The diagnostic approach to thyroid disease

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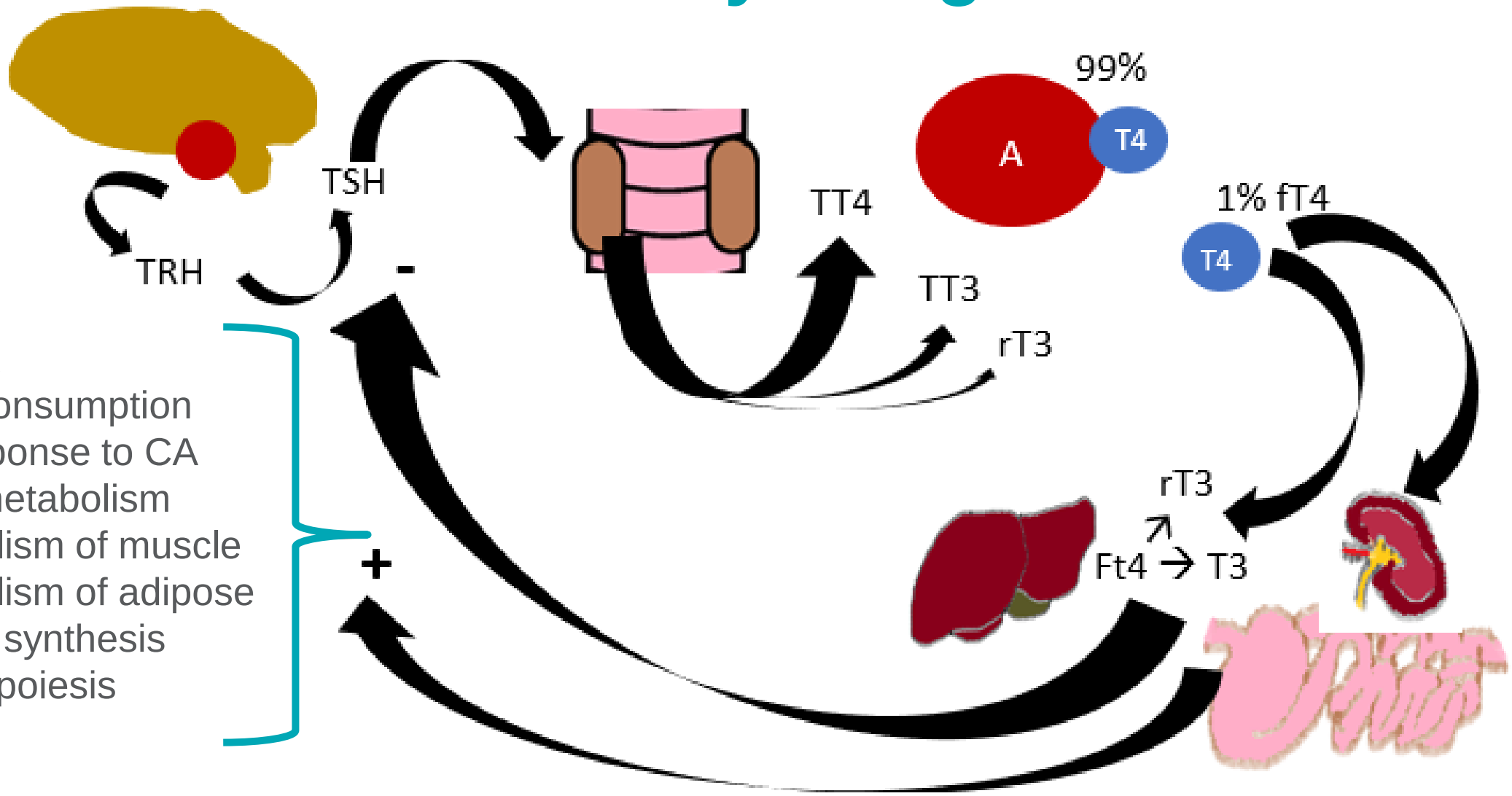
Overview

- Physiology of the thyroid gland
- Clinical features of hypothyroidism in dogs and hyperthyroidism in cats
- How to detect 'significant' results from a clinical and biochemical perspective
- A case-based approach to some common patterns of results

What does the thyroid gland do?

- ↑ BMR
- ↑ O_2 consumption
- ↑ Response to CA
- Bone metabolism
- Catabolism of muscle
- Catabolism of adipose
- Protein synthesis
- Erythropoiesis



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When things go wrong….

Primary acquired loss of thyroid tissue

Lymphocytic thyroiditis ➡ Idiopathic atrophy

Other aetiologies:

- Thyroid carcinoma
- Congenital
- Radiation therapy
- Central hypothyroidism

Rare

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When things go wrong….

