14769

Sample Submission Form

Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
Davis, CA 95616
Tel: (530)7525058, Fax: (530)752-4698

http://www.vetmed.ucdavis.edu/vmb/labs/aal/index.cfm

UC CUSTOMERS ONLY:
Non-federal funds ID/Account Number to bill:_____

Vet/Tech Contac (b) (6)
Company Name:
Address:

Email: (b) (6)
Tel: **Fax:** (b) (6)

Billing Contact: (b) (6) **TAX ID:**
Email: (b) (6) **Tel:** (b) (6)

Patient Name: (b) (6)
Species: Feline
Owner's Name: (b) (6)

Sample Type: ☐ Plasma ☑ Whole Blood ☐ Urine ☐ Food ☐ Other:_____
Test Items: ☐ Taurine ☐ Complete Amino Acid ☐ Other:_____

Taurine Results (nmol/ml)

Plasma:_____ Whole Blood: 124 Urine:_____ Food:_____

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	>150

14771

Sample Submission Form

Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
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Tel: (530)752-5058, Fax: (530)752-4698

http://www.vetmed.ucdavis.edu/vmb/labs/aal/index.cfm

UC CUSTOMERS ONLY:
Non-federal funds ID/Account Number to bill:_____

Vet/Tech Contact:_____
Company Name:_____
Address:_____
(b) (6)

Email: (b) (6)
Tel:_____ Fax: (b) (6)

Billing Contact: (b) (6) TAX ID:
Email: (b) (6) Tel: (b) (6)

Patient Name: (b) (6)
Species: Feline
Owner's Name: (b) (6)

Sample Type: ☐ Plasma ☒ Whole Blood ☐ Urine ☐ Food ☐ Other:_____
Test Items: ☐ Taurine ☐ Complete Amino Acid ☐ Other:_____

Taurine Results (nmol/ml)

Plasma:_____ Whole Blood: 536 Urine:_____ Food:_____

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	>150

Congestive Heart Failure Due to Reversible Cardiomyopathy in Patients With Hyperthyroidism

GUILLERMO E. UMPIERREZ, MD,* SRIDEVI CHALLAPALLI, MD,*
CAM PATTERSON, MD†

ABSTRACT: The authors describe the clinical characteristics and response to therapy of seven patients with hyperthyroidism, dilated cardiomyopathy, and low-output cardiac failure. All patients (4 women and 3 men, age 47 ± 4 years, mean ± standard error of the mean) were admitted with the primary diagnosis of congestive heart failure. The cause of hyperthyroidism was Graves' disease in six patients, and toxic multinodular goiter in one. On admission, the mean serum T_4 was 21 ± 1 μg/dL and mean serum T_3: 411 ± 77 ng/mL, and serum thyroid-stimulating hormone was suppressed (<0.03 μU/mL) in all patients. Two-dimensional echocardiogram showed biventricular or four chamber dilatation and impaired left ventricular performance. Therapy of heart failure and hyperthyroidism resulted in rapid clinical improvement. During follow-up (5 months to 9 years), left ventricular ejection fraction improved from a mean of 28% to a mean ejection fraction of 55% ($P < 0.01$). Resolution of dilated cardiomyopathy with normalization of systolic function was achieved in five patients, and improvement from severe to mild left ventricular dysfunction was observed in two patients. We conclude that some patients with hyperthyroidism may have a reversible form of dilated cardiomyopathy and "low-output failure." Assessment of thyroid hormone status in patients with heart failure might permit the identification of patients with dilated cardiomyopathy and thyrotoxicosis who are likely to have reversible cardiac dysfunction. KEY INDEXING TERMS: Hyperthyroidism; Dilated cardiomyopathy; Heart failure. [Am J Med Sci 1995;310(3):99–102.]

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Submitted October 14, 1994; accepted April 3, 1995.

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The association of hyperthyroidism and cardiovascular dysfunction is well established.[1–4] Hyperthyroidism is one of the most common causes of sustained hyperkinetic circulatory disease.[5,6] This high-output state results from a direct effect of thyroid hormones that increase heart rate and cardiac contractility,[7,8] and from an indirect effect of thyroid hormones on the peripheral circulation that results in increased blood volume and peripheral vasodilatation.[8] This increase in cardiac work leads to cardiac hypertrophy and increased ejection fraction.[9–11] Paradoxically, in some patients with hyperthyroidism, high-output congestive heart failure develops despite increased cardiac performance.[1,6,7] Likoff and Levine,[3] in 1943, reported that among 409 cases of thyrotoxicosis, 21 patients had congestive heart failure in the absence of other forms of heart disease. Similarly, Sandler and Wilson[2] reported that 150 of 462 patients with thyrotoxicosis had evidence of cardiac dysfunction—auricular fibrillation, congestive heart failure, cardiomegaly, or all three. More recently, there have been several reports of a reversible cardiomyopathy in thyrotoxicosis, especially in children.[12,13]

For several years, we recognized that some patients with hyperthyroidism may have low-output heart failure. Although they often had moderate to severe symptoms of heart failure and echocardiographic documented dilated cardiomyopathy, they usually experience a rapid improvement with conventional treatment of heart failure and hyperthyroidism. In this article, we describe the clinical characteristics and initial echocardiographic findings at presentation, and the response to therapy of seven patients with hyperthyroidism who had low-output heart failure and bi-ventricular dilatation and hypokinesis.

Material and Methods

Seven patients, admitted with both hyperthyroidism and congestive heart failure due to dilated cardiomyopathy, served as the study population. All patients were seen by the endocrinology consult service at Grady Memorial Hospital between 1985 and 1994. The pri-

Table 1. Patient Characteristics and Admission Laboratory Values in Patients With Thyrotoxic Heart Failure

#	Age	Sex	T_4 μg/dL	T_3 ng/mL	T_3RU %	TSH uU/mL	Cause of Hyperthyroidism	Therapy of Hyperthyroidism
1	44	F	23	381	60	<0.03	Graves	RAI
2	82	F	20	196	48	<0.03	Toxic MNG	Surgery
3	28	F	26	800	69	<0.1	Graves	RAI
4	35	M	16	287	37	<0.1	Graves	RAI
5	65	F	21	434	68	0.1	Graves	RAI
6	29	M	19	271	36	<0.03	Graves	RAI
7	41	M	22	509	50	<0.01	Graves	RAI

T_4 = serum thyroxine, T_3 = triiodothyronine; TSH = thyrotropin (thyroid-stimulating hormone); MNG = multinodular goiter; RAI = radioactive iodine therapy.

mary diagnosis on admission was congestive heart failure. The diagnosis of heart failure was based on the Framingham criteria[14] and confirmed by the presence of cardiomegaly and evidence of pulmonary edema on chest x-ray. Patients were excluded from the study population if they had a history of valvular heart disease, angina pectoris, myocardial infarction, alcoholism, or longstanding systemic arterial hypertension. All patients on admission had a cardiac evaluation that included a 12-lead electrocardiogram and a two-dimensional (2-D) echocardiogram to determine left ventricular performance, cardiac chamber dimensions, and valvular integrity, and to exclude regional wall motion abnormalities. Left ventricular performance was assessed by the fractional shortening of the left ventricle. Fractional shortening (%) was calculated from the diastolic septal–posterolateral axes measured at the level of the chordae tendineae of the mitral valve[15] using the formula:

(left ventricular diastolic diameter

− left ventricular systolic diameter)/

(left ventricular diastolic diameter × 100).

Normal values of fractional shortening of the left ventricle in adults ranged from 27–37%. Determination of fractional shortening of the left ventricle allows rapid and noninvasive estimation of systolic ejective fraction (ejection fraction: % fractional shortening × 1.7).[16]

The diagnosis of hyperthyroidism was based on history and signs of hyperthyroidism, with laboratory data including elevated serum thyroxine (normal 5–12 μg/dL) and triiodothyronine (normal 70–190 ng/dL) concentrations and suppressed thyrotropin (thyroid-stimulating hormone, normal 0.4–3.5 μU/mL) levels. The response of left ventricular function to antithyroid therapy was assessed clinically and by repeat 2-D echocardiogram after thyroid function had returned to normal.

Congestive heart failure was treated with a combination of diuretics, digitalis, angiotensin-converting-enzyme inhibitors and oxygen therapy. Low dose propranolol (30–60 mg daily) was used in 4 patients. Patients were treated initially with propylthiouracil (450–800 mg daily) or methimazole (30–60 mg daily). Once clinical symptoms improved, euthyroidism was maintained for several months with lower doses of antithyroid drugs, followed by definitive therapy with radioactive iodine or surgery.

Results

The clinical characteristics and results of thyroid function tests on admission are shown in Table 1. Seven patients with hyperthyroidism—four women and three men—with a mean age of 47 ± 4 years (range 28–82 years) are reported. The primary diagnosis on admission in all patients was congestive heart failure. The diagnosis of hyperthyroidism was known before admission in two patients. In the other patients, the diagnosis was suspected on clinical grounds and confirmed by elevated thyroid hormones. Six patients had Graves' disease and one had toxic multinodular goiter. The duration of hyperthyroid symptoms was greater than 1 year in most patients (range 4 months to 6 years). On admission, the mean serum T_4 concentration was 21 ± 1 μg/dL, serum T_3 concentration: 411 ± 77 ng/dL, and T_3RU: 51 ± 5%, and serum thyroid-stimulating hormone was suppressed in all patients.

Therapy of heart failure and hyperthyroidism resulted in a rapid clinical improvement in all patients. Treatment of hyperthyroidism was started on admission in the two patients with known hyperthyroidism or as soon after the diagnosis was confirmed by laboratory studies. Symptoms of heart failure improved within 1–4 days of medical therapy, and hyperthyroidism was controlled within 2 months of antithyroid therapy. A maintenance regimen of antithyroidal medication was administered for 2–6 months and was followed by definitive therapy of hyperthyroidism with radioactive iodine or surgery. I^{131} was given to six patients, and one patient underwent surgery for coexistent toxic multinodular goiter and primary hyperparathyroidism.

