From the Skin to Within: Canine endocrine disease from the internist and dermatologist perspective

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CONFLICT OF INTEREST DISCLOSURE

Christina Gentry: I receive honoraria from IDEXX.

Patty Lathan: I receive honoraria from IDEXX, Dechra, and Boehringer Ingelheim. I consult for Boehringer Ingelheim and ScoutBio.

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Learning Objectives

- **Describe the clinical presentation and diagnostic approach** to hypercortisolism and hypothyroidism from both internal medicine and dermatology perspectives.
- **Identify and manage concurrent dermatologic conditions** such as cutaneous infections, calcinosis cutis, and demodicosis in patients with endocrine disease.
- **Recognize the impact of allergic disease** on the diagnosis and treatment of hypercortisolism and hypothyroidism.
- **Develop treatment plans** for cutaneous and systemic signs of endocrine disease

The Patient

Symmetrical alopecia of the trunk without erythema in a medium sized, middle age dog

The patient is not pruritic.

Differential diagnosis: hypothyroidism, hypercortisolism, sex hormone dermatosis, hair cycle arrest, follicular dysplasia, alopecia areata

Cutaneous clinical signs of canine hypothyroidism

Alopecia- Initially at wear and tear areas such as collar line, bridge of nose elbows, and lateral trunk

Skin may be scaly (seborrhea) and may be hyperpigmented

Hair coat dry, dull, and brittle, regrows slowly if at all post clipping

Dry and dull coat in a golden retriever with hypothyroidism

Canine Hypothyroidism

‘Wear and tear’ alopecia of the collar line and proximal dorsal thorax and lateral trunk with patchy regrowth

Cutaneous myxedema

Uncommon sign of canine hypothyroidism

Myxedema caused by increase in mucin (mostly hyaluronic acid) in the skin.

This appears as skin swelling and extra skin folds

Tragic expression of hypothyroidism with redundant skin

Canine Hypercortisolism

- Symmetric alopecia- generally truncal
- Thin skin (cutaneous atrophy) +/- fine to small adherent scale
- Bruising, delayed wound healing, visible dermal vasculature
- Comedones
- Calcinosis cutis
- ‘Pot belly’

Calcinosis cutis, visible vasculature, cutaneous atrophy, and alopecia secondary to topical steroid administration

Canine hypercortisolism

‘pot belly’, patchy alopecia, and dropped carpi

Close up image of the flank fold of the same patient showing cutaneous atrophy

Severe cutaneous atrophy

Alopecia, thin skin and visible cutaneous vessels

Cutaneous atrophy, bruising, and calcinosis cutis

Hypothyroidism vs Hypercortisolism: Systemic Signs

Age

- Hypercortisolism: Mean age 10+
- Hypothyroidism: Mean age <8 years old
  - 5 y if antibody positive (thyroglobulin)
  - Peaks at 5-8 years if antibody negative

Is the Dog PU/PD?

- Yes--> Look for Cushing's
- No--> Check a UA
  - Owners may not have noticed
  - If concentrated, less likely Cushing’s

- But…15% of dogs with Cushing’s aren’t…

Other Clinical Signs

- Cushing's
  - Obesity
  - Panting
  - Polyphagia
- Hypothyroidism
  - Obesity
  - Lethargy, decreased interaction
  - Neuro signs

Endocrine disease and pruritus(itch)

Patients that only have endocrine disease should be non-pruritic prior to the development of infections

Infections lead to variable pruritus

**Patients with concurrent unmanaged allergy may have pruritus prior to infections

Cutaneous diagnostics for suspected endocrine disease

- Skin and ear cytology- evaluate for yeast and bacterial overgrowth.
- Skin scraping or trichogram- evaluate for *Demodex* mite overgrowth
- Suspected that allergic inflammation and skin infection will decrease total T4 levels (euthyroid sick syndrome)
- Corticosteroid containing oral and topical medication can affect endocrine testing

Bacterial pyoderma and endocrine disease

Bacterial pyoderma is common in both hypothyroidism and hypercortisolism.

