/L.
- She was started on 20 mg Trilostane oid (2.5 mg/kg oid)
- After 4 weeks no real improvement was seen and dose was increased to 30mg bid (3.5mg/kg bid).

111

Physical examination

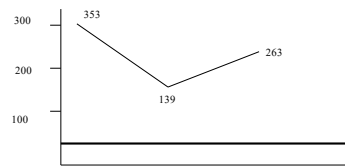
- On presentation Lexi was bright, alert and responsive.
- Her clinical parameters were within normal limits.
- Abdomen had an obvious potbellied appearance.
- The abdominal skin is thin, with prominent vasculature.
- The skin is dry and scaly.
- Lexi also had bilateral patella luxation (Grade 2?)

112

Question?

This low dose dexamethasone suppression test is consistent with:

- a) Adrenal dependent Hyperadrenocorticism (ADH)
- b) Pituitary dependent Hyperadrenocorticism (PDH)
- c) A false positive test result
- d) A false negative test result
- e) The test cannot distinguish between PDH and ADH



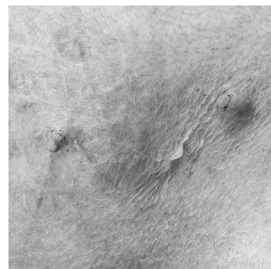
113

Abdomen



114

Abdominal skin close up



115

Haematology – 16 October 2020

TEST	RESULT	UNITS	REF RANGE
HAEMOGLOBIN	205	H g/L	120 - 180
RED CELL COUNT	8.12	x10 ¹² /L	5.5 - 8.5
HAEMATOCRIT	0.62	H L/L	37 - 55
MEAN CORPUSCULAR VOLUME	74.8	fL	60 - 77
MEAN CORPUSCULAR HAEMOGLOBIN	25.2	pg	No Reference Range
MEAN CORPUSCULAR HAEMOGLOBIN CONCENTRATION	33.0	g/dL	32 - 36
RED CELL DISTRIBUTION WIDTH	13.2	%	No Reference Range
WHITE CELL COUNT	13.59	x10 ⁹ /L	6 - 15
SEGMENTED NEUTROPHIL	11.69	H x10 ⁹ /L	3 - 11.5
BAND NEUTROPHIL	0.00	x10 ⁹ /L	0 - 5
LYMPHOCYTE	1.09	x10 ⁹ /L	1 - 4.8
MONOCYTE	0.82	x10 ⁹ /L	15 - 136
EOSINOPHIL	0.00	L x10 ⁹ /L	1 - 1.25
BASOPHIL	0.00	x10 ⁹ /L	0 - 1
OTHER	0.00	%	No Reference Range
PLATELET COUNT	443	x10 ⁹ /L	200 - 500
NRBC/100 WBC	4		0 - 9
MORPHOLOGY	1+ ANISOCYTOSIS, 1+ POLYCHROMASIA, MILD NEUTROCYTE ACTIVITY, MANY NEUTROPHILS		

116

Serum chemistry - 16 October 2020

... CHEMISTRY			
TEST	RESULT	UNITS	REF RANGE
TOTAL SERUM PROTEIN	57.4	g/L	56 - 73
ALBUMIN	33.3	g/L	28 - 41
GLOBULIN	24.1	g/L	20 - 41
AVG RATIO	1.4		0.6 - 1.7
ALANINE AMINOTRANSFERASE	53.2	U/L	9 - 73
ALKALINE PHOSPHATASE	218	H U/L	20 - 165
UREA NITROGEN	18.6	H mmol/L	2.3 - 8.9
CREATININE	79	umol/L	59 - 109
PLASMA SERUM CONDITION	CLEAR		No Reference Range

... BLOOD GAS & ELECTROLYTES			
TEST	RESULT	UNITS	REF RANGE
SODIUM	148	mmol/L	142 - 151
POTASSIUM	5.76	H mmol/L	3.6 - 5.1