Common clinical findings

- Lethargy
- Obesity
- Dermatopathy
  - Symmetrical alopecia
  - Myxoedema
  - Dull/dry coat
  - Poor regrowth
  - Hyperkeratosis, hyperpigmentation
  - Secondary pyodermas
  - Demodicosis
  - Seborrhoea
  - Ceruminous otitis

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When things go wrong….

Typical haematological and biochemical changes

- Hypertriglyceridemia (<90%)
- Hypercholesterolemia (75%)

} Severity is helpful!

- Normocytic normochromic anaemia (25-30%)
- Hyponatremia <30%

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When your patient reads the textbook…

Harvey, 8 yo MN cross breed

Clinical history:

- Lethargic
- Alopecic
- Recurrent demodex and sarcoptes

Bloods:

- Mild non-regenerative anaemia
- Hypercholesterolemia
- Hypertriglyceridemia

Endocrinology

TEST	RESULT	REFERENCE VALUE	
Total T4	4.9	13.0 - 51.0 nmol/L	L
cTSH	3.17	0.00 - 0.50 ng/mL	H

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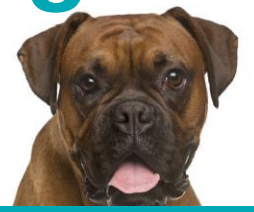
Bruce, 4yo ME Boxer: Lethargy, weight gain



- Dull dry hair coat
- Ceruminous otitis
- Urinalysis: USG 1.040, Otherwise unremarkable

Is Bruce hypothyroid?

What would be an approp

TEST	RESULT	REFERENCE VALUE	
Total T4	**7.8**	**13.0 - 51.0 nmol/L**	
cTSH	0.35	0.00 - 0.50 ng/mL	
Free T4	**<3.9**	**7.7 - 47.6 pmol/L**	L

~15-25% hypothyroid dogs have TSH within RI

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Fred, 4yo MN Westie, off colour

Mild anaemia and borderline low T4 in house

Haematology

TEST		RESULT	REFERENCE VALUE	
Reticulocytes	a	37.2	<= 110.0 K/µL	
Reticulocyte Haemoglobin		21.9	24.5 - 31.8 pg	L
WBC		8.5	4.9 - 17.6 x10^9/L	
Platelets		281	143 - 448 x10^9/L	
Blood Film Evaluation		Moderate anisocytosis. No increase in polychromasia. Moderate poikilocytosis with schistocytes and few keratocytes seen No abnormal white cells seen. Platelet clumps are seen. Platelet count should be considered the minimum value.		

Is Fred hypothyroid?

TEST	RESULT	REFERENCE VALUE	
Total T4	15.6	13.0 - 51.0 nmol/L	
cTSH	0.66	0.00 - 0.50 ng/mL	H

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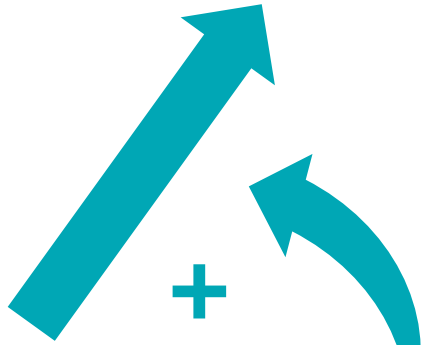
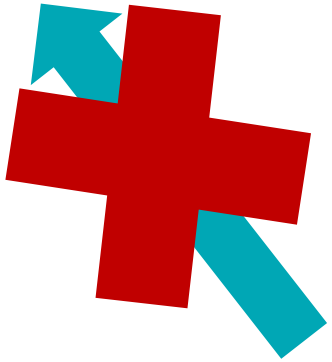
Reasons to measure Free T4/TSH



Clinical suspicion based on presenting signs

+

Suggestive haem or biochem changes



Low T4 on bloodwork

Needs to be backed up by the clinical picture

- Low Total T4, normal TSH
- Borderline T4/TSH results
- Concurrent disease
- Drug interferences (e.g. steroids, antiepileptics)

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Normal T4 with elevated TSH

Physiological

- Transient, unexplained
- Recovery from non-thyroidal illness
- Recovery from drug induced hypothyroidism (e.g. TMPS)

Pathological

- Early hypothyroidism (query associated clinical signs)

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Fred, 4yo MN Westie, off colour

Mild anaemia and low T4 in house

Haematology

TEST	RESULT	REFERENCE VALUE	
RBC	4.89	5.39 - 8.70 x10^12/L	L
Haematocrit	0.321	0.383 - 0.565 L/L	L
Haemoglobin	103	134 - 207 g/L	L
MCV	65.6	59.0 - 76.0 fL	
MCH	21.1	21.9 - 26.1 pg	L
MCHC	321	326 - 392 g/L	L
Reticulocytes [a]	37.2	<= 110.0 K/µL	
Reticulocyte Haemoglobin	21.9	24.5 - 31.8 pg	L
WBC	8.5	4.9 - 17.6 x10^9/L	
Platelets	281	143 - 448 x10^9/L	
Blood Film Evaluation	Moderate anisocytosis. No increase in polychromasia. Moderate poikilocytosis with schistocytes and few keratocytes seen No abnormal white cells seen. Platelet clumps are seen. Platelet count should be considered the minimum value.		