With hypercortisolism pustules can be larger than seen in allergic pyoderma due to immunocompromise

Bacterial Pyoderma Classification

Surface (hot spot)	• Moist erythematous skin without hair follicle involvement • Treat with topical antiseptic therapy for ~2 weeks
Superficial	Papules →Pustules → Annular Crusts → Epidermal collarettes → +/- Alopecia • Treat with topical antiseptic therapy+/- oral antibiotics (2-4 weeks)
Deep (furunculosis)	Papules, furuncles, nodules, draining tracts, ulceration, • Treat with topical antiseptic therapy + oral antibiotics (3-6 weeks)

Canine Demodicosis

Erythema alopecia and crusting on a middle-aged Shih Tzu

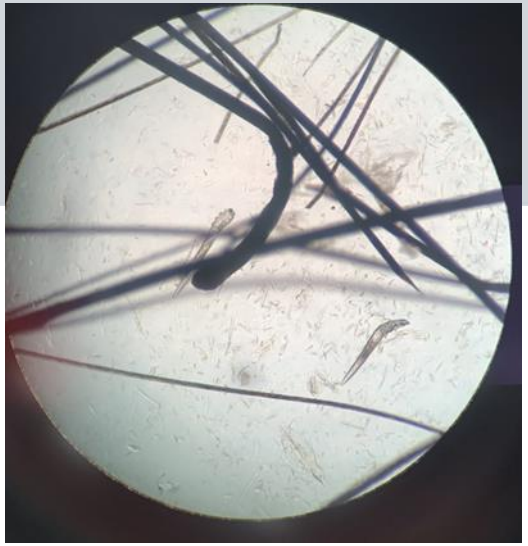
Furuncles(nodules caused by ruptured hair follicles and erythema in a dog on oclacitinib

Furuncles (nodules caused by ruptured hair follicles) in a dog with lymphoma

Treatment of canine Demodicosis

Recommended – Isoxazolines

- Off label use/on label dose and frequency



Alternative

- Oral daily ivermectin at 300-600 **ug**/kg -off label dose/frequency
- Advantage Multi ®(Imidacloprid/Moxidectin)- on label dose/ off label frequency- every 2 weeks

Calcinosis Cutis

Dorsal neck is most common initial lesion site. May progress the entire dorsum, lateral trunk, face and rarely the oral cavity. Chronic lesions may progress to osteoma cutis (lamellar bone deposition)

Dystrophic calcinosis cutis- Hypercortisolism

Reduce or eliminate exogenous topical or systemic corticosteroids

Break up calcium faster with DMSO or Sodium thiosulfate in Zinc Oxide

Close up view of calcinosis cutis lesion showing yellow to white granules in hard erythematous plaques

Itchy after beginning treatment: Cushing's and Self-medication

- Cortisol is anti-inflammatory
- Trilostane decreases cortisol
- Unmanaged allergies may get worse after trilostane
  - And calcinosis cutis
- And…
  - Brain tumors (get images from neuro!)
  - DJD
  - Other?

How does concurrent skin infection, skin inflammation, and potential concurrent allergy affect thyroid test results? Is there a ‘best testing panel’ when patients have other inflammatory disease? Should we treat infections and inflammation before thyroid testing?

Thyroid testing in the face of allergic inflammation and skin/ear infections

- Allergic inflammation +/- pyoderma, yeast dermatitis, and otitis anecdotally lowers total T4. Some patients will also have decreases in free T4.
  - Treat infections promptly
  - Improve allergic inflammation (ideally with non corticosteroid product)
  - If thyroid testing is needed NOW- consider panel that measures auto-antibodies
- Post pill T4 results can be lower when patients are experiencing a severe allergic flare.
  - Wait until after allergy flare is treated before post pill testing is performed