Admission electrocardiograms revealed sinus tachycardia in 4 patients, atrial flutter with 2:1 block in two patients, and atrial fibrillation in one patient. Electro-

cardiographic abnormalities resolved in all patients after treatment of hyperthyroidism. Similarly, radiologic evidence of cardiomegaly and pulmonary congestion improved in most patients during follow-up.

In Table 2, the echocardiographic findings on admission and during follow-up are shown. 2-D echocardiograms performed soon after admission had either bi-ventricular or four chamber dilatation and impaired systolic function. The left atrium diameter was 45 ± 1 mm (mean ± standard error), the left ventricular diastolic diameter (LVDd) was 55 ± 1 mm, and the left ventricular systolic diameter (LVDs) was 46 ± 1 mm. The mean fractional shortening of the left ventricle (LVDd − LVDs/LVDd, percent) was 17 ± 1%, with a an estimated ejection fraction of 28 ± 2%. Therapy of heart failure and hyperthyroidism resulted in rapid clinical improvement, with resolution of signs and symptoms of heart failure in all patients. Repeat 2-D echocardiogram within 6–12 months of resolution of hyperthyroidism showed resolution of dilated cardiomyopathy with normalization of systolic function in five patients, and improvement from severe to mild ventricular dysfunction in the other two patients (Figure 1). The mean left ventricular ejection fraction improved from 28 ± 2% to 55 ± 5% after resolution of hyperthyroidism. Cardiovascular drugs were discontinued in the five patients with normal left ventricular ejection fraction, while the other two patients were continued on a low dose of angiotensin-converting-enzyme inhibitors.

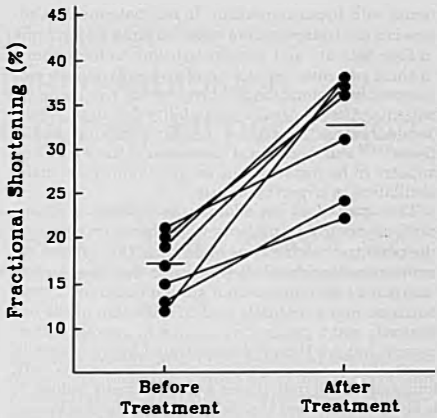

Figure 1. Left ventricular performance assessed by the fractional shortening of the left ventricle (%) in seven patients with dilated cardiomyopathy, congestive heart failure, and hyperthyroidism.

Discussion

The major importance of this study is the documentation of a reversible low-output heart failure due to dilated cardiomyopathy in hyperthyroidism. Admission 2-D echocardiogram showed biventricular or four chamber dilatation and markedly impaired systolic function in all patients. Complete echocardiographic resolution of dilated cardiomyopathy and normalization of left ventricular systolic function was achieved in 5 of 7 patients, and improvement from severe to mild cardiomyopathy was observed in 2 patients (Figure 1). The most important historical finding was the long duration of symptoms of untreated hyperthyroidism (4 months to 6 years). This is in agreement with previous reports.[2,3] Likoff and Levine[3] reported that the duration of thyrotoxicosis in patients with clinical evidence of severe heart failure was 55 months, with moderate heart failure duration was 12 months, and with no failure it was 8 months.

Table 2. Echocardiographic Measurements Before and After Treatment of Hyperthyroidism

	Before/After Treatment		
#	Left Atrial Size (mm)	Fractional Shortening (%)	Ejection Fraction (%)
1	45/34	12/40	20/68
2	46/35	21/31	36/53
3	39/26	19/38	32/65
4	45/35	15/22	25/38
5	44/33	17/37	29/62
6	42/35	13/24	22/40
7	46/32	20/36	34/61
M ± SE	45 ± 1/33 ± 1	17 ± 1/33 ± 3	28 ± 2/55 ± 5

The fractional shortening of the left ventricle was calculated by the formal (LVDd − LVDs/LVDd) × 100. Left Ventricular ejection fraction: % fractional shortening × 1.7.[16]

Left ventricular dilatation, congestive heart failure, and death have been reported in necropsy studies in humans with hyperthyroidism[17-18] and in spontaneously hyperthyroid animals,[19] in the absence of other forms of heart disease. Histologically, interstitial and perivascular fibrosis, myocardial hypertrophy, necrosis, and cell edema are reported. Ultrastructurally, increased number, size, and complexity of cardiac mitochondria have been described in animal models of hyperthyroidism.[20] In addition, based on recent evidence, excess thyroid hormone causes reversible replacement of the normal myosin isoenzyme concentrations.[21,22] Although abnormalities in myosin isotypes in myocardial tissues from patients with thyrotoxic cardiomyopathy have not been described, changes in myosin concentration with different contractile properties may prove to be important in the development of thyrotoxicosic heart disease.

Thyrotoxicosis has long been recognized as a major cause of tachyarrhythmias.[2,23] Atrial fibrillation is the most common arrhythmia, occurring in 7–21% of pa-

tients with hyperthyroidism. In our patients, the admission electrocardiogram revealed sinus tachycardia in four patients and supraventricular tachyrhythmia in three patients. Correction of hyperthyroidism was followed by restoration of normal sinus rhythm in all patients. Altered cardiac excitability due to increased beta-adrenergic receptor density in myocardial tissue[6,23,24] and mechanical distension of the left atrium appears to be important in the development of atrial fibrillation in hyperthyroidism.[25]

This study does not address the etiology of dilated cardiomyopathy in patients with thyrotoxicosis, and the potential mechanisms underlying this process remain to be elucidated. It is possible that long-lasting tachycardia and high-output state induced by thyroid hormone may eventually lead to dilatation of the left ventricle and a progressive decline in systolic performance. Indeed, Ikram[5] demonstrated improvement in contractile function after treatment in patients with longstanding thyrotoxicosis and overt heart failure. It is also plausible that thyroid hormone, which is known to translocate to the nucleus of cardiac cells in association with its receptor and to act as a trans-activating factor,[26,27] may alter the expression of certain cardiac proteins (myosin heavy chain, sarcoplasmic reticulum calcium-activated adenosine triphosphatase) in cardiomyocytes,[22,28] which may result in contractile dysfunction in patients with hyperthyroidism.

In summary, we suggest, with this report, that in addition to the "high-output congestive heart failure" commonly described in patients with hyperthyroidism, some patients may have a reversible form of dilated cardiomyopathy and "low-output congestive heart failure." Conventional treatment of hyperthyroidism usually results in rapid resolution of the clinical manifestations of heart failure, in partial or complete reversal of cardiomyopathy and in marked improvement of left ventricular systolic function. Assessment of thyroid hormone status in patients with dilated cardiomyopathy might permit the identification of patients who have thyrotoxicosis and are, therefore, likely to have reversible cardiac dysfunction.

Acknowledgment

The authors thank Lewis S. Blevins, MD, and Nelson B. Watts, MD, for critical review of the manuscript.

References

1. **Woeber KA.** Thyrotoxicosis and the heart. N Engl J Med. 1992;327:94–8.
2. **Sandler G, Wilson GM.** The nature and prognosis of heart disease in thyrotoxicosis: A review of 150 patients treated with ^{131}I. Q J Med. 1959;28:347–69.
3. **Likoff WB, Levine SA.** Thyrotoxicosis as the sole cause of heart failure. Am J Med. 1943;206:425–34.
4. **Forfar JC, Muir AL, Sawers SA, Toft AD.** Abnormal left ventricular function in hyperthyroidism: Evidence for a possible reversible cardiomyopathy. N Engl J Med. 1982;307:1165–70.
5. **Ikram H.** The nature and prognosis of thyrotoxic heart disease. Q J Med. 1985;54:19–28.
6. **DeGroot WJ, Leonard JJ.** Hyperthyroidism as a high cardiac output state. Am Heart J. 1970;79:265–75.
7. **Polikar R, Burger AG, Scherrer U, Nicod P.** The thyroid and the heart. Circulation. 1993;87:1435–41.
8. **Klein I.** Thyroid hormone and the cardiovascular system. Am J Med. 1990;88:631–7.
9. **Merillon JP, Passa PH, Chastre J, Wolf A, Gourgon R.** Left ventricular function and hyperthyroidism. Br Heart J. 1981;46:137–43.
10. **Grossman W, Robin NI, Johnson LW, Brooks HL, Selenkow HA, Dexter L.** The enhanced myocardial contractility of thyrotoxicosis: Role of beta adrenergic receptor. Ann Intern Med. 1971;74:869–74.
11. **Biondi B, Fazio S, Carella C, et al.** Control of adrenergic overactivity by *B*-blockade improves the quality of life in patients receiving long term suppressive therapy with levothyroxine. J Clin Endocrinol Metab. 1994;78:1028–33.
12. **Cavallo A, Casta A, Fawcett HD.** Is there is a thyrotoxic cardiomyopathy in children? J Pediatr. 1985;107:531–6.
13. **Shapiro S, Steier M, Dimich I.** Congestive heart failure in neonatal thyrotoxicosis. Clin Pediatr. 1975;14:1155–6.
14. **McKee PA, Castelli WP, McNamara PM, et al.** The natural history of congestive heart failure: The Framingham Study. N Engl J Med. 1971;285:1441–6.
15. **Folland ED, Parisi AF, Moynihan PF, et al.** Assessment of left ventricular ejection fraction and volumes by real-time, two-dimensional echocardiography. Circulation. 1979;60:760–6.
16. **Quinones MA, Pickering E, Alexander JA.** Percentage of shortening of the echocardiographic left ventricular dimension: Its use in determining ejection fraction and stroke volume. Chest. 1978;74:59–65.
17. **Shirani J, Barron MM, Pierre-Louis ML, Roberts WC.** Congestive heart failure, dilated cardiac ventricles, and sudden death in hyperthyroidism. Am J Cardiol. 1993;72:365–8.
18. **Saphir O.** Myocarditis: A general review, with an analysis of two hundred and forty cases. Arch Pathol. 1942;33:88–137.
19. **Liu S, Peterson ME, Fox PR.** Hypertrophic cardiomyopathy and hyperthyroidism in the cat. J Am Vet Med Assoc. 1984;185:52–7.
20. **Page E, McCallister LP.** Quantitative electron microscopic description of heart muscle cells-application to normal, hypertrophied and thyroxin-stimulated hearts. Am J Cardiol. 1973;31:172–81.
21. **Chizzonite RA, Everett AW, Prior G, Zak R.** Comparison of myosin heavy chains in atria and ventricles from hyperthyroid, hypothyroid, and euthyroid rabbits. J Biol Chem. 1984;259:15564–71.
22. **Rohrer DK, Hartong R, Dillmann WH.** Influence of thyroid hormone and retinoic acid on slow sarcoplasmic reticulum Ca^{++} ATPase and myosin heavy chain alpha gene expression in cardiac myocytes. J Biol Chem. 1991;266:8638–46.
23. **Olshansen KV, Bischoff S, Hahaly G, et al.** Cardiac arrhythmias and heart rate in hyperthyroidism. Am J Cardiol. 1989;63:930–3.
24. **Golf S, Lovstad R, Hansson V.** *B*-adrenoceptor density and relative number of *B*-adrenoceptor subtypes in biopsies from human right atrial, left ventricular, and right ventricular myocardium. Cardiovasc Res. 1985;19:636–41.
25. **Iwasaki T, Naka M, Hiramatsu K, et al.** Echocardiographic studies on the relationship between atrial fibrillation and atrial enlargement in patients with hyperthyroidism of Graves' disease. Cardiology. 1989;76:10–7.
26. **Izumo S, Nadal-Ginard B, Mahdavi V.** All members of the MHC gene family respond to thyroid hormone in a highly tissue-specific manner. Science. 1986;231:597–600.
27. **Izumo S, Lompre AM, Matsuoka R, et al.** Myosin heavy chain messenger RNA and protein isoform transitions during cardiac hypertrophy. Interaction between hemodynamic and thyroid hormone-induced signals. J Clin Invest. 1987;79:970–7.
28. **Klein I, Ojamaa K.** Cardiovascular manifestations of endocrine disease. J Clin Endocrinol Metab. 1992;75:339–42.