Endocrinology

12/11/2022 (Order Received)
12/11/2022 3:08 PM (Last Updated)

TEST	RESULT	REFERENCE VALUE	
Total T4	15.6	13.0 - 51.0 nmol/L	
cTSH	0.66	0.00 - 0.50 ng/mL	H

Monitor **IF** ongoing clinical suspicion

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Trick, 12 yo Bichon Frisé

- Long-term steroid therapy
- Recent bout of gastritis but otherwise clinically well

Is Trick hypothyroid?

Chemistry

ALT	145.5	19.8 - 124.0 U/L	H
Calcium	2.95	2.36 - 2.84 mmol/L	H
Sodium	152.5	135.0 - 155.0 mmol/L	
Potassium	4.57	3.60 - 5.60 mmol/L	
Na: K Ratio	33.37	28.80 - 40.00	
Chloride	110.5	100.0 - 116.0 mmol/L	
Total Protein	72.3	54.9 - 75.3 g/L	
Albumin	36.0	26.3 - 38.2 g/L	
Globulin	36.3	23.4 - 42.2 g/L	
Albumin: Globulin Ratio	0.99	0.70 - 1.40	
Lipase	105.2	<= 200.0 U/L	

Endocrinology

1/7/2022 (Order Received)
5/7/2022 12:53 PM (Last Updated)

TEST	RESULT	REFERENCE VALUE	
Total T4	12.8	13.0 - 51.0 nmol/L	L
cTSH	0.82	0.00 - 0.50 ng/mL	H
Thyroglobulin Autoantibody	NEGATIVE		

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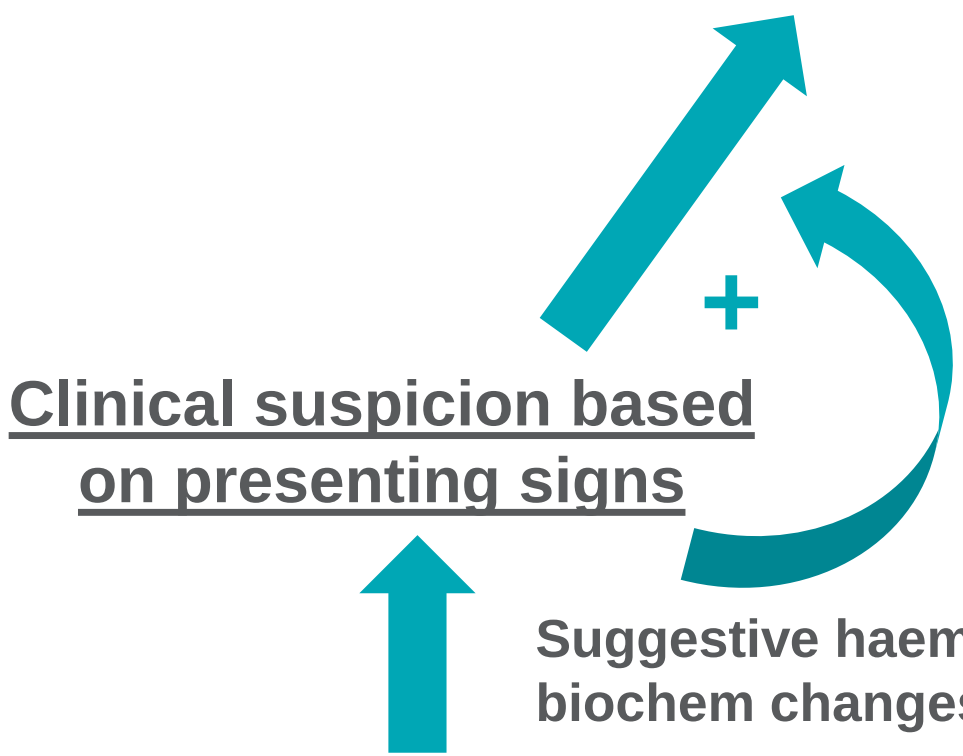
Reasons to measure Free T4/TSH



- Low Total T4, normal TSH
- Borderline T4/TSH results
- Concurrent disease
- Drug interferences (e.g. steroids, antiepileptics)

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Trick, 12 yo Bichon Frisé

- Long-term steroid therapy
- Recent bout of gastritis but otherwise clinically well

Endocrinology

1/7/2022 (Order Received)
5/7/2022 12:53 PM (Last Updated)

TEST		RESULT	REFERENCE VALUE	
Total T4		**12.8**	**13.0 - 51.0 nmol/L**	L
Free T4	a	13.5	7.7 - 47.6 pmol/L	
cTSH		**0.82**	**0.00 - 0.50 ng/mL**	H
Thyroglobulin Autoantibody		NEGATIVE		

Clinical Trial > Vet Dermatol. 2011 Apr;22(2):202-5. doi: 10.1111/j.1365-3164.2010.00932.x. Epub 2010 Nov 11.