Thyroid testing

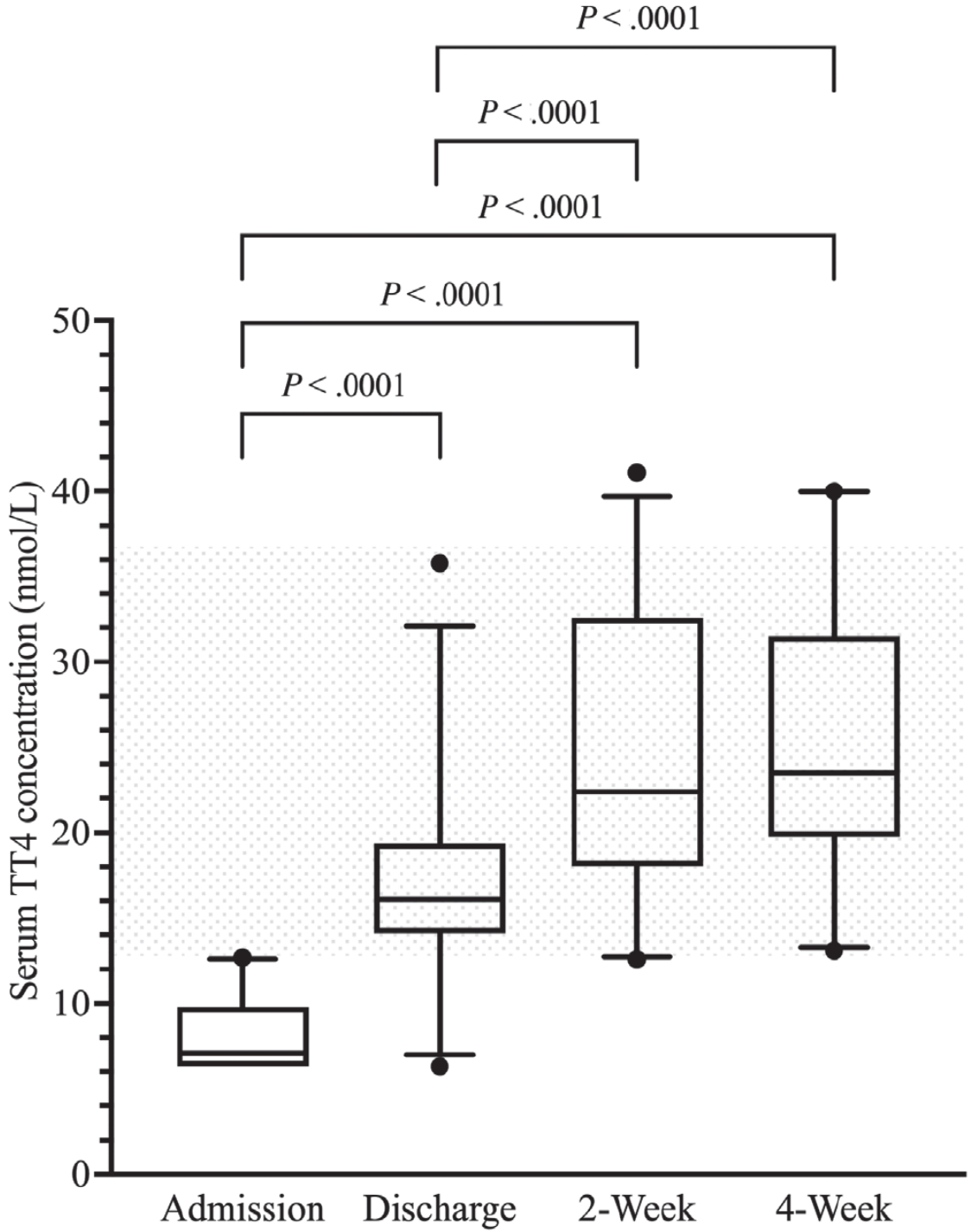
- Illness (including inflammatory disease) causes decreased TT4
- Low TT4 + high TSH → Hypothyroidism
  - Lack of high TSH in 30% of hypothyroid dogs
    - Low FT4 by equilibrium dialysis helps confirm
    - MUST USE equilibrium dialysis!
    - FT4 performed without equilibrium dialysis step is no more useful than TT4