(b) (6)

(b) (6)

Client ID:	(b) (6)	Patient ID:	(b) (6)
Client Name:	(b) (6)	Name:	(b) (6)
Spouse/Other:	(b) (6)	Breed:	Retriever, Labrador Mix
Address:	(b) (6)	Sex:	Spayed Female
	(b) (6)	Color:	Brindle
Telephone:	(b) (6)	Age:	6 Yrs. 9 Mos.
		DOB:	(b) (6)

Referring Veterinarian:	(b) (6)	Dr. Jennifer Jones
Practice:	(b) (6)	FDA
Phone:	(b) (6)	
FAX:	(b) (6)	

Dear Dr. Jones,

Please find attached the normal results of the iron panel on (b) (6). Please let me know if you have any other recommendations in (b) (6)

I would love to discuss our findings on dilated cardiomyopathy and dietary relationships in our clinic over the past year. In particular, 75% of our DCM cases in 2017 for which we have adequate dietary histories were on grain free diets. We have started to do a survey of other cardiac patients during the same time period to see if we can get an idea of what percentage of our referral population were feeding these type of diets so we can see if this is truly significant. As we have been looking harder at these cases, we have found some other interesting things. For instance, two patients that were found to be taurine deficient were being fed Zignature diets. One was on the kangaroo variety and the other the pork variety. There continues to be a lot of discussion about diets and dilated cardiomyopathy on our list serve, but I can see it degenerating into I diagnosed DCM and the dog is on this diet so therefore this is a problem, which may or may not be true evidence to support a causative role of the diet.

I am not sure what information the FDA would want on all this at this point. We are certainly concerned that there may be a wider concern than simply the kangaroo and lentil diets that we first identified as a potential problem. Feel free to give me a call if you wish to discuss this further, or if you can suggest a direction for us to go with this inquiry. My clinic number is (b) (6) and I am in the clinics Monday through Thursday, or my cell phone is (b) (6).

Sincerely,

(b) (6)

		800.218-sub 1	800.218-sub 2	800.218-sub 6	
		Case Sample	Storebought	Case sample	Label
		California Naturals Kangaroo & Lentil	California Naturals Kangaroo & Lentil	California Naturals Kangaroo & Lentil	Product Nutrient Analysis (website label)
(b) (4)	Ca	1.30%	1%	0.93%	0.83%
	Mg	0.13%	0.14%	0.15%	0.17%
	P	0.74%	0.67%	0.68%	0.71%
	Fe	30 mg/kg	30 mg/kg	31 mg/kg	305 mg/kg
	Co	0.12 mg/kg	0.14 mg/kg	.14 mg/kg	n/a
	Cu	21 mg/kg	19 mg/kg	16 mg/kg	13.61 mg/kg
	Zn	240 mg/kg	280 mg/kg	200 mg/kg	193.37 mg/kg
	Se	0.7 mg/kg	0.65 mg/kg	.68 mg/kg	0.08 mg/kg
	Ca:P	1.76:1	1.49:1	1.37:1	
	Cu:Zn	0.09:1	0.07:1	0.08:1	
(b) (4)	Tau	~0.26%	1.06 mg/g = ~0.11%	1.22 mg/g = ~0.12%	
	Cystine	2.32 mg/g = ~0.23%	2.31 mg/g = ~0.23%	2.5 mg/g = ~0.25%	
	Met	5.78 mg/g = ~0.58%	5.53 mg/g = ~0.55%	7.78 mg/g = ~0.78%	0.61%
	Met-Cys	~0.81%	~0.78%	~1.03%	0.97%
MSU	Iodine	not tested	4.04 ug/g (ppm)	1.87 ug/g (ppm)	

AAFCO	
AAFCO-Adult Maint	Issues
0.5 to 2.5%	none
0.06%	none
0.4 to 1.6 %	none
40 mg/kg	below AAFCO & Label
25 mg/kg-chicks/rats/sheep max	unlikely
7.3 mg/kg	none
80 mg/kg	none
0.35 to 2 mg/kg	label should be higher to align w/ AAFCO maintenance claim
1:1 to 2:1	none
0.09:1-not AAFCO	none
0.1% in Cats	
n/a	
0.33%	none
0.65%	none
1 ppm (min) to 11 ppm (max)	none

http://www.californianaturalpet.com/products/1741

Report Details - EON-266814

ICSR:	1053335
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Both
Reporting Type:	Voluntary
Report Submission Date:	2016-06-06 11:15:17 EDT

Reported Problem:

Problem Description:	Presented 5/8/2016 for lethargy; on physical exam the patient was dyspneic and pleural effusion identified on cursory ultrasound and DV thoracic x-rays - given lasix and placed in oxygen. Transferred to cardiology service; evaluation including echocardiogram on 5/9/16 revealed dilated cardiomyopathy, moderate left atrial enlargement, pleural effusion and azotemia. Plasma taurine was submitted to University of Wisconsin. Lab results received 5/15/16 - plasma taurine 24nmol/ml (ref range 60-120, critical level <40). Recheck echocardiogram on 5/15/16 revealed same changes as prior and a thrombus in her left ventricle. Medications/supplements included taurine 250mg PO BID, Mirtazepine 15mg tablets (Give 1/4 tablet PO every 3d PRN), Furosemide 12.5 mg tablets (Give 1/4 tablet PO SID), Pimobendan 1.5mg tiny tabs (Give 1 tablet PO BID). Patient presented on (b)(6) for partial aortic thromboembolism and owner's elected euthanasia. Review of patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe feline dry for approximately 3 years. The 4 remaining cats were tested for taurine deficiency and 2/4 had whole blood levels indicating deficiency: 5/21/2016 - Whole Blood Taurine submitted at the University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results were received on 5/27/2016 (b)(6): 9yr male neutered domestic long hair: 196 nmol/ml (b)(6): 8y female spayed domestic short hair: 368 nmol/ml (b)(6): 9yr male neutered domestic long hair: 124 nmol/ml - (b)(6): 9yr male neutered domestic long hair: 536 nmol/ml
Date Problem Started:	05/08/2016
Concurrent Medical Problem:	No
Outcome to Date:	Died Euthanized
Date of Death:	(b)(6)

Product Information:

Product Name:	Merrick Purrfect Bistro Grain Free Real Chicken Recipe
Product Type:	Pet Food
Lot Number:	**Lot Number:** 16025 DL1 38310 14131 **Expiration Date:** 07/26/2017
UPC:	22808383 10
Package Type:	BAG
Package Size:	5.4 kilogram
Purchase Date:	05/01/2016
Number Purchased:	1
Possess Unopened Product:	No
Possess Opened Product:	Yes
Storage Conditions:	Stored in bag indoors
Product Use Information:	**Description:** Fed to cats in bowl **Last Exposure Date:** 05/08/2016 **Time Interval between Product Use and Adverse Event:** 3 Months **Product Use Stopped After the Onset of the** Yes

		Adverse Event:	
		Adverse Event Abate After Product Stop:	No
		Product Use Started Again:	No
		Perceived Relatedness to Adverse Event:	Definitely related
		Other Foods or Products Given to the Animal During This Time Period:	Yes
	Manufacturer/Distributor Information:	Name:	Merrick Pet Care, Inc
		Type(s):	Manufacturer
		Address:	P.O. Box 9800 Amarillo Texas 79105 United States
		Contact:	Phone: 18006647387 Web Address: www.merrickpetcare.com
		Possess One or More Labels from This Product:	Yes
	Purchase Location Information:	Name:	(b) (6)
		Address:	(b)(6) United States
Animal Information:	Name:		(b)(6)
	Type Of Species:		Cat
	Type Of Breed:		Mixed (Cat)
	Gender:		Female
	Reproductive Status:		Neutered
	Weight:		5.3 Kilogram
	Age:		12 Years
	Assessment of Prior Health:		Good
	Number of Animals Given the Product:		5
	Number of Animals Reacted:		3
	Owner Information:	Owner Information provided:	Yes
		Contact:	Name: (b)(6) Phone: (b)(6)
		Address:	(b)(6) United States
	Healthcare Professional	Practice Name:	(b) (6)