Effect of an anti-inflammatory dose of prednisone on thyroid hormone monitoring in hypothyroid dogs

Sarah H O'Neill [1], Linda A Frank, Lisa M Reynolds

Affiliations + expand

PMID: 21070400 DOI: 10.1111/j.1365-3164.2010.00932.x

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Betty, 8yo FE Rottweiler, facial nerve paralysis

Chronically overweight

Chemistry

TEST	RESULT	REFERENCE VALUE	
Glucose	5.8	3.6 - 7.0 mmol/L	
IDEXX SDMA	11	1 - 14 µg/dL	
Creatinine	72.0	44.0 - 133.0 µmol/L	
Urea	5.3	3.1 - 10.1 mmol/L	
Phosphorus	**0.68**	**0.80 - 1.60 mmol/L**	L
Calcium	**2.26**	**2.36 - 2.84 mmol/L**	L
Sodium	148.3	135.0 - 155.0 mmol/L	
Potassium	4.83	3.60 - 5.60 mmol/L	
Na: K Ratio	30.70	28.80 - 40.00	
Chloride	**117.5**	**100.0 - 116.0 mmol/L**	H
Total Protein	59.1	54.9 - 75.3 g/L	
Albumin	**23.8**	**26.3 - 38.2 g/L**	L
Globulin	35.3	23.4 - 42.2 g/L	
Albumin: Globulin Ratio	**0.67**	**0.70 - 1.40**	L
ALT	**124.1**	**19.8 - 124.0 U/L**	H
ALP	120.0	<= 130.0 U/L	
GGT	**16.0**	**2.0 - 5.7 U/L**	H
Cholesterol	**> 18.00**	**3.20 - 6.20 mmol/L**	H

?

?

Endocrinology

TEST	RESULT	REFERENCE VALUE	
Total T4	**9.0**	**13.0 - 51.0 nmol/L**	L
Free T4	**< 3.9**	**7.7 - 47.6 pmol/L**	L
cTSH	**0.95**	**0.00 - 0.50 ng/mL**	H

Don’t forget hypothyroidism with unexplained neuropathy, myopathy, thromboembolic disease

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Sadie, 2 year old FE Labrador

- Lethargy, picky appetite, weight gain, recurrent pyoderma
- Mild anaemia, mild ↑ in ALT, ALP, hypercholesterolemia, hypertriglyceridemia

Endocrinology

14/02/22

TEST	RESULT	REFERENCE VALUE	
Total T4	**7.8**	**13.0 - 51.0 nmol/L**	L
cTSH	0.35	0.00 - 0.50 ng/mL	

Endocrinology

28/03/22

TEST	RESULT	REFERENCE VALUE
Total T4	14.5	13.0 - 51.0 nmol/L
Free T4	19.9	7.7 - 47.6 pmol/L
Thyroglobulin Autoantibody	POSITIVE	

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Sadie, 2 year old FE Labrador

- Persistent lethargy, picky appetite, weight gain, recurrent pyoderma
- High suspicion of hypothyroidism with questionable results
- Elevated TGAA to support thyroiditis

Endocrinology

28/03/22

TEST	RESULT	REFERENCE VALUE	
Total T4	14.5	13.0 - 51.0 nmol/L	
Free T4	19.9	7.7 - 47.6 pmol/L	
Thyroglobulin Autoantibody	POSITIVE		
Free T4 by ED	**5.3**	**6.0 - 40.0 pmol/L**	L

- Biological variation?
- Analytical variation?
- **Free T4 questionable**
- No issues with validity check?
- Interference?

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What does a positive Thyroglobulin autoantibody result mean?

Inflammation in the thyroid gland (thyroiditis)

<30% { May get Ig against thyroid protein (thyroglobulin)

<10% { If Ig is associated with a T3/T4 storage site – cross reactivity
T3/T4 autoantibodies (potential interference)

Positive Thyroglobulin autoantibody doesn't mean hypothyroidism!