117

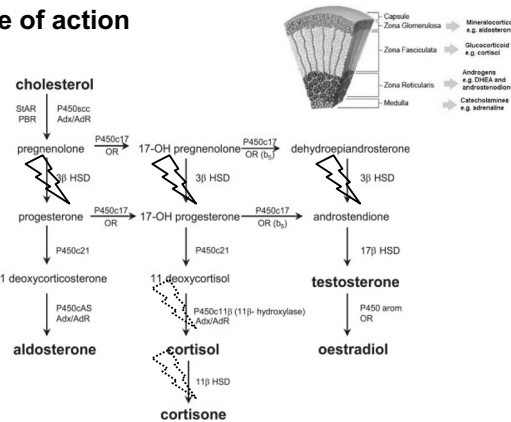
Question?

What is the most likely cause of the hyperkalaemia?

- a) Hyperaldosteronaemia
- b) Trilostane therapy
- c) Cushing's syndrome
- d) Thrombocytosis
- e) Polycythaemia

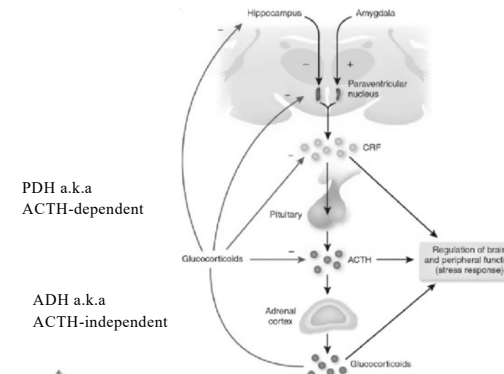
118

Mode of action



119

Different forms of HAC

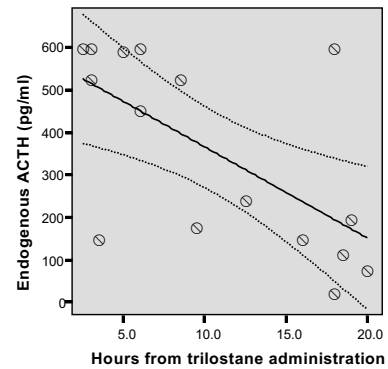


120

120

Endogenous ACTH

ACTH increases after Trilostane is given



Witt and Neiger (2004) *Vet Record* 154: 399-400

121

US left adrenal cranial pole 11 mm (< 6mm)



122

Ultrasound L adrenal cdl pole 13 mm (<6mm)



123

Ultrasound right adrenal 11 mm (< 6mm)



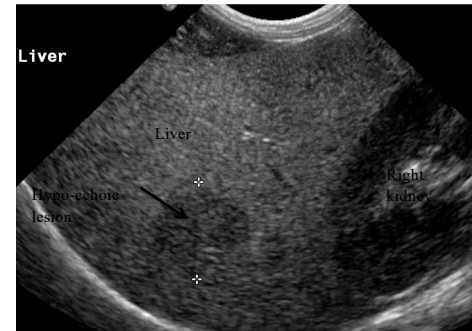
124

Gall bladder sludge



125

Liver



126

Question?

- The liver is often enlarged in cases of hyperadrenocorticism and tends to have a hyper-echoic appearance on ultrasound.
- DD's for the hypoechoic lesion seen?

127



128

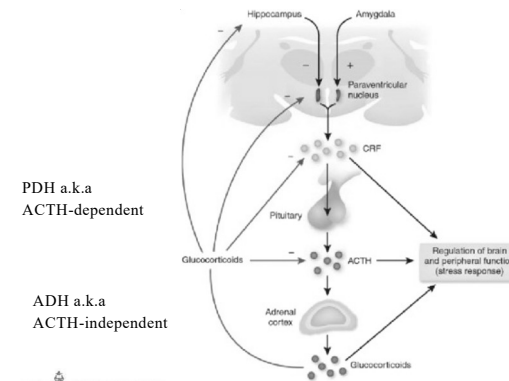
Question?

The above signalment and diagnostic findings are consistent with?