	Information:	Contact:	Name: (b)(6) Phone: (b)(6) Email: (b)(6)
		Address:	(b)(6) United States
Sender Information:	Name:	(b)(6)	
	Address:	(b)(6) United States	
	Contact:	Phone: (b)(6) Email: (b)(6)	
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
	Reported to Other Parties:	Manufacturer	
Additional Documents:			

Report Details - EON-266821

ICSR:	1053339
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2016-06-06 11:44:41 EDT

Reported Problem:

Problem Description:	Another household cat diagnosed with dilated cardiomyopathy and taurine deficiency - separate report filed (FDA ICSR ID 1053335). Euthanized or (b)(6) due to aortic thromboembolism. Review of the patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe Feline dry for approximately 3 years. Remaining 4 cats in household tested for taurine deficiency - whole blood samples submitted to University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results received on 5/27/16 - (b)(6) 196nmol/ml - started on taurine supplementation 250mg PO BID for 2-3 weeks. Diet was changed at the time of other cat's diagnosis (5/15/15). Patient also diagnosed with hyperthyroidism on same day as blood submitted for taurine testing - history of weight loss. An echo was not performed on this patient therefore it is unknown if he had evidence of DCM.
Date Problem Started:	05/27/2016
Concurrent Medical Problem:	No
Outcome to Date:	Not Applicable

Product Information:

Product Name:	Merrick Purrfect Bistro Grain Free Real Chicken Recipe	
Product Type:	Pet Food	
Lot Number:	**Lot Number:**	16025 DL1e38310d4131
	Expiration Date:	07/26/2017
UPC:	2280838310	
Package Type:	BAG	
Package Size:	5.4 kilogram	
Number Purchased:	1	
Possess Opened Product:	Yes	
Storage Conditions:	stored in bag indoors	
Product Use Information:	**Description:**	fed to cats in bowl
	Last Exposure Date:	05/15/2016
	Product Use Stopped After the Onset of the Adverse Event:	Yes
	Perceived Relatedness to Adverse Event:	Definitely related
	Other Foods or Products Given to the Animal During This Time Period:	No
Manufacturer/Distributor Information:	**Name:**	Merrick Pet Care, Inc
	Type(s):	Manufacturer
	Address:	P.O. Box 9800 Amarillo Texas 79105 United States

	Contact:	Phone:	18006647387
		Web Address:	www.merrickpetcare.com
	Possess One or More Labels from This Product:	Yes	
	Purchase Location Information:	Name:	(b) (6)
		Address:	(b)(6) United States
Animal Information:	Name:	(b)(6)	
	Type Of Species:	Cat	
	Type Of Breed:	Mixed (Cat)	
	Gender:	Male	
	Reproductive Status:	Neutered	
	Weight:	4.4 Kilogram	
	Age:	9 Years	
	Assessment of Prior Health:	Fair	
	Number of Animals Given the Product:	5	
	Number of Animals Reacted:	3	
	Owner Information:	Owner Information provided:	Yes
		Contact:	Name: (b)(6)
			Phone: (b)(6)
		Address:	(b)(6) United States
	Healthcare Professional Information:	Practice Name:	(b)(6)
		Contact:	Name: (b)(6)
			Phone: (b)(6)
			Email: (b)(6)
		Address:	(b)(6) United States
Sender Information:	Name:	(b)(6)	
	Address:	(b)(6) United States	
	Contact:	Phone:	(b)(6)
		Email:	(b) (6)
	Permission To Contact Sender:	Yes	

	Preferred Method Of Contact:	Email
	Reported to Other Parties:	Manufacturer
Additional Documents:		

Report Details - EON-266827

ICSR:	1053345
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Both
Reporting Type:	Voluntary
Report Submission Date:	2016-06-06 12:11:20 EDT

Reported Problem:

Problem Description:	Another household cat diagnosed with dilated cardiomyopathy and taurine deficiency - separate report filed (FDA ICSR ID 1053335). Euthanized on (b)(6) due to aortic thromboembolism. Review of the patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe Feline dry for approximately 3 years. Remaining 4 cats in household tested for taurine deficiency - whole blood samples submitted to University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results received on 5/27/16 - (b)(6) 124nmol/ml - started on taurine supplementation 250mg PO BID for 2-3 weeks. Diet was changed at the time of other cat's diagnosis (5/15/15). An echo was not performed on this patient therefore it is unknown if he had evidence of DCM.
Date Problem Started:	05/27/2016
Concurrent Medical Problem:	Yes
Pre Existing Conditions:	patient is obese
Outcome to Date:	Not Applicable

Product Information:

Product Name:	Merrick Purrfect Bistro Grain Free Real Chicken Recipe
Product Type:	Pet Food
Lot Number:	**Lot Number:** 16025 DL1e38310e14131
	Expiration Date: 07/26/2017
UPC:	2280838310
Package Type:	BAG
Package Size:	5.4 kilogram
Purchase Date:	05/01/2016
Number Purchased:	1
Possess Unopened Product:	No
Possess Opened Product:	Yes
Storage Conditions:	stored in bag indoors

Product Use Information:

Description:	fed to cats in bowl
Last Exposure Date:	05/15/2016
Product Use Stopped After the Onset of the Adverse Event:	Yes
Perceived Relatedness to Adverse Event:	Definitely related
Other Foods or Products Given to the Animal During This Time Period:	No

Manufacturer/Distributor Information:

Name:	Merrick Pet Care, Inc
Type(s):	Manufacturer
Address:	P.O. Box 9800 Amarillo

			Texas 79105 United States
		Contact:	Phone: 18006647387
			Web Address: www.merrickpetcare.com
		Possess One or More Labels from This Product:	Yes
	Purchase Location Information:	Name:	(b) (6)
		Address:	(b)(6) United States
Animal Information:	Name:	(b) (6)	
	Type Of Species:	Cat	
	Type Of Breed:	Mixed (Cat)	
	Gender:	Male	
	Reproductive Status:	Neutered	
	Weight:	9.5 Kilogram	
	Age:	9 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	5	
	Number of Animals Reacted:	3	
	Owner Information:	Owner Information provided:	Yes
		Contact:	Name: (b)(6)
			Phone: (b) (6)
		Address:	(b)(6) United States
	Healthcare Professional Information:	Practice Name:	(b)(6)
		Contact:	Name: (b)(6)
			Phone: (b)(6)
			Email: (b)(6)
		Address:	(b)(6) United States
Sender Information:	Name:	(b)(6)	
	Address:	(b)(6) United States	
	Contact:	Phone:	(b)(6)

	Email:	(b) (6)
	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
Additional Documents:		

Follow-up Case Information Uniform Data Entry Form
Vet-LIRN

Date (mm/dd/yy): Jun 9, 2016

EON/CC Number: 266,814

PATIENT INFORMATION

Pet Name: (b) (6)

○ Dog ◉ Cat

Breed: DSH

Age in years (if < 6 months, put 0.5): 12

Gender:

○ M ○ MN ○ F ◉ FS

This form serves as a Uniform Data Entry Form to capture additional case specific information not clear from the Consumer Complaint or Medical Records in a standardized manner. Because each follow-up interview made with owners features questions tailored specifically to the case, each box of information contained in this Uniform Data Entry Form may not be completed.

HISTORY-Additional Comments from Owner

Owner's Description of What Happened: lethargic, difficulty moving, not herself

Any Health Problems Prior to the Event (e.g. allergies, surgeries): (b) (6): none; none in the past; all house cats

Sensitive GI tract (e.g. stomach upset when switching foods, eats a lot of grass) ☐ Yes

Changes to the pet's diet prior to illness ☐ Yes

Date Diet Change:

CLINICAL INFORMATION--Additional Comments from Owner on What Happened

Appetite ☐ Increased ☐ Decreased

Vomiting ☐ Yes

Diarrhea ☐ Yes

Duration of Diarrhea (days):

Blood in Feces ☐ Fresh,Red ☐ Coffee Ground ☐ Black,Tarry

Water Consumption ☐ Increased ☐ Decreased

Urination ☐ Increased ☐ Decreased

Lethargy ☐ Yes

Other:

MEDICATIONS-Taken Prior to the Event and Mentioned by Owner

List medications mentioned by owner (e.g. NSAIDs, steroids, heartworm/flea prevention, antibiotics, etc.)

List probiotics, vitamins, or supplements mentioned by owner:

Continued otherside

Follow-up Case Information Uniform Data Entry Form
Vet-LIRN

EON/CC Number: 266,814

Owner: (b) (6)

Pet's Name: (b) (6)

DIET-Any other foods the owner mentions were given to the animal during this period. (check all that apply)

☒ Commercial Dry — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

List Product Label Name: Merrick Grain Free Bistro Chicken-started in January of 2014, print out of all pet food purchases thru Jan 2014 –> on the Chicken pretty much the entire time; owner has a listing of all purchases from pet

☐ Commercial Wet-Canned — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

List Product Label Name: Fancy Feast Wet food given to (b) (6) to stimulate her appetite after her illness onset, but she only licked the gravy. So for ~1 week before the other 4 house cats were tested for taurine, only (b) (6)

☐ Commercial Wet-Pouch — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

List Product Label Name:

☐ Commercial-Raw — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

List Product Label Name:

☐ Homemade-Raw — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

Describe Product Type:

☐ Homemade-Cooked — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

Describe Product Type:

☐ Table Scraps/Human Food (as an occasional contribution to diet) — Describe Product Type(s): not in past 5 years

☐ Pet Treat Products — Product Use as Part of Diet: ☐ Primary ☐ Secondary ☐ Occasional

☐ Commercial	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	
☐ Rawhides or Pig Ears	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	
☐ Marrow Bones	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	
☐ Chicken Jerky	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	
☐ Duck Jerky	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	
☐ Sweet Potato Jerky or Treats	Product Label Name/Lot:		Date first fed	
	How Product Administered:		Date last fed	

Continued otherside

Follow-up Case Information Uniform Data Entry Form
Vet-LIRN

EON/CC Number: 266,814

Owner: (b) (6)

Pet's Name: (b) (6)

DIET-*continued*-Any other foods the owner mentions were given to the animal during this period. (check all that apply)

☐ Other Treats

Product Label Name/Lot:

Date first fed

How Product Administered

Date last fed

ENVIRONMENTAL EXPOSURES-Environmental Exposures Mentioned by the Owner Potentially Affecting the Animal's Overall State of Health Prior to the Event . (check all that apply)

☒ Indoor ☐ Outdoor ☐ Indoor & Outdoor ☐ Carrion ☐ Rodents ☐ Grapes or Raisins ☐ Nuts

☐ Plants ☐ Trash ☐ Hunt ☐ Pet Shows ☐ Sporting Events ☐ Pet Recreation Facilities

☐ Livestock ☐ Poultry ☐ Reptiles ☐ Pet Birds ☐ Small Mammals ☐ Untreated Surface Water

☐ Anti-freeze ☐ Mushrooms ☐ Heavy Metals ☐ Ticks ☐ Urban ☐ Suburban ☐ Rural

Comments:

HOUSEHOLD-Signalment of Additional Animals Given the Product mentioned by the owner.