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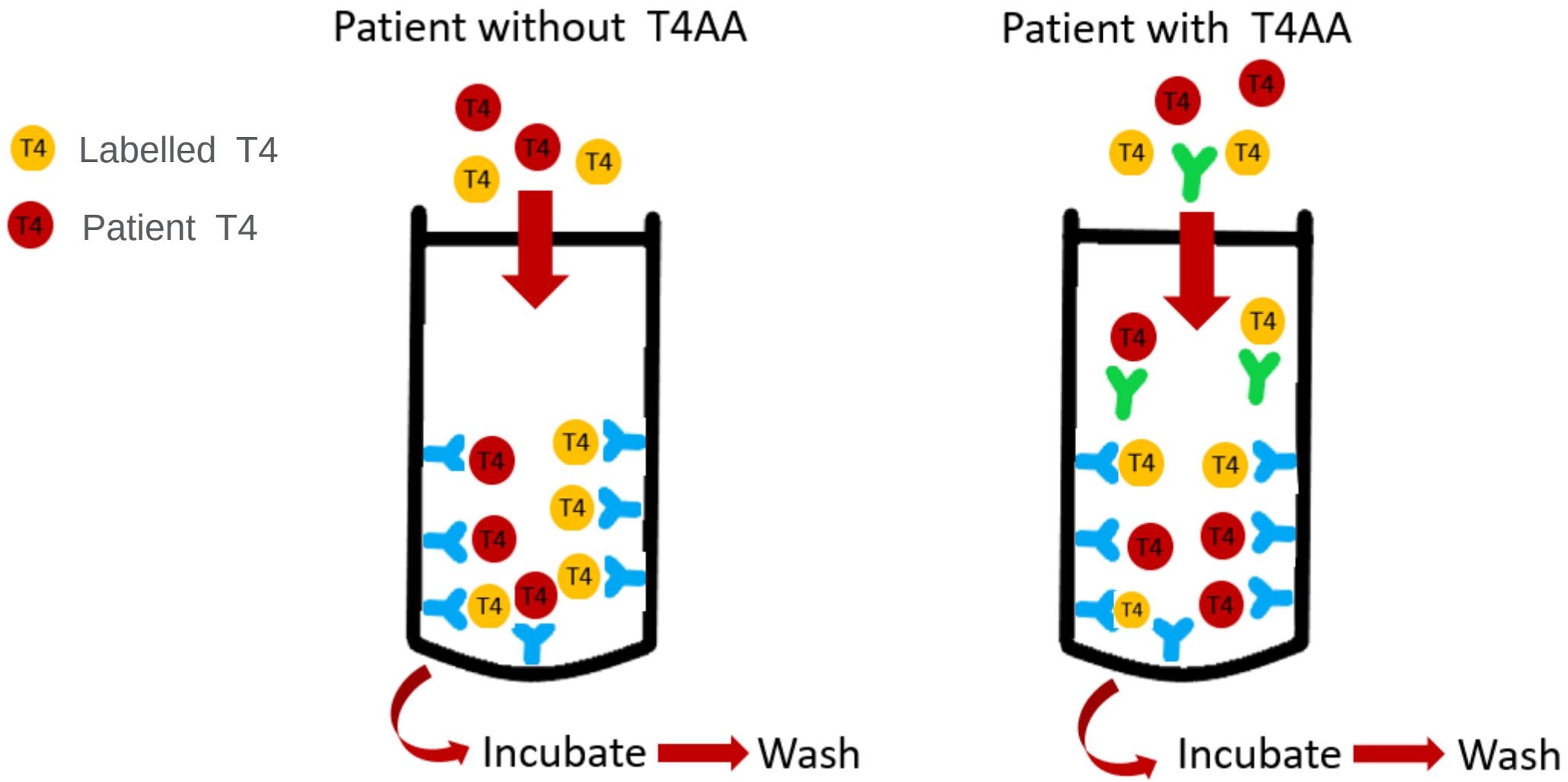
Effect of autoantibodies on measurement of T4