STANDARD ARTICLE

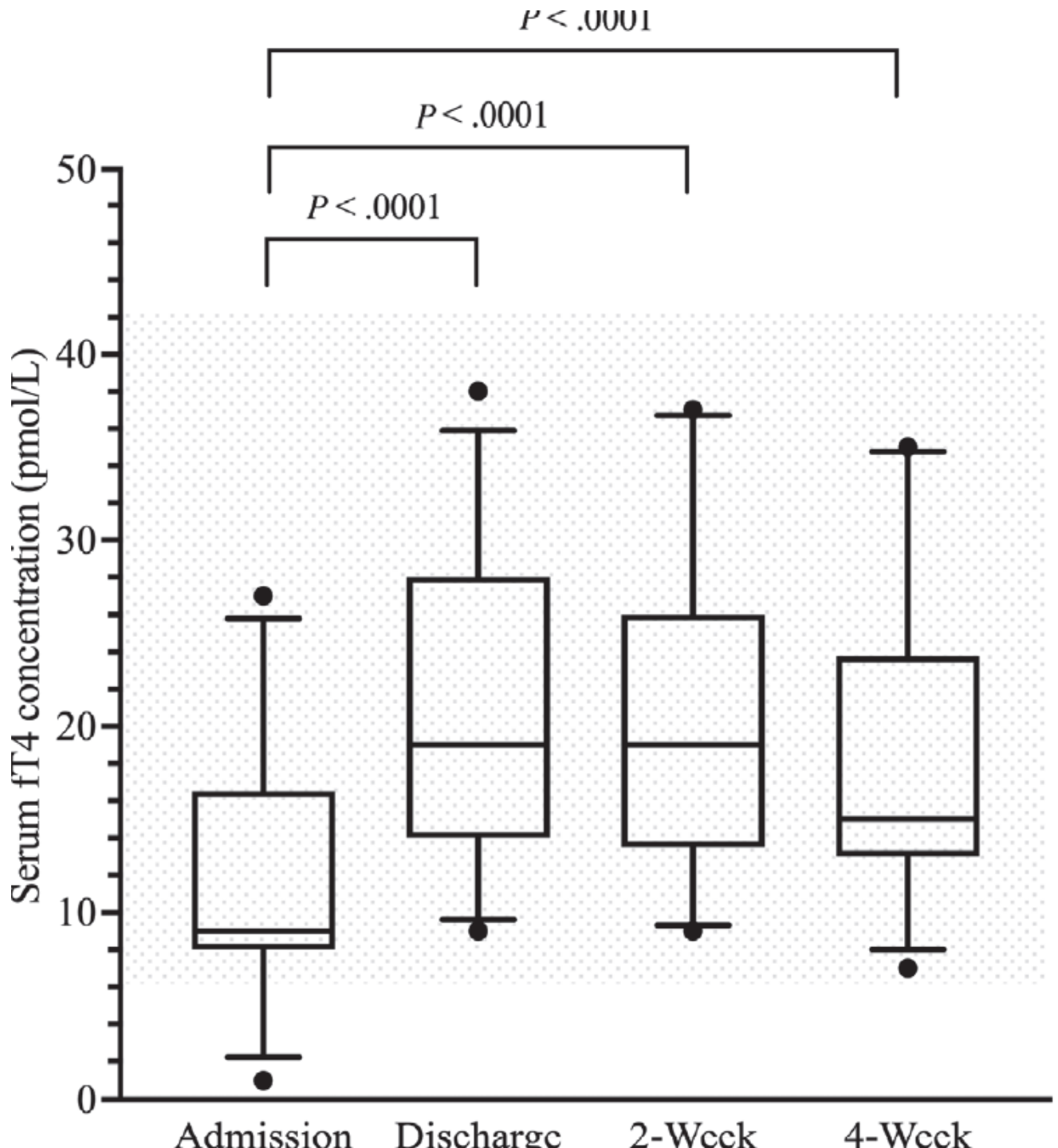
Journal of Veterinary Internal Medicine Open Access
ACVIM American College of Veterinary Internal Medicine

Thyroid function tests during nonthyroidal illness syndrome and recovery in acutely ill dogs

Timothy A. Bolton | David L. Panciera | Caylie D. Voudren | Matthew I. Crawford-Jennings



FT4 (ED)


P < .0001
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Serum fT4 concentration (pmol/L)
50
40
30
20
10
0
Admission
Discharge
2-Week
4-Week

Journal of Veterinary Internal Medicine
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J Vet Intern Med 2015;29:877–881

Free Thyroxine Concentrations by Equilibrium Dialysis and Chemiluminescent Immunoassays in 13 Hypothyroid Dogs Positive for Thyroglobulin Antibody