Animal 1 ☐ Reacted

Animal 2 ☐ Reacted

Animal 3 ☐ Reacted

Comments

Submit

Food and Drug Administration Office of Regulatory Affairs

Summary Report

For Sample Number: 958500

TD Sample Number: **Import Sample Number**

This is an accurate reproduction of the original electronic record as of 08/24/2016

Sample Class: Normal Everyday Sample
Sample Origin: Domestic
Sample Basis: Surveillance
Sample Flag:
Sample Type: Official
Collecting District: NWJ-DO
Home District:
Orig C/R and Records To: NWJ-DO
Collection PACs: 71R801

Product Name: Poultry Prod Pet Cat Food; Not Elsewhere Classified (NEC); Packaged Food (Not Commercially Sterile)

Product Description: See Remarks Section.

Collection Reason: Sample collected per FACTS Assignment ID #11650647 and OP ID # 8660426 referencing Consumer Complaint #146048 reporting the illness of multiple cats from the same household. Sample testing request: Taurine.

Lab: SRL **Split Num:** 0 **Date Received:** 06/29/2016 **Date Out of Lab:** 08/04/2016

District Conclusion: No Action Indicated (NAI)
District Conclusion Made By: Tweedley, Karen P
District 08/12/2016

Disposition Reason: NAI By Examining District
Disposition Authorized By: Tweedley, Karen P
Disposition Authorized Date: 08/12/2016

Performing Org	PAC	LID	PAF	Compliance No	Lab Class-Description	Laboratory Status
ACNA-N	71R801		NAR		1 - In Compliance	Completed

Lab Conclusion

Sample Narrative - Method: AccQTag AAA(Waters) Analysis - Taurine
Amt Found - 0.187% (dry matter basis)
Meets AAFCO minimum requirement of 0.10%

Sample Narrative - Method: Instrument Manual (Denver Instrumentst IR60)/ AOAC 930.15 Analysis - Moisture
Amt Found - 2.20%
Amt Declared - 11.00% max

Lab Conclusion Date	Lab Conclusion Made By
08/04/2016	Hawes,Brian M

Food and Drug Administration Office of Regulatory Affairs

Summary Report

For Sample Number: 958501

TD Sample Number: **Import Sample Number**

This is an accurate reproduction of the original electronic record as of 08/24/2016

Sample Class: Normal Everyday Sample
Sample Origin: Domestic
Sample Basis: Surveillance
Sample Flag:
Sample Type: Official
Collecting District: NWJ-DO
Home District:
Orig C/R and Records To: NWJ-DO
Collection PACs: 71R801

Product Name: Poultry Prod Pet Cat Food; Not Elsewhere Classified (NEC); Packaged Food (Not Commercially Sterile)

Product Description: See Remarks

Collection Reason: Sample collected per FACTS Assignment ID #11650647 and OP ID # 8660426 referencing Consumer Complaint #146048 reporting the illness of multiple cats from the same household. Sample testing request: Taurine.

Lab: SRL **Split Num:** 0
Date Received: 06/29/2016
Date Out of Lab: 08/04/2016

District Conclusion: No Action Indicated (NAI)
District Conclusion Made By: Tweedley, Karen P
District 08/12/2016

Disposition Reason: NAI By Examining District
Disposition Authorized By: Tweedley, Karen P
Disposition Authorized Date: 08/12/2016

Performing Org	PAC	LID	PAF	Compliance No	Lab Class-Description	Laboratory Status
ACNA-N	71R801		NAR		1 - In Compliance	Completed

Lab Conclusion

Sample Narrative - Method: AccQTag AAA Analysis - Taurine
Amt Found - 0.156% (dry matter basis)
Meets AAFCO minimum requirement of 0.10%

Sample Narrative - Method: Instrument Manual (Denver Instrumentst IR60)/ AOAC 930.15 Analysis - Moisture
Amt Found - 1.99%
Amt Declared - 11.00% max

Lab Conclusion Date	Lab Conclusion Made By
08/04/2016	Hawes,Brian M

Food and Drug Administration Office of Regulatory Affairs

Summary Report

For Sample Number: 958504

TD Sample Number: **Import Sample Number**

This is an accurate reproduction of the original electronic record as of 08/24/2016

Sample Class: Normal Everyday Sample
Sample Origin: Domestic
Sample Basis: Surveillance
Sample Flag:
Sample Type: Official
Collecting District: NWJ-DO
Home District:
Orig C/R and Records To: NWJ-DO
Collection PACs: 71R801

Product Name: Poultry Prod Pet Cat Food; Not Elsewhere Classified (NEC); Packaged Food (Not Commercially Sterile)

Product Description: See Remarks Section.

Collection Reason: Sample collected per FACTS Assignment ID #11650647 and OP ID # 8660426 referencing Consumer Complaint #146048 reporting the illness of multiple cats from the same household. Sample testing request: Taurine.

Lab: SRL **Split Num:** 0
Date Received: 06/29/2016
Date Out of Lab: 08/04/2016

District Conclusion: No Action Indicated (NAI)
District Conclusion Made By: Ciaccia, Andrew
District 08/17/2016

Disposition Reason: NAI By Home District
Disposition Authorized By: Ciaccia, Andrew
Disposition Authorized Date: 08/17/2016

Performing Org	PAC	LID	PAF	Compliance No	Lab Class-Description	Laboratory Status
ACNA-N	71R801		NAR		1 - In Compliance	Completed

Lab Conclusion

Sample Narrative - Method: AccQTag AAA Waters Analysis - Taurine
Amt Found - 0.176% (dry matter basis)
Meets AAFCO minimum requirement of 0.10%

Sample Narrative - Method: Instrument Manual (Denver Instrumentst IR60)/AOAC 930.15 Analysis - Moisture
Amt Found - 2.79%
Amt Declared - 11.00% max

Lab Conclusion Date	Lab Conclusion Made By
08/04/2016	Hawes,Brian M

OR Final Report

A. Study Identification:

Study Number: 800.180

Study Director: Renate Reimschuessel, VMD PhD

Division: Vet-LIRN

Division Code: HFV – 500

Other Investigators:

Jennifer Jones	Vet-LIRN
Sarah Nemser	Vet-LIRN
Olgica Ceric	Vet-LIRN
Jake Guag	Vet-LIRN
David Rostein	OS&C

B. Descriptive Title of Study:

Investigation into the death of one cat and low blood taurine levels of two other cats after consumer Merrick Purrfect Bistro Grain Free Chicken Recipe cat food

Name and Address of Testing Facilities:

Mod II
Vet-LIRN and DAFM
Center for Veterinary Medicine
Office of Research
8401 Muirkirk Road
Laurel, MD 20708

C. Starting and Completion Date: Starting Date: 6/7/2016
Ending Date: 6/13/2016
Final Report Submitted Date: 9/2/2016

Case Summary

Complaint: June 7, 2016 Vet-LIRN received consumer complaints, EON-226814, EON-226821, and EON-226827, reporting the death of one cat and low blood taurine levels of 2 others after consuming Merrick Purrfect Bistro Grain Free Real Chicken Recipe food for cats.

Signalment: (b)(6)-12 year old female spayed (FS) domestic shorthair (DSH); (b)(6)-9 year old male castrated (MC) domestic longhair (DLH); (b)(6)-8 year old FS DSH; (b)(6)-9 year old MC DLH; (b)(6)-9 year old MC DLH

Signs: congestive heart failure, dilated cardiomyopathy (DCM), an aortic thromboembolism, low plasma taurine levels, weight loss, hair loss

Medical Records: Medical records were received and reviewed.