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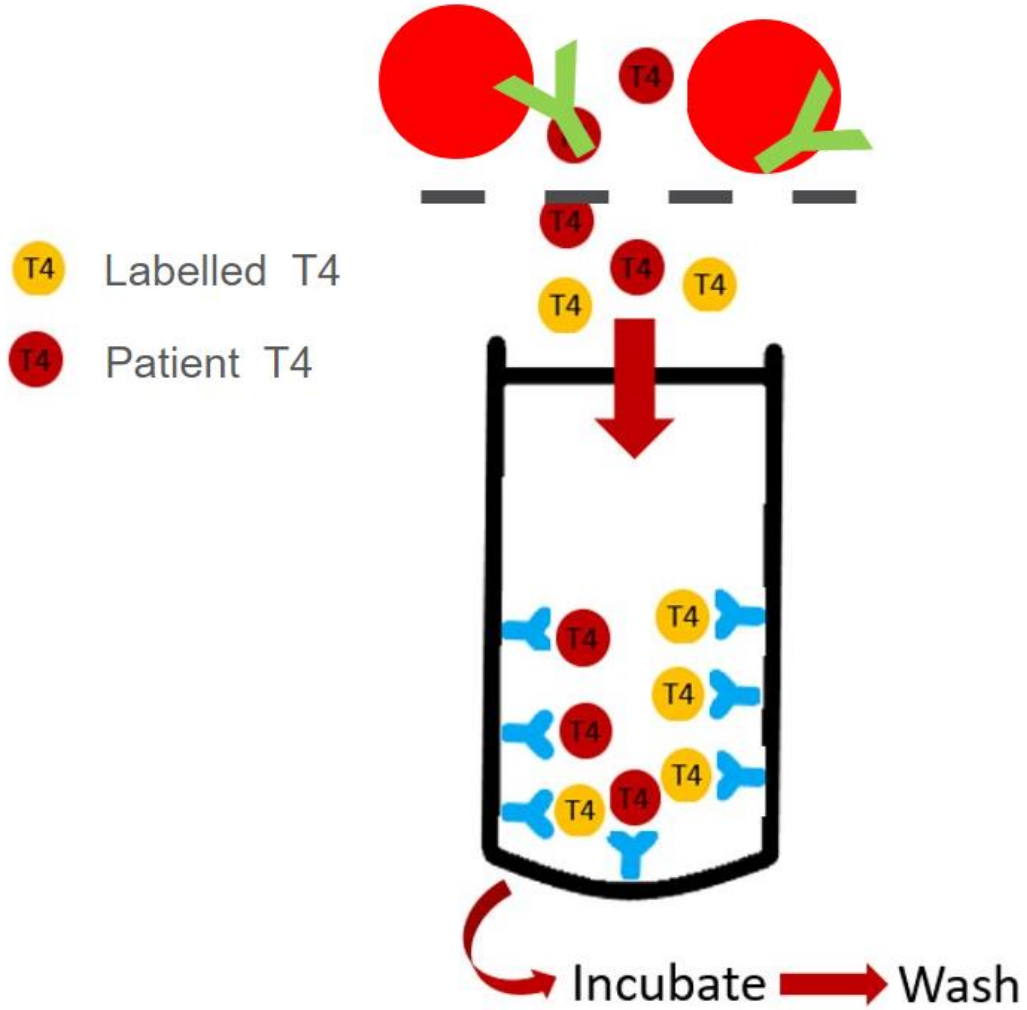
Concept of Free T4 by equilibrium dialysis



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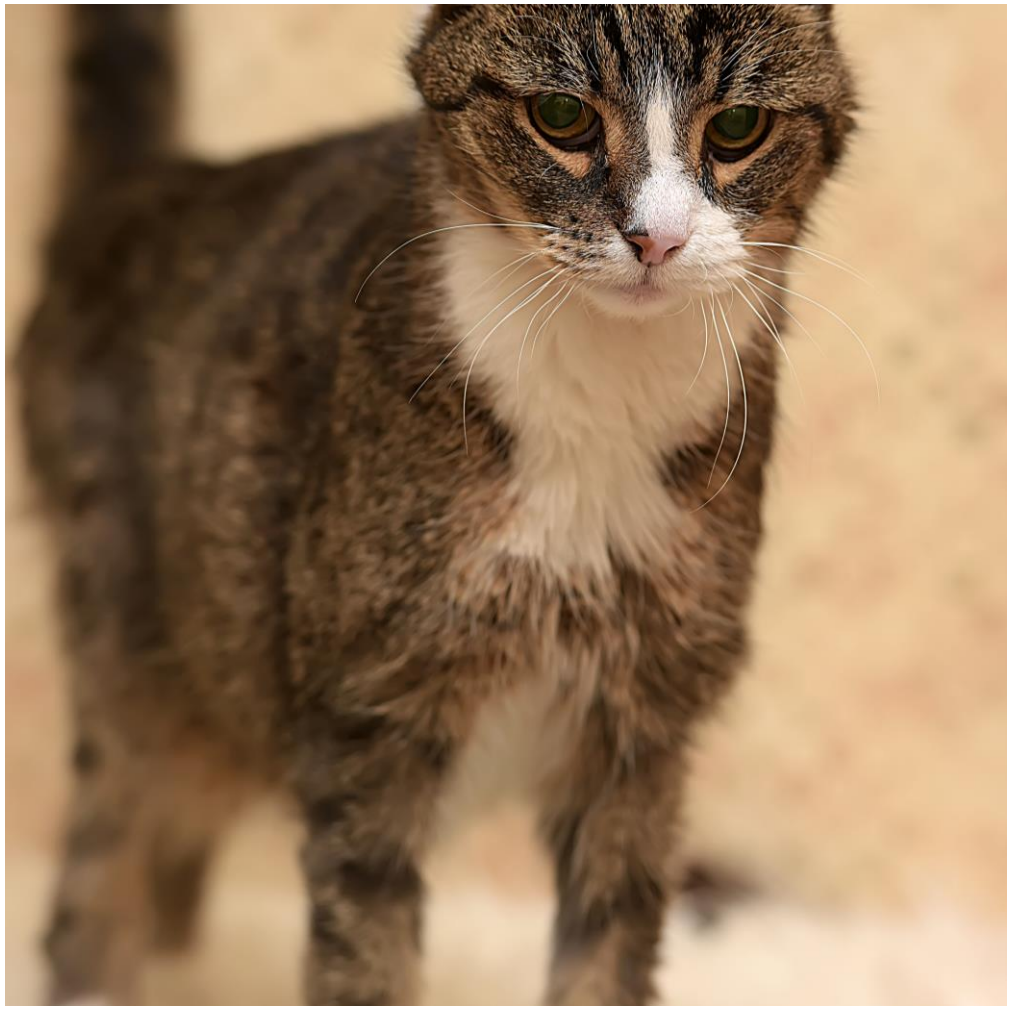
What about cats?....Hyperthyroidism