J.F. Randolph, S.V. Lamb, J.L. Cheraskin, B.J. Schanbacher, V.J. Salerno, K.M. Mack, J.M. Scarlett, and N.J. Place

- 13 dogs with hypothyroidism
  - Based on low FT4 by equilibrium dialysis (ED)
- WITH anti-thyroglobulin antibodies
- Measured TT4 and FT4 on Immulite (NOT ED)
  - Commonly used by state labs and Idexx when ED NOT chosen
- FT4 in or above rr in 2/8 dogs on Immulite

Montana

- 3 yo MN Great Pyrenees
- Decrease energy level, per owner
- Cholesterol increased

Specimen	Test Name	Result	Ref. Range- Result	Flag
Montana - Mammalia - Carnivora - Canidae - Dog (Domestic) - Great Pyrenees - Castrated - 3 Years				
Serum/Plasma - 1	PANEL: TT4, fT4 and TSH, (ChL) Screening			
	TT4 Screening (Immunoassay)	13.6 nmol/L	8.7 - 42.8 nmol/L	Suspect
	FT4 Screening (Immunoassay)	50.7 pmol/L	6.7 - 31.1 pmol/L	High
	TSH (Immunoassay)	5.77 ng/mL	0 - 0.5 ng/mL	High
	.			

Procedure		Ref Range	Units
Total Thyroxine (TT4) (CLIA)	8 L	[9-52]	nmol/L
Total Triiodothyronine (TT3) (RIA)	0.0 L	[0.8-2.1]	nmol/L
Free T4 by dialysis (RIA)	2 L	[6-42]	pmol/L
T4 Autoantibody (RIA)	63 H	[0-20]	%
T3 Autoantibody (RIA)	88 H	[0-10]	%
Thyroid Stimulating Hormone (CLIA)	5.19 H	[0.00-0.58]	ng/mL
Thyroglobulin Autoantibody (ELISA) *	221 H	[0-35]	%
Endocrinology Comment	See Below		

1/25/2024 12:20:00 PM Thyroglobulin Autoantibody (ELISA):

< 20% Negative

20 - 35 % Inconclusive

> 35% Positive

Steroids and Thyroid Function

- Humans
  - Steroids suppress the HPT axis
  - Inhibit conversion of T4 to T3
  - Decreased TT4, FT4, and TSH
- Dogs
  - Anti-inflammatory pred (1 mg/kg/d) x 3-5 weeks
    - May decrease TT4 (studies vary)
    - TSH unaffected
  - Immunosuppressive pred (2-4 mg/kg/d) x 3 weeks
    - Decreases TT4 and FT4; unchanged TSH
  - Topical dexamethasone decreases TT4
- Recommendation: Withdrawal of steroids for 2 weeks prior to testing

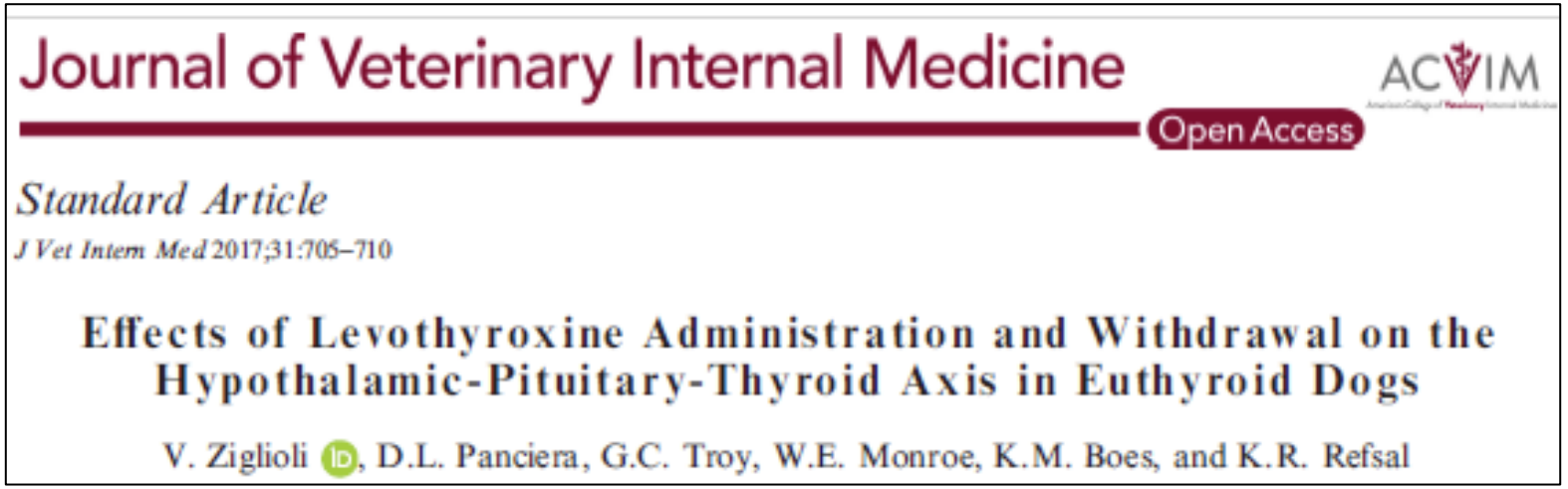
Effects of spontaneous hyperadrenocorticism on serum thyroid hormone concentrations in the dog