(b)(6)**: 12 yo FS DSH-euthanized**

Presenting complaint 5/8/2016: lethargy starting (b), indoor only → recheck (b)(6) b/c very weak, PD, difficulty walking, inappetant → (b)(6), feed Merrick Purrfect Bistro Grain Free Real chicken recipe ~3 yr, prior to this fed Dick Van Pattons Indoor Dry-Chicken & Salmon; vet called Merrick → bag purchased 2 weeks prior per owner. Vet doesn't think a single bag/lot issue because takes several months to develop → urinating & defecating outside litterbox, soft stool, no change to appetite, ambulating well → (b)(6) dyspnea beginning (b)(6), recheck → by (b)(6) weak hindlimbs → by (b)(6) 1 hindlimb worse than other → by (b)(6), recheck b/c dragging right hindlimb → euthanized, vet spoke w/ Merrick QA team and the taurine in that lot # was sufficient

PE 5/8: BCS 7/9, T 93, HR 150, RR 60, muffled heart sounds, inc respiratory effort, dull lung sounds

-5.9: heart sounds slightly muffled, RR 30 w/ slight effort
-5.10: cat PD, inappetant, RR ~28
-5.25: tachypneic, mild inc resp effort, RR 48, faint referred upper airway noise
(b)(6) tachypneic, moderate dyspnea, RR 48-60, non-weight baring Right hindlimb, Right HL: no femoral pulse, cold paw pad; T 94.8, laterally recumbent

Labs:

5.9.2016	**BGA:** Hct 40, Na 146.3 (146.2-156.2), K 4.99 (3.41-4.71), Cl 107.8 (117-125.3), Ca 1.17 (1.16-1.35), Mg 1.08 (0.33-0.49), Glu 156 (72-132), Lac 9.7 (0.7-1.9), BUN 67 (20-33), Ct 5.3 (1.1-3.5)
	-5.9 Renal panel: ALP 11 (14-111), ALT 140 (12-130), BUN 74 (16-36), Cl 100 (112-129), Na 138 (150-165), Ct 1.4 (0.8-2.4)
	-5.15 BGA: Hct 43, Na 145.3, K 3.33, Cl 104.5, BUN 61, Ct 3.1
	-5.25 BGA: Hct 34, Na 147.3, K 6.65, Cl 115.1, BUN 31, Ct 1.3
5.9	**PCV/TS:** 42/6.8
	-5.15 PCV/TS: 39/7.8
	-5.25 PCV/TS: 32/6
5.9	**Plasma taurine:** 24 (60-120, critical <40)

5/8 Cursory US: mild-moderate pleural effusion, R>L

5/8 Rads: cardiac silhouette difficult to visualize, pleural effusion, moderate inc opacity area caudal to left cranial lung lobe

5/9 Echocardiogram: mod LA enlargement, LV enlarged, mild RA & RV enlargement, trivial MR &

TR, dec aortic & pulmonary flow, moderate volume Pleural effusion → DCM

-5.15: small volume PE, no pericardial effusion, large mass in LV-thrombus

-5.25: thrombus unchanged

(b) (6) small vol PE, large LV thrombus

Treatments: Lasix, thoracocentesis: 5/8 (25mL), 5/9 (120 mL), 5/25 (160 mL), O2, pimobendan, taurine, mirtazapine, MaxCal, buprenex, telazol, acepromazine, butorphanol, beuthanasia

Name	Clinical Signs	Lab work Abnormalities	Taurine Level (300-600)**	Outcome	Comments
(b) (6)	Chronic weight & hair loss, polyphagia, BCS 1.5-2/5, alopecia	ALP 174 (hi) ALT 243 (hi) TT4 20.2 (hi)	196	Supplement taurine, treat hyperthyroidism	Lives above garage
(b) (6)	Copious otic debris-AU, resorptive tooth lesion (UR PM3)	TP 9.1 (hi) Glob 6.5 (hi) Gamma Globulins 3.6 (hi)	368	Treat ears; Potential Diagnosis of: Lymphoma, myeloma, or chronic inflammatory disease	Lives above garage
(b) (6)	Moderate tartar, some matted hair	nsf	124	Supplement taurine	Lives above garage
(b) (6)	Significant gingivitis, heavy tartar PM3's, loose canine tooth (UR)	nsf	536	None	Lives **in house** because (b) (6) is aggressive toward him

**Taurine Level >200 associated with No Risk of DCM.

nsf = No significant findings

Owner Interview: An owner interview was completed in order to understand the feeding history and the impact of any potential environmental exposures. The owner also sent a copy of her cat food purchase history. According to the document, Merrick Grain Free Bistro Chicken Adult cat food was most frequently purchased.

Presenting complaint: (b) (6) had lethargy, difficulty moving, not acting like herself. Indoor cats

Prior MHx: none significant for all cats (5) in household

Diet: Merrick Grain Free Bistro Chicken-started in January of 2014, --> on the Chicken variety pretty much the entire time; owner has a listing of all purchases from pet store and she will send us a copy tomorrow; fed prior to the Merrick food was Dick Van Pattens Natural Balance-2 indoor cat formulas-owner thinks the chicken & salmon type but not 100% sure, she can find out if needed: owner mentions the consistency changed when the company was purchased by Del Monte which prompted her to switch foods to Merrick; After the illness onset for (b) (6), Fancy Feast Wet food fed to stimulate her appetite, but she only licked the gravy. So for ~1 week before the other 4 house cats were tested for taurine, only (b) (6) got the Fancy Feast leftovers (solid chunks) not consumed by (b) (6)

Response: Vet-LIRN collected medical records for review and completed an owner interview for more information on the feeding history and potential environmental exposures. The Office of Regulatory Affairs (ORA) local district office sampled and tested product.

Results: Three regulatory samples were collected. The measured taurine content for each was 0.187%, 0.156%, and 0.176%, on a dry matter basis.

Conclusion: The medical records showed three of five cats in a household had low blood taurine levels. One cat, (b) (6), had low blood taurine and dilated cardiomyopathy (DCM). DCM can be caused by low dietary and blood taurine levels. She was euthanized due to a thromboembolism, a complication arising from DCM. (b) (6) lived above the garage with three other cats: (b) (6), (b) (6) and (b) (6) also had low blood taurine levels (<200 nMol/mL), which increase the risk for developing DCM. Neither cat had an echocardiogram, and it is unclear if they had any evidence of DCM. One cat, (b) (6), who lived separately from the other cats, had the highest blood taurine level. (b) (6) received a supplemental wet food for approximately one week prior to the blood taurine level check. The dietary interview and purchase history indicate the chicken variety cat food was fed most frequently. Over time, if the food were deficient in taurine, the cats could develop low blood taurine and thus DCM. If all cats ate the same diet deficient in taurine, you would expect all cats to have low blood taurine levels. (b) (6) normal blood taurine level could be due to individual variation. (b) (6) had the highest blood taurine level of all the cats. His blood taurine level prior to eating the supplemental wet food is unknown. However, if he were taurine deficient, it is possible for the supplemental wet food to improve his blood taurine level. This could explain why (b) (6) had the highest blood taurine level of all the cats.

According to AAFCO, cat food must contain a minimum of 0.10% taurine on a dry matter basis. All three cat food samples tested by ORA are in compliance. Because taurine deficiency develops over time, the cats would have had to consume taurine deficient product over a period of months to years. It is unknown if prior lots or varieties of the food contained adequate taurine levels. It is unlikely this lot of food caused the cats' taurine deficiency.

Supplemental Information

01-800.180-EON-multiple (b) (6)	CC: Consumer complaints
02-800.180-EON-multiple	MedRec: Medical records
03-800.180-EON-multiple	Interview: Owner interview
04-800.180-EON-multiple	Feed: Purchase history
05-800.180-EON-multiple	Results: District testing results
06-800.180-EON-multiple	Summary: Vet-LIRN summary document

SIGNATURES

_____

Deputy Director OR Date

_____

Director OR Date

_____

Study Director Date

Vet-LIRN Case Summary Document

Vet-LIRN Case Number:	800.180
EON/CC #:	EON-226814-226821-226827
Vet-LIRN Initiation Date:	6.7.2016
MedRec: Requested:	6.7.2016
MedRec: Received:	6.7.2016
MedRec: Significant finding:	(b) (6)-DCM,
Vet-LIRN Tests (planned):	MRx, owner interview, ORS to sample
Vet-LIRN Test Results:	ORS sample-in compliance
Result Interpretation:	
IF NFA, justification:	Completed MRx, Interview

COMPLAINT:

#1-for (b) (6)-12 yo FS Mixed Breed Feline: Presented 5/8/2016 for lethargy; on physical exam the patient was dyspneic and pleural effusion identified on cursory ultrasound and DV thoracic x-rays – given lasix and placed in oxygen. Transferred to cardiology service; evaluation including echocardiogram on 5/9/16 revealed dilated cardiomyopathy, moderate left atrial enlargement, pleural effusion and azotemia. Plasma taurine was submitted to University of Wisconsin. Lab results received 5/15/16 - plasma taurine 24nmol/ml (ref range 60-120, critical level <40). Recheck echocardiogram on 5/15/16 revealed same changes as prior and a thrombus in her left ventricle. Medications/supplements included taurine 250mg PO BID, Mirtazepine 15mg tablets (Give 1/4 tablet PO every 3d PRN), Furosemide 12.5 mg tablets (Give ¼ tablet PO SID), Pimobendan 1.5mg tiny tabs (Give 1 tablet PO BID). Patient presented on (b) (6) for partial aortic thromboembolism and owner's elected euthanasia. Review of patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe feline dry for approximately 3 years. The 4 remaining cats were tested for taurine deficiency and 2/4 had whole blood levels indicating deficiency: 5/21/2016 - Whole Blood Taurine submitted at the University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results were received on 5/27/2016 - (b) (6): 9yr male neutered domestic long hair: 196 nmol/ml (b) (6): 8y female spayed domestic short hair: 368 nmol/ml (b) (6): 9yr male neutered domestic long hair: 124 nmol/ml (b) (6): 9yr male neutered domestic long hair: 536 nmol/ml

For #2 for (b) (6)-9yo MC Mixed Breed feline: Another household cat diagnosed with dilated cardiomyopathy and taurine deficiency - separate report filed (FDA ICSR ID 1053335). Euthanized on (b) (6) due to aortic thromboembolism. Review of the patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe Feline dry for approximately 3 years. Remaining 4 cats in household tested for taurine deficiency - whole blood samples submitted to University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results received on 5/27/16 (b) (6) 196nmol/ml - started on taurine supplementation 250mg PO BID for 2-3 weeks. Diet was changed at the time of other cat's diagnosis (5/15/15). Patient also diagnosed with hyperthyroidism on same day as blood submitted for taurine testing - history of weight loss. An echo was not performed on this patient therefore it is unknown if he had evidence of DCM.

#3 (b) (6)-9yo MC Mixed breed feline-OBESE- for Another household cat diagnosed with dilated cardiomyopathy and taurine deficiency - separate report filed (FDA ICSR ID 1053335). Euthanized on (b) (6) due to aortic thromboembolism. Review of the patient's diet history revealed that all 5 cats in household had been fed Merrick Purrfect Bistro Grain Free Real Chicken Recipe Feline dry for approximately 3 years. Remaining 4 cats in household tested for taurine deficiency - whole blood samples submitted to University of California Davis (normal 300-600 nmol/ml, no known risk for deficiency >200), results received on 5/27/16 - (b) (6) 124nmol/ml - started on taurine supplementation 250mg PO BID for 2-3 weeks. Diet was changed at the time of other cat's diagnosis (5/15/15). An echo was not performed on this patient therefore it is unknown if he had evidence of DCM.