Clinical features

- Hyperactivity
- Polyphagia
- Weight loss
- Tachycardia
- PUPD
- Diarrhoea

Clinicopathological changes

- Erythrocytosis
- ↑ ALT +/ ↑ ALP (>90%)
- Hyperphosphatemia
- >90% have elevated TT4

- ↑ TT4 alone is enough to reach a diagnosis, in line with relevant symptoms

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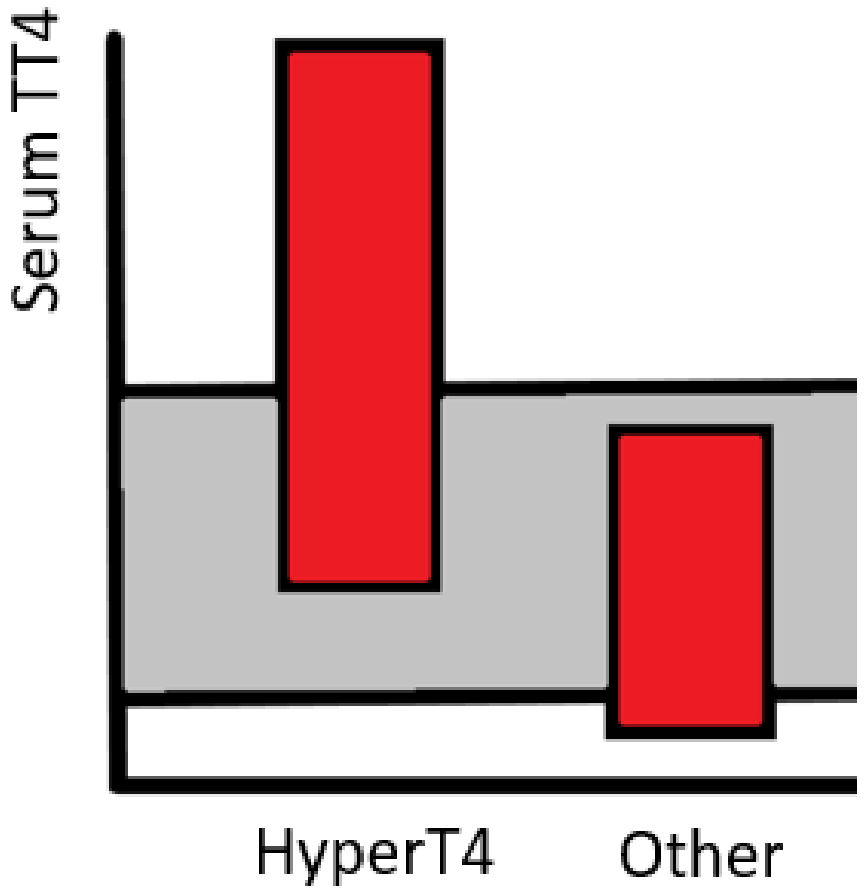
Why its not so simple



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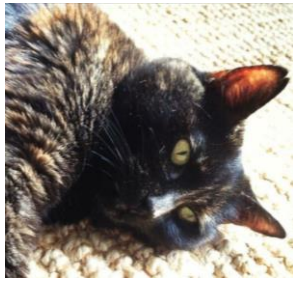
Lucy, 14yo FN DSH



- Weight loss
- Possible pupd
- BCS 3/9
- HR 240 with gallop rhythm

Chemistry

TEST	RESULT	REFERENCE VALUE	
Creatinine	200	71 - 212 µmol/L	
Urea	6.8	5.7 - 12.9 mmol/L	
BUN: Creatinine Ratio	19		
Phosphorus	1.38	1.00 - 2.42 mmol/L	
Calcium	2.51	1.95 - 2.83 mmol/L	
Sodium	**167**	**150 - 165 mmol/L**	H
Potassium	3.7	3.5 - 5.8 mmol/L	
Na: K Ratio	45		
Chloride	117	112 - 129 mmol/L	
Total Protein	73	57 - 89 g/L	
Albumin	34	23 - 39 g/L	
Globulin	39	28 - 51 g/L	
Albumin: Globulin Ratio	0.9		
ALT	**144**	**12 - 130 U/L**	H
ALP	60	14 - 111 U/L	
GGT	0	0 - 4 U/L	
Bilirubin - Total	2	0 - 15 µmol/L	
Cholesterol	**6.15**	**1.68 - 5.81 mmol/L**	H
Amylase	665	500 - 1,500 U/L	
Lipase	544	100 - 1,400 U/L	
Total T4	53	10 - 60 nmol/L	

What are the most clinically significant results here?