Mark E. Peterson, DVM; Duncan C. Ferguson, VMD, PhD; Peter P. Kintzer, BS; William D. Drucker, MD

The effect of trilostane treatment on circulating thyroid hormone concentrations in dogs with pituitary-dependent hyperadrenocorticism

- AJVR, 1984, Peterson
  - 57% of dogs with HC had low TT4
- JSAP, 2007, Kenefick and Neiger
  - 20% “ had low TT4 pre-tx, none post-tx
    - Increase in TT4 in 14/20 dogs with trilostane therapy
  - 10% had low FT4(ED) before tx; 5% post-tx
  - No dog with low TT4 or FT4(ED) had increased TSH

When a dermatologist is referred an allergic patient that was started on thyroid supplementation after low total 4 alone, how do we decide if that patient is truly hypothyroid?



Journal of Veterinary Internal Medicine
ACVIM
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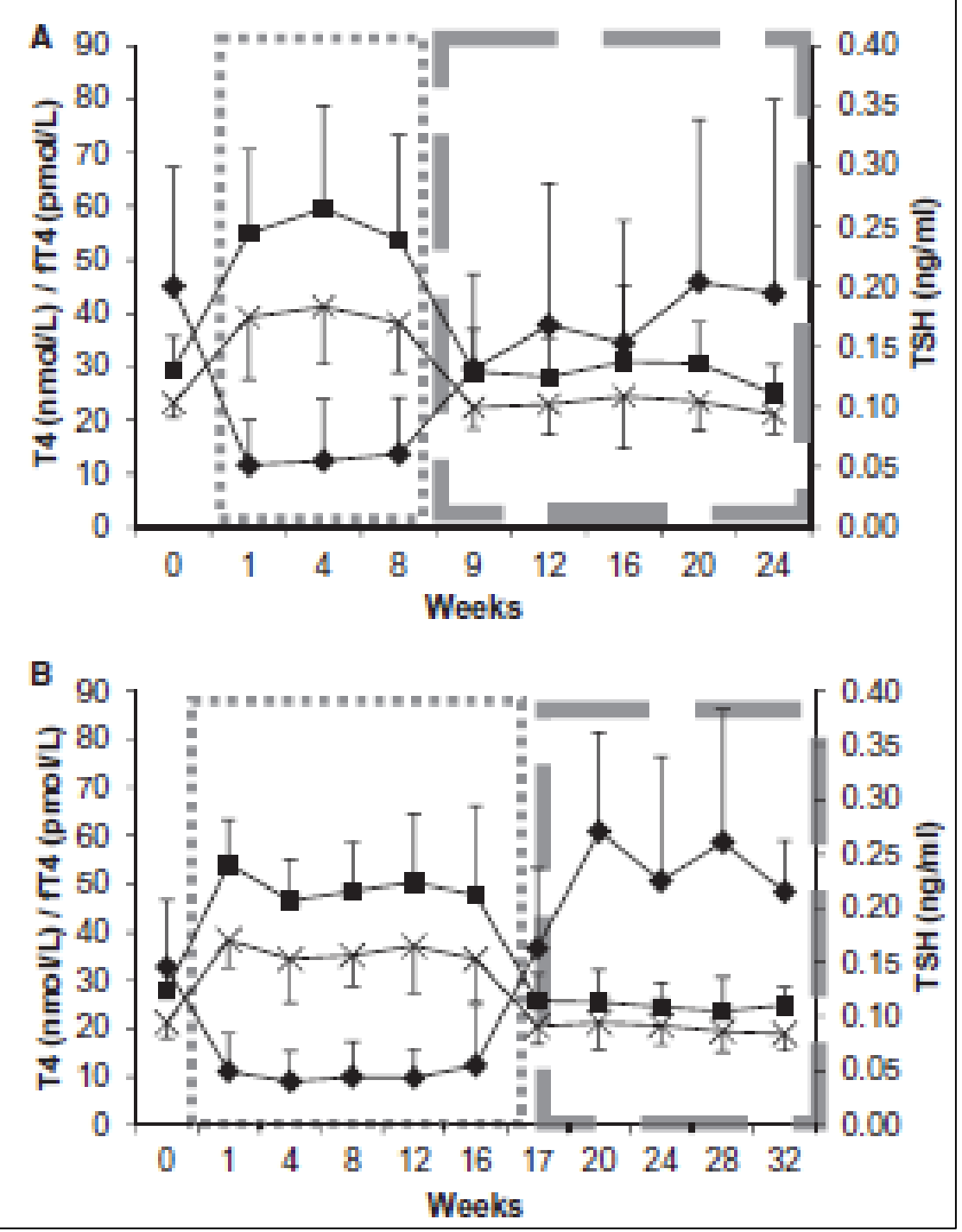
Standard Article
J Vet Intern Med 2017;31:705–710