- a) Adrenal-dependent hyperadrenocorticism (ADH)
- b) Pituitary dependent hyperadrenocorticism (PDH)

129

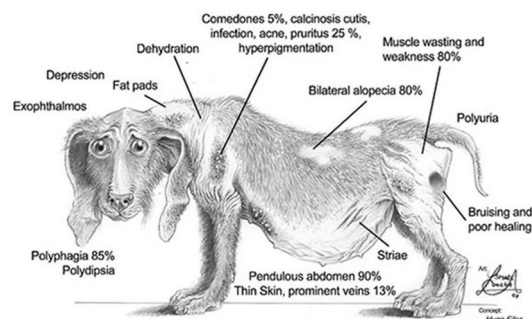
Different forms of HAC



130

130

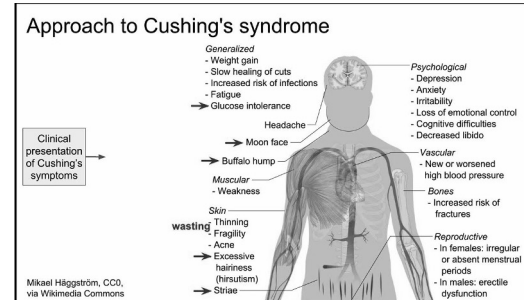
Canine hyperadrenocorticism



131

131

Wide-ranging effects of cortisol



132

Which test is next?

- a) Low dose dexamethasone suppression test
- b) ACTH stimulation test
- c) Water deprivation test
- d) Urine cortisol: Urine creatinine ratio

133

ACTH stimulation test results

- Basal cortisol 148 nmol/l (10 – 160)
- ACTH-stimulated cortisol 295 nmol/l (220 – 450)
- UPC = 9.35 (normal < 0.5)

134

Continued treatment

- Trilostane @ 1 mg/kg bid

135

Questionnaire to assess the stability of a patient with Hyperadrenocorticism (Cushing's disease)

This prototype questionnaire is an adaptation from Macfarlane et al. Pre-Trilostane and three-hour post-Trilostane cortisol to monitor Trilostane therapy in dogs. Vet Record, 2020, Dec 10.

Patient Name: _____ Date: 23/11/2020

Questions	1 (Bad/out of control)	2	3	4	5 (Normal)
Maximum score for dogs experiencing very good control is 45					
1. Thirst					
2. Urine volume					
3. Appetite					
4. Panting					
5. Exercise tolerance					
6. Coat quality					
7. Demeanour					
8. GIT signs					
9. Owner's overall impression of control					
Total score					/45

The next six variables are absolute values, not on an ordinal scale

Urine SG:
Pre-Trilostane basal cortisol (40 – 138 nmol/l):
Trilostane dose and time:
Basal cortisol 3 hours post-Trilostane (> 27.6 nmol/l):
Post ACTH cortisol (100 – 200 nmol/l) (if ACTH stimulation test is done):
ACTH dose and volume:

136

136

Follow up 23 November 2020

-- CHEMISTRY

TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
CREATININE	89	umol/L	59 - 109	11/23/2020 02:13pm
UREA NITROGEN	17.0 H	mmol/L	2.3 - 8.9	11/23/2020 02:14pm

-- BLOOD-GAS & ELECTROLYTES

TEST	RESULT	UNITS	REF RANGE	RESULT DATETIME
POTASSIUM	4.78	mmol/L	3.6 - 5.1	11/23/2020 02:13pm
SODIUM	151	mmol/L	142 - 151	11/23/2020 02:13pm

137

Follow up ACTH stim test results 23/11/2020

- Basal cortisol 287 nmol/l (10 – 160)
- ACTH-stimulated cortisol 444 nmol/l (220 – 450)
- UPC = 16.68 (normal < 0.5)

138

Remaining issues with Trilostane

- Mode of action still unclear
- Starting dose needs refinement
- Monitoring needs improvement
- Optimise treatment of Adrenal-dependent disease
- Effects on adrenals are a concern

139

139

Future plan?