TEST	RESULT	REFERENCE VALUE	
Free T4	**44.1**	**9.0 - 33.5 pmol/L**	H
IDEXX SDMA [a]	**16**	0 - 14 µg/dL	H

Journal of Veterinary Internal Medicine Open Access

J Vet Intern Med. 2018 Jan-Feb; 32(1): 295–304. PMCID: PMC5787157
Published online 2018 Jan 28. doi: 10.1111/jvim.15036 PMID: 29377360

Evaluation of Serum Symmetric Dimethylarginine Concentration as a Marker for Masked Chronic Kidney Disease in Cats With Hyperthyroidism

M.E. Peterson,[1,2] F.V. Varela,[1] M. Rishniw,[2,3] and D.J. Polzin[4]

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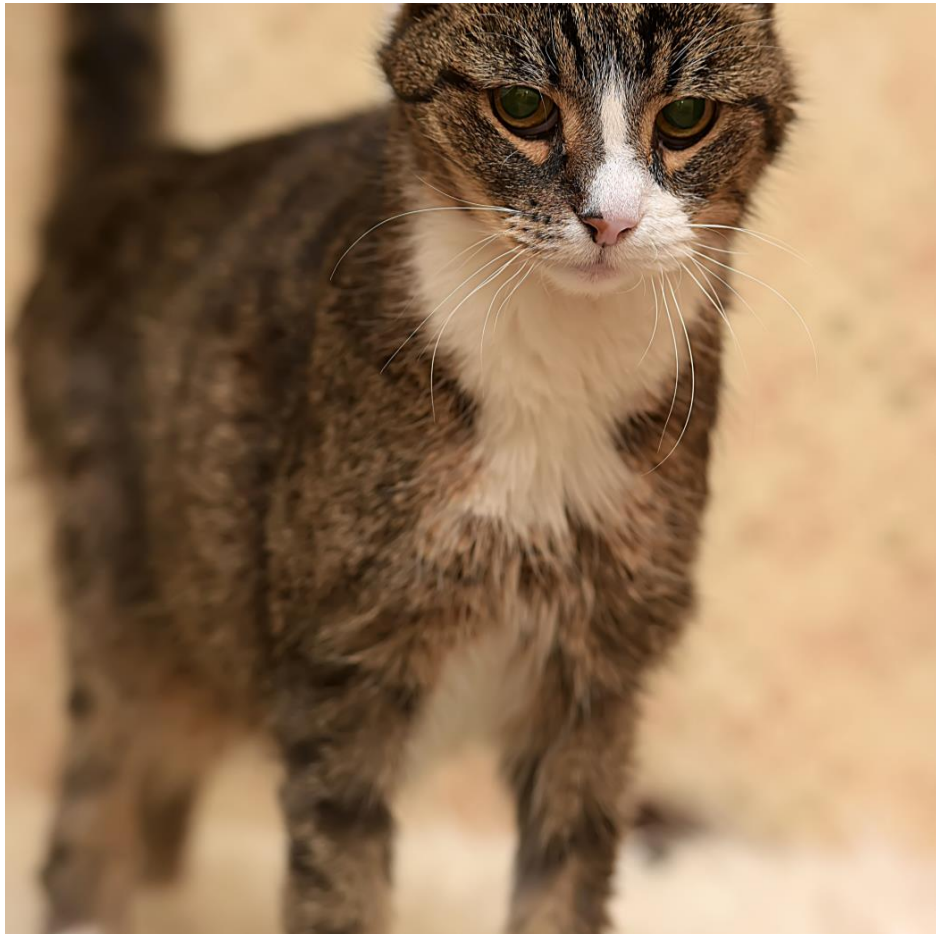
Interpreting Free T4 in cats



- Often helps reach a diagnosis with ‘grey zone’ total T4
- Mild elevations may be non-thyroidal illness
- ALWAYS correlate with Total T4 and Clinical signs (especially if 30-60pmol/L)
- Monitoring Total T4 may be appropriate alternative

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Investigating thyroid disease

To summarise

- Investigate based on the presence of clinical symptoms
- Haematological/biochemical changes may add weight to clinical suspicion
- Don’t use any single ‘test’ in isolation
- Understand the limit of one-off values and decision thresholds
- Remember potential interferences; drugs, concurrent disease
- Consider biological variation; age, breed etc.

Questions?

IDEXX is green

Please project (don’t print) this presentation.