Signalments: 5 cats in household

- (b) (6)-deceased-12 yo FS Feline Mix, DCM and Aortic Thromboembolism
- (b) (6)-9 yo MC DLH, no echocardiogram, hyperthyroidism, low plasma taurine
- (b) (6)-8 yo FS DSH, plasma taurine wnl
- (b) (6)-9 yo MC DLH, no echocardiogram, low plasma taurine
- (b) (6)-9 yo MC DLH, plasma taurine wnl

Signs: 5 cat household: congestive heart failure in 1 cat with dilated cardiomyopathy and aortic thromboembolism, low plasma taurine → euthanized; other 4 living cats unknown if DCM present because no echocardiogram performed; 2 of 4 living cats had low plasma taurine and supplementation begun; 1 cat with low taurine also diagnosed w/ hyperthyroidism and had a history of weight loss

Food: Merrick Purrfect Bistro Grain Free Real Chicken Recipe feline dry for approximately 3 years

Owner: (b) (6)

Vet: (b) (6)

Vet-LIRN PLAN OF ACTION: MRx and owner interview, ORA regulatory sampling based on interview results

FINAL CONCLUSION: pending

Follow-up: email vet permission to contact owner and requesting MRx

6.8.2016
JJ-Vet calling owner to let them know we'll be calling (were ok with it when the vet submitted the report). Vet sent MRx.

MRx summary:

(b) (6)-8 yo FS DSH:
Presenting complaint 5/21/2016: taurine check. Lives in a room above the garage with 3 other cats, indoor only, no Rx → recheck 6/1 protein electrophoresis, ddx: LSA vs myeloma vs chronic inflam
PE: FORL right upper PM3, mild tartar, copious black otic debris-AU that is mildly pruritic on cleaning
Labs: 5.21.2016 **CBC:** nsf
Chem: TP 9.1 (5.2-8.8), Glob 6.5 (2.3-5.3)

Taurine: 368 (300-600, no risk if >200)

6.1 **Protein Electrophoresis:** TP 8.2 (5.2-8.8), Glob 5.3 (2.3-5.3), alpha 0.3 (norm), alpha 2 0.7 (norm), beta 0.6 (0.3-0.9), Gamma 3.6 (0.3-2.5)

Treatments: tresaderm

(b) (6) -9 yo MC DLH

Presenting complaint 5/21/2016: one of 4 cats kept in finished room above garage, chronic weight loss past few months & taurine check, was losing hair >1 yr but told related to anxiety, voracious appetite, indoor only, no Rx

PE: slightly feisty, alopecia caudal dorsum/ventrum/lateral thighs, BCS 1.5-2/5

Labs: 5.21.2016 **CBC:** nsf
Chem: ALP 174 (6-102), ALT 243 (10-100)
T4: 20.2 (0.8-4)
Taurine: 196 (300-600, no risk if >200)

Treatments: Tapazole (methimazole), taurine

(b) (6) : 9 yo MC DLH

Presenting complaint 5/21/2016: lives in the owner's house, not above the garage b/c (b) (6) is aggressive to him, no Rx, Diet: Merrick;

PE: right upper canine loose, significant gingivitis, heavy tartar PM3's

Labs: 5.21.2016 **CBC:** nsf
Chem: nsf
Taurine: 536 (300-600, no risk if >200)

(b) (6) : 9 yo MC DLH

Presenting complaint 5/21/2016: taurine check, one of 4 cats living above garage in a room; 2 dogs in house, Diet: Merrick; no Rx

PE: some matted hair, BCS 4/5, moderate tartar overall

Labs: 5.21.2016 **CBC:** MCHC 30.8 (30-38), Plt 188 (200-500)-clumped
Chem: Glob 5.3 (2.3-5.3)
Taurine: 124 (300-600, no risk if >200)

Treatments: Taurine

(b) (6) : 12 yo FS DSH-euthanized

Presenting complaint 5/8/2016: lethargy starting 5/7, indoor only → recheck 5/15 b/c very weak, PD, difficulty walking, inappetant → 5/19, feed Merrick Purrfect Bistro Grain Free Real chicken recipe ~3 yr, prior to this fed Dick Van Pattons Indoor Dry-Chicken & Salmon; vet called Merrick → bag purchased 2 weeks prior per owner. Vet doesn't think a single bag/lot issue because takes several months to develop → urinating & defecating outside litterbox, soft stool, no change to appetite, ambulating well → 5/25 dyspnea beginning 5/24, recheck → by 5/26 weak hindlimbs → by 5/29 1 hindlimb worse than other → by (b) (6) recheck b/c dragging right hindlimb → euthanized, vet spoke w/ Merrick QA team and the taurine in that lot # was sufficient

PE 5/8: BCS 7/9, T 93, HR 150, RR 60, muffled heart sounds, inc respiratory effort, dull lung sounds

-5.9: heart sounds slightly muffled, RR 30 w/ slight effort

-5.10: cat PD, inappetant, RR ~28

-5.25: tachypneic, mild inc resp effort, RR 48, faint referred upper airway noise

(b) (6) : tachypneic, moderate dyspnea, RR 48-60, non-weight baring Right hindlimb, Right HL: no femoral pulse, cold paw pad; T 94.8, laterally recumbent

Labs: 5.9.2016 **BGA:** Hct 40, Na 146.3 (146.2-156.2), K 4.99 (3.41-4.71), Cl 107.8 (117-125.3), Ca 1.17 (1.16-1.35), Mg 1.08 (0.33-0.49), Glu 156 (72-132), Lac 9.7 (0.7-1.9), BUN 67 (20-33), Ct 5.3 (1.1-3.5)

-5.9 Renal panel: ALP 11 (14-111), ALT 140 (12-130), BUN 74 (16-36), Cl 100 (112-129), Na 138 (150-165), Ct 1.4 (0.8-2.4)

-5.15 BGA: Hct 43, Na 145.3, K 3.33, Cl 104.5, BUN 61, Ct 3.1

-5.25 BGA: Hct 34, Na 147.3, K 6.65, Cl 115.1, BUN 31, Ct 1.3

5.9 **PCV/TS:** 42/6.8

-5.15 PCV/TS: 39/7.8

-5.25 PCV/TS: 32/6

5.9 **Plasma taurine:** 24 (60-120, critical <40)

5/8 Cursory US: mild-moderate pleural effusion, R>L

5/8 Rads: cardiac silhouette difficult to visualize, pleural effusion, moderate inc opacity area caudal to left cranial lung lobe

5/9 Echocardiogram: mod LA enlargement, LV enlarged, mild RA & RV enlargement, trivial MR & TR, dec aortic & pulmonary flow, moderate volume Pleural effusion → DCM

-5.15: small volume PE, no pericardial effusion, large mass in LV-thrombus

-5.25: thrombus unchanged

-6.1: small vol PE, large LV thrombus

Treatments: Lasix, thoracocentesis: 5/8 (25mL), 5/9 (120 mL), 5/25 (160 mL), O2, pimobendan, taurine, mirtazapine, MaxCal, buprenex, telazol, acepromazine, butorphanol, beuthanasia

Thoughts: since (b) (6) lives in house with owners, could he be getting more supplements of taurine (e.g. table scraps of meat) vs the other 4 cats living above the garage. The clinician commented that if food was the source of the taurine deficiency, it was interesting the array of presentations/levels in the 5 cats.

Left msg for owners to arrange interview.

JJ-Owner sent follow-up email & voicemail. Will email to arrange interview.

6.9.2016
JJ-Owner interview:

Presenting complaint: (b) (6) had lethargy, difficulty moving, not acting like herself. Indoor cats
Prior MHx: none significant for all cats (5) in household
Diet: Merrick Grain Free Bistro Chicken-started in January of 2014, –> on the Chicken variety pretty much the entire time; owner has a listing of all purchases from pet store and she will send us a copy tomorrow; fed prior to the Merrick food was Dick Van Pattens Natural Balance-2 indoor cat formulas-owner thinks the chicken & salmon type but not 100% sure, she can find out if needed: owner mentions the consistency changed when the company was purchased by Del Monte which prompted her to switch foods to Merrick;
After the illness onset for (b) (6), Fancy Feast Wet food fed to stimulate her appetite, but she only licked the gravy. So for ~1 week before the other 4 house cats were tested for taurine, only (b) (6) got the Fancy Feast leftovers (solid chunks) not consumed by (b) (6). (Could this explain his higher blood taurine than the other housemates???)

Owner will send the list of pet food purchases from Merrick tomorrow. Will forward to group.

6.13.2016
JJ-Received owner's receipts from her food purchase history. Forwarded to DR on 6/10. NFA-completed interview and MRx review.

Final conclusion: Based on the medical records, 3 of the 5 cats in the household had low blood taurine levels. One cat, (b) (6), had documented low blood taurine and was euthanized due to a thromboembolism, a complication arising from dilated cardiomyopathy (DCM). DCM can be caused by low dietary and blood taurine levels. (b) (6) lived above the garage with 3 other cats: (b) (6) also had low blood taurine levels (<200 nMol/mL) associated with risk for DCM. Neither cat had echocardiograms to confirm DCM. It is unclear why (b) (6) had taurine levels within reference range, but may be due to individual variation. One cat, (b) (6), who lived separately from the other cats, had the highest blood taurine level. (b) (6) received a supplemental wet food for approximately 1 week prior to the taurine level check. If the dry food regular diet were deficient in taurine, it is possible the supplemental wet food could have improved his taurine levels. This may explain why (b) (6) had the highest blood taurine levels of all the cats, which were within normal range. The dietary interview and purchase history indicate the Chicken variety was most often fed to the cats. Over time, if the food were deficient in taurine, the cats could develop low blood taurine and thus DCM. The ORS product sampling and taurine testing will provide more information on the food taurine content.

7.21.2016
JJ-Checked w/ DR. Testing results from ORA still pending.

7/27/2016
Taurine results received

7/28/16
JJ-DAF reviewing the taurine results.