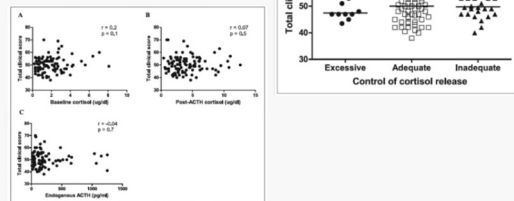
- Increase dose of Trilostane?
- Image the pituitary?
- MRI vs. CT scan
- If macroadenoma, consider hypophysectomy

140

Lack of association between clinical signs and laboratory parameters in dogs with hyperadrenocorticism before and during trilostane treatment

F. S. Boretto¹, J. Holzthum¹, C. E. Reusch¹, N. S. Sieber-Ruckstuhl¹

¹Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich
Band 158, Heft 9, September 2016, 631–638, © GST | SVS



141

Lab vs. Clinical score (continued)



Objectives of the study:

To compare the recommended laboratory variables, including serial basal cortisol concentrations in a cohort of dogs treated with trilostane.

Patients: 22 dogs with PDH

Results:

No single variable or group of variables reliably discriminated between adequately-controlled dogs and suboptimal-controlled dogs

142

Final recommendations

- Indications for Trilostane
 - Use in both PDH and ADH
- Mode of action
 - Who knows how it works – 3B-HSD isoforms in breeds
- Dose
 - Use a starting dose of 0.5 mg/kg bid (under constant revision)
- Monitor
 - Ask the owner what to do ? (Questionnaire will help)
 - Measure the USG on a few urine samples
 - Check Electrolytes & Creatinine
 - Basal cortisol measurements – Alert to over-treatment !
 - ACTH stimulation test – under specific circumstances !
- Efficacy
 - 75%
- Adverse effects
 - Can occur without warning !

143

Case 9: Mina – 12 yo Shar Pei



144

History and clinical findings

- Mina presented for a second opinion due to severe polyuria and polydipsia, weight gain and lethargy
- Clinical examination showed bilaterally symmetrical alopecia
- Magnetic resonance imaging revealed marked enlargement of her pituitary gland
- Abdominal ultrasound revealed bilateral adrenal enlargement



145

Mina – 12 yo Shar Pei



146

Considerations

- Hormones released by the different parts of the pituitary gland
- Causes of pituitary enlargement
- Effect of different neoplasms of the pituitary on their respective effector organs in the body



147

Final diagnoses

- Mina was ultimately diagnosed with
 - hyperadrenocorticism,
 - diabetes insipidus and
 - central/secondary hypothyroidism
- Diabetes insipidus in dogs
 - Causes
 - Diagnosis
 - Treatment



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Case 10: 13 year old Boston Terrier



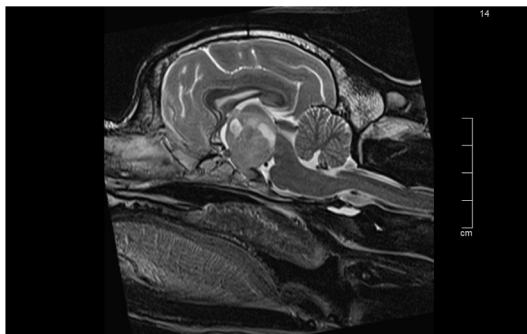
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13 year old Boston Terrier



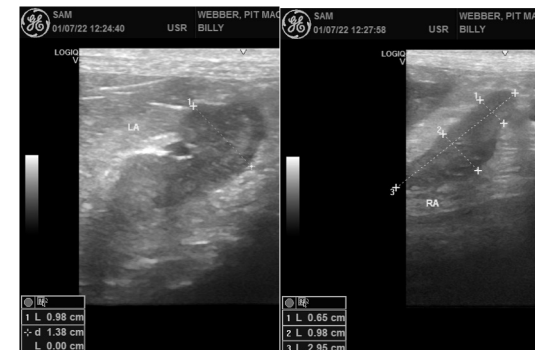
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13 year old Boston Terrier
30 May 2022