Effects of Levothyroxine Administration and Withdrawal on the Hypothalamic-Pituitary-Thyroid Axis in Euthyroid Dogs

V. Ziglioli, D.L. Panciera, G.C. Troy, W.E. Monroe, K.M. Boes, and K.R. Refsal

- LT4 given to euthyroid dogs x 8 wks or 16 wks
- TT4, TT4(ED), TSH measured q weeks during and after tx (x 16 wks)
- STATISTICALLY “Recovered” 1 week following withdrawal
  - TSH was higher than baseline after the 1 week period
  - 1 dog had high TSH for 14 months (but normal TT4 and FT4)



Square = TT4
X = FT4 (ED)
Diamond = TSH

What diagnostic tests are recommended for diagnosis of endogenous hypercortisolism? What other lab work is recommended? What concurrent conditions are you expecting to find?

Minimum Data Base

- CBC
  - Stress leukogram, nRBCs(?!)
- Chemistry
  - ALP, cholesterol
- Urinalysis
- Urine culture…???

Clinical and microbiological characterization of subclinical bacteriuria and sporadic bacterial cystitis in dogs with spontaneous hypercortisolism

Letícia Machado [a], Milena Cleff de Oliveira [b], Cláudia Ruga Barbieri [b], Camila Impérico Riboldi [b], Vanessa Bielefeldt Leotti [c], Félix Hilário Díaz González [a,d], Stella de Faria Valle [a,d], Franciele Maboni Siqueira [a,d], Álan Gomes Pöppl [a,e,*]

- 2021, Comparative Immuno, Micro, and Infx Dz
- Most positive cultures were from subclinical bacteriuria patients
- Persistent infections only in SB dogs treated with abx, which became more resistant
- Do we culture if they’re not clinical???

Definitive Diagnosis

- LDDS
  - More sensitive
  - Able to help differentiate
  - More time consuming
  - Less specific
    - *Esp with concurrent disease
- ACTH stimulation test
  - Faster
  - Unable to differentiate
  - Less sensitive
  - More specific
    - Probably better with significant concurrent disease

What are the baseline skin diagnostics performed? What are you concerned about may happen to skin in future?

How does development of calcinosis cutis affect your treatment plan?

...

Trilostane treatment

- SID vs BID? TID?
- 2-3 mg/kg/d
- Monitoring
  - Clinical signs
    - BUT…what if they're derm???
  - ACTH stimulation test
  - Pre-pill cortisol
  - Other?

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