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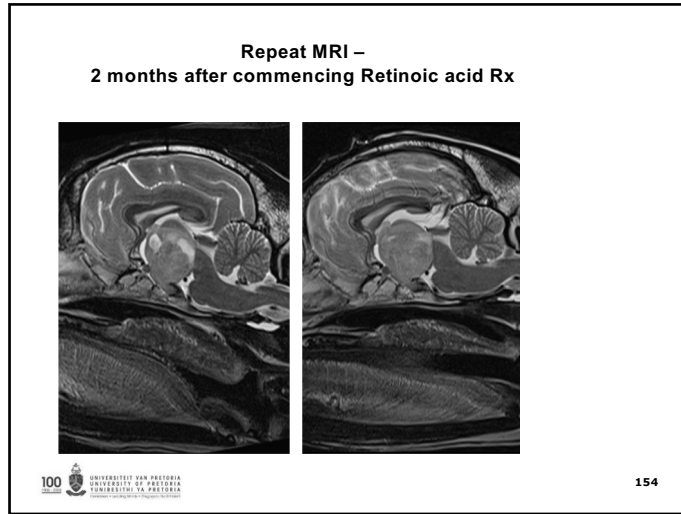
13 yo Boston Terrier
1 July 2022



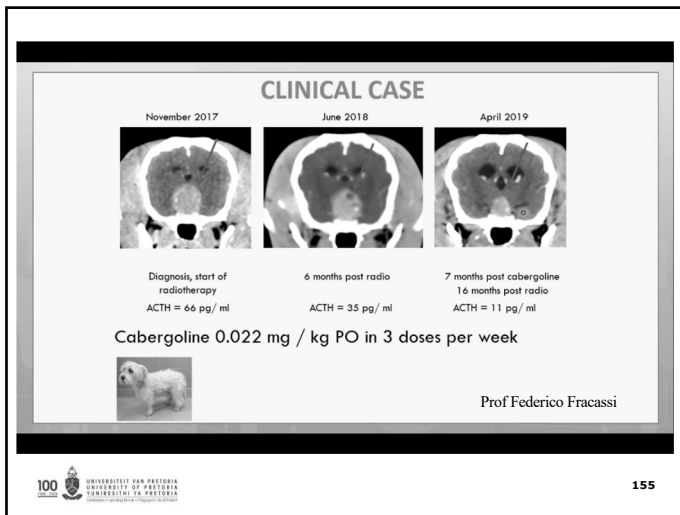
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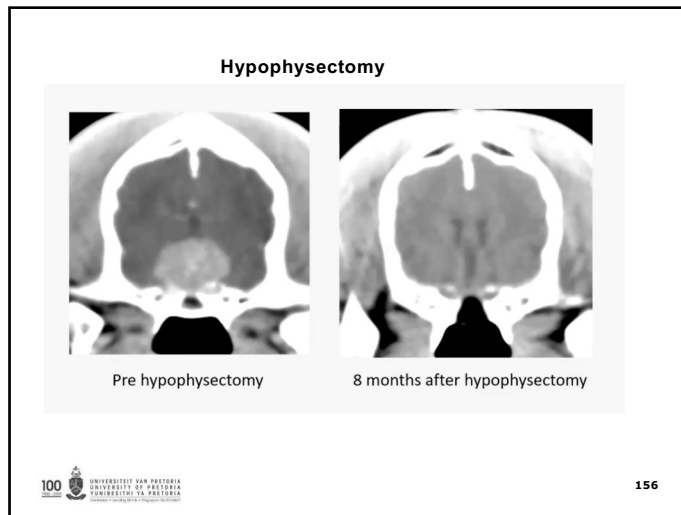
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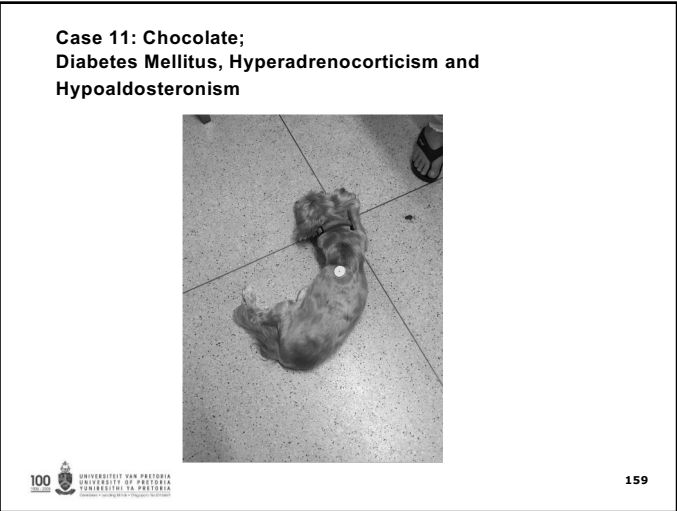
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159



160

Chocolate



161

Chocolate



162

Chocolate



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Chocolate Treatment regimen

- Glargine 5IU tid
- DOCP injection @ 2.2 mg/kg every 14 days
- Trilostane @ 1mg/kg BID

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> Vet Surg. 2016 Aug;45(8):790-7. doi: 10.1111/vsu.12514. Epub 2016 Jul 11.

Peroperative Management and Outcome of Bilateral Adrenalectomy in 9 Dogs

Michelle L Oblak¹, Nicholas J Bacon², Jennifer L Covey³

Affiliations + expand
PMID: 27388811 DOI: 10.1111/vsu.12514

Abstract

Objective: To report peroperative care, postoperative management, and long-term outcomes in dogs undergoing bilateral adrenalectomy.

Study design: Retrospective case series.

Animals: Dogs undergoing bilateral adrenalectomy from 2008 to 2013 (n=9).

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Bilateral adrenalectomy (abstract)

Animals: Dogs undergoing bilateral adrenalectomy from 2008 to 2013 (n=9).

Methods: Data retrieved from the record, when available, included signalment, preoperative clinical signs, laboratory data, diagnostic imaging, blood pressure measurement, preoperative treatment for adrenal gland disease, intraoperative procedures, treatments and complications, postoperative treatment and diagnostics during hospitalization, diagnostics and management following discharge, histopathologic diagnosis, and survival.

Results: Seven dogs underwent concurrent bilateral adrenalectomy and 2 dogs had staged adrenalectomy. Surgery was uncomplicated in most cases. All dogs received IV dexamethasone SP intraoperatively. Eight dogs received intramuscular desoxycorticosterone pivalate intraoperatively. Histopathology revealed adrenocortical adenoma (7 dogs), adrenocortical carcinoma (4), pheochromocytoma (6), and adrenocortical atrophy (1). One dog died perioperatively and the remainder died due to unrelated causes. Postoperative management of hypoadrenocorticism included oral prednisone and intramuscular desoxycorticosterone pivalate (6 dogs), oral prednisone and fludrocortisone (1), and oral fludrocortisone alone (1). The median survival time in dogs surviving to hospital discharge was 525 days (range 67–966 days). No dogs developed metastatic disease or died due to signs of hypoadrenocorticism.

Conclusion: Based on the cases reported here, the perioperative mortality in dogs undergoing bilateral adrenalectomy may be lower than previously reported. Management of hypoadrenocorticism is both achievable and straightforward.

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Surgery for Cushing's disease



Harvey Cushing, 1932



Bjorn Meij, 2015



100
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Trans-sphenoidal hypophysectomy

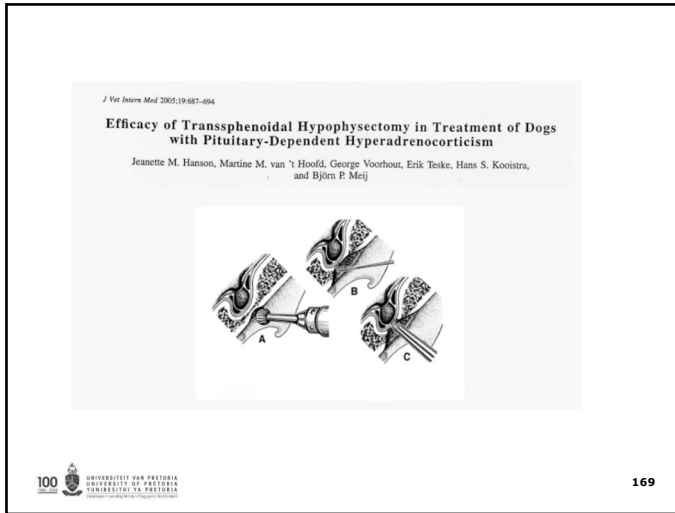


Photo: Björn Meij

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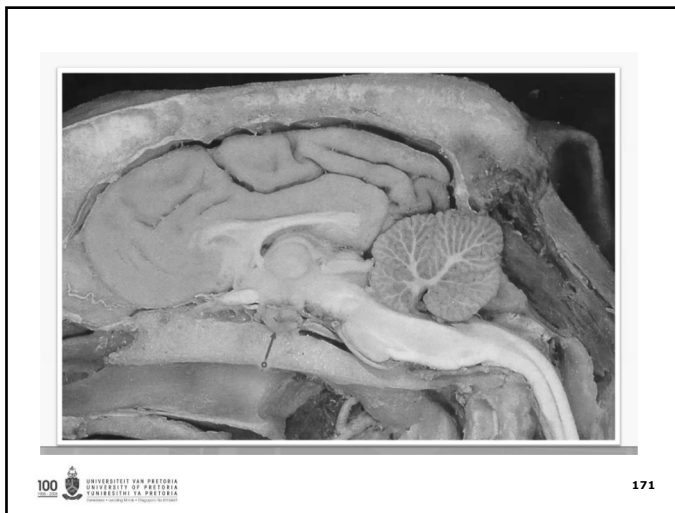
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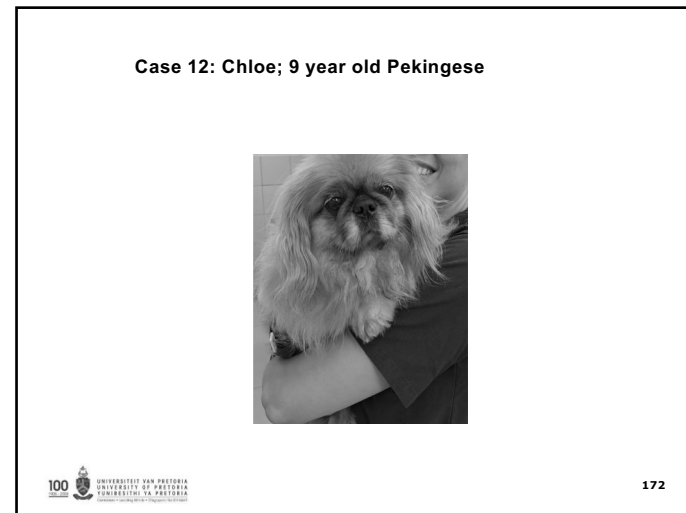
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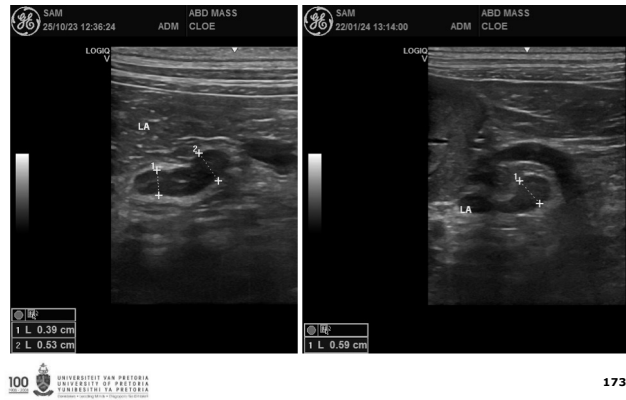


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Cloe; 9 year old Pekingese cross



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Chloe: 9yo Pekingese



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Any questions?

johanpschoeman@gmail.com



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