8.24.2016
JJ-DAF reviewed the results:

OK Everyone. The product appears to be a dry extruded product, for which the AAFCO Cat Food Nutrient Profiles content for taurine is 0.10% on a dry matter basis. Clearly all three samples were analyzed to contain more than that amount of taurine. On a dry matter basis the concentration of taurine in the samples was analyzed to be:

FACTS #	Amount Taurine Found	%Moisture	%Dry Matter	Amount Taurine on a Dry Matter Basis
958500	0.183g/100g ≈ 0.18%	2.20%	100 – 2.20 = 97.80%	0.183/0.9780 = 0.187%
958501	0.153g/100g ≈ 0.15%	1.99%	100 – 1.99 = 98.01%	0.153/0.9801 = 0.156%
958504	0.171g/100g ≈ 0.17%	2.79%	100 – 2.79 = 97.21%	0.171/0.9721 = 0.176%

All of the Dry Matter Taurine percentages are above 0.10%. IF any of the samples were canned cat food, they would not be in compliance with the AAFCO Cat Food Nutrient Profiles for the recommended minimum taurine content and IF the label indicated the product was formulated to meet the AAFCO Cat Food Nutrient Profiles the product would be misbranded.

The answer to the question of consequence/causation of the taurine content in the product from which these three samples originated to the cats in the consumer complaint is that this(ese) lot(s) of product are not indicated to be causative. However, dilated cardiomyopathy from taurine deficiency occurs over a long period of exposure to a deficient diet (months to a year or more), so, if these cats were eating the Merrick Purrfect Bistro Grain Free Real Chicken Recipe feline dry for the 3 years indicated in the complaint, it is possible that the product was deficient for some long interval of time during that three year period and that a return to "normal" taurine levels in the diet were insufficient to correct the problem in the three cats that developed low blood taurine and the two with dilated cardiomyopathy. Treatment for dilated cardiomyopathy caused by taurine deficiency takes higher daily doses of taurine for several months than normal dietary amounts and is not completely curative.

Recommendations for regulatory steps to consider: (b) (5)

NFA.

8.25.2016
JJ-ORA final results received from DR. Filed.

3 subs taurine content: 0.176%, 0.187%, 0.156% on dry matter basis → in compliance w/ 0.10% minimum set by AAFCO

10/14/16

OC-received FOIA request related to the case, preparing documentation. Deadline: 10/26/16.

(b) (6)

16879

Sample Submission Form

UC CUSTOMERS ONLY:
Non-federal funds ID/Account Number to bill:_____

Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
Davis, CA 95616
Tel: (530)752-5058, Fax: (530)752-4698

http://www.vetmed.ucdavis.edu/vmb/aal/aal.html

Vet/Tech Contact: (b) (6) / Contact: (b) (6) Date: 6-20-17
Company Name: (b) (6)
Address: (b) (6)
(b) (6)

Email: (b) (6)
Tel: (b) (6) **Fax:** (b) (6)

Billing Contact: (b)(6) **TAX ID:**
Email: (b) (6) **Tel:** (b) (6)

Patient Name: (b) (6)
Species: Canine
Owner's Name (b) (6)

Sample Type: ☐ Plasma ☑ Whole Blood ☐ Urine ☐ Food ☐ Other:_____
Test Items: ☑ Taurine ☐ Complete Amino Acid ☐ Other:_____

Taurine Results (nmol/ml)

Plasma:___ Whole Blood: 276 Urine:_____ Food:_____

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	>150

(b) (4)

(b) (6)

PET OWNER:	(b) (6)		(b) (6)	LAB ID:	2600050841
SPECIES:	Canine			ORDER ID:	105299928
BREED:				COLLECTION DATE:	6/18/17
GENDER:	Male		(b) (6)	DATE OF RECEIPT:	6/19/17
AGE:	8 Years	ACCOUNT #:	(b) (6)	DATE OF RESULT:	6/19/17
PATIENT ID:	(b) (6)	ATTENDING VET:	(b) (6)		

(b) (4) HealthChek™ - Standard CBC

Hematology

6/19/17 (Order Received)
6/19/17 5:44 PM (Last Updated)

TEST	RESULT	REFERENCE VALUE	
RBC	4.98	5.39 - 8.7 M/µL	L
Hematocrit	35.0	38.3 - 56.5 %	L
Hemoglobin	12.2	13.4 - 20.7 g/dL	L
MCV	70	59 - 76 fL	
MCH	24.5	21.9 - 26.1 pg	
MCHC	34.9	32.6 - 39.2 g/dL	
% Reticulocyte	2.3	%	
Reticulocyte	115	10 - 110 K/µL	H
Reticulocyte Comment	A reticulocyte count of greater than 110 K/uL of blood is considered evidence of bone marrow response to an increased peripheral demand. Depending on the degree of anemia, a reticulocyte count <110 K/uL may indicate an inadequate bone marrow response. Serial monitoring of the erythrogram and reticulocyte count may be useful to evaluate bone marrow responsiveness over time. The following chart may be used as a guideline to determine appropriateness of regenerative response. Degree of bone marrow response (K/uL): Mild 110-150 Moderate 150-300 Marked >300		
WBC	9.1	4.9 - 17.6 K/µL	
% Neutrophil	58.6	%	
% Lymphocyte	29.8	%	
% Monocyte	8.7	%	
% Eosinophil	2.9	%	
% Basophil	0.0	%	
Neutrophil	5.333	2.94 - 12.67 K/µL	
Lymphocyte	2.712	1.06 - 4.95 K/µL	
Monocyte	0.792	0.13 - 1.15 K/µL	
Eosinophil	0.264	0.07 - 1.49 K/µL	
Basophil	0	0 - 0.1 K/µL	

(b) (4)

(b) (6) PET OWNER: (b) (6) DATE OF RESULT: **6/19/17** LAB ID: 2600050841

Hematology (continued)

TEST	RESULT	REFERENCE VALUE	
Platelet	208	143 - 448 K/µL	

Chemistry

6/19/17 (Order Received)
6/19/17 5:44 PM (Last Updated)

TEST	RESULT	REFERENCE VALUE	
Glucose	84	63 - 114 mg/dL	
(b) (4)SDMA [a]	14	0 - 14 µg/dL	
Creatinine	0.5	0.5 - 1.5 mg/dL	
BUN	16	9 - 31 mg/dL	
BUN:Creatinine Ratio	32.0		
Phosphorus	5.6	2.5 - 6.1 mg/dL	
Calcium	11.3	8.4 - 11.8 mg/dL	
Sodium	154	142 - 152 mmol/L	H
Potassium	5.4	4.0 - 5.4 mmol/L	
Na:K Ratio	29	28 - 37	
Chloride	107	108 - 119 mmol/L	L
TCO2 (Bicarbonate)	30	13 - 27 mmol/L	H
Anion Gap	22	11 - 26 mmol/L	
Total Protein	6.5	5.5 - 7.5 g/dL	
Albumin	4.1	2.7 - 3.9 g/dL	H
Globulin	2.4	2.4 - 4.0 g/dL	
Alb:Glob Ratio	1.7	0.7 - 1.5	H
ALT	57	18 - 121 U/L	
AST	83	16 - 55 U/L	H
ALP	84	5 - 160 U/L	
GGT	4	0 - 13 U/L	
Bilirubin - Total	<0.1	0.0 - 0.3 mg/dL	
Bilirubin - Unconjugated	0.0	0.0 - 0.2 mg/dL	
Bilirubin - Conjugated	0.1	0.0 - 0.1 mg/dL	
Cholesterol	159	131 - 345 mg/dL	

(b) (4)

PET OWNER: DATE OF RESULT: **6/19/17** LAB ID: 2600050841

Chemistry (continued)

TEST	RESULT	REFERENCE VALUE	
Creatine Kinase	1,162	10 - 200 U/L	H
Hemolysis Index [b]	1+		
Lipemia Index [c]	N		

[a] BOTH SDMA AND CREATININE ARE WITHIN THE REFERENCE INTERVAL which indicates kidney function is likely good. Evaluate a complete urinalysis and confirm there is no other evidence of kidney disease.

[b] Index of N, 1+, 2+ exhibits no significant effect on chemistry values.

[c] Index of N, 1+, 2+ exhibits no significant effect on chemistry values.

Case Description

Patient Information		Case Information	
Patient name:	(b) (6)	Referrer:	(b) (6)
Species:	Canine	Created:	06/19/2017 4:38:15pm
Breed:	Mix	Modified:	06/19/2017 4:52:56pm
Age:	8yr MN	Clinic:	(b) (6)
		Clinician:	(b) (6)
		Modality:	CR
		Patient ID:	(b) (6)
		Sex:	M
		Description:	THORAX II VIEWS

History

history of chronic cough-worsening, not responsive to cough tabs or sid lasix, still eating and dirinking well

Physical Findings

4/6 murmur, clear lungs, soft not painful abdomen

Report

Radiographic Findings

3 thoracic radiographs made to June 19, 2017. Previous radiographs from the referring veterinarian are on the server but cannot be evaluated for comparison due to image transfer artifact.

There is moderate generalized cardiomegaly. The heart measures approximately 11.5 VHS. Peripheral pulmonary vessels are normal in diameter. There is dorsal displacement of the carina by the enlarged heart. The lungs are normal. There is no evidence of cardiogenic pulmonary edema or free pleural fluid. The trachea is normal in diameter.

Conclusion

1. Cardiomegaly. Valvular endocardiosis and insufficiency as most likely. Concurrent pulmonary hypertension is not excluded. There is no evidence of congestive heart failure.
2. Irritation/compression of the carina/principal bronchi by the enlarged heart could be contributing to the cough.
3. Allergic/inflammatory bronchitis or infectious tracheobronchitis may be present without radiographic changes and could also be an underlying cause for chronic cough.

Consider cardiology consult for echocardiography. Consider treatment for bronchitis.

(b) (6)

06/19/2017 4:52:56pm

Radiology Report powered by Remedy View

(b) (6)

(b) (6)

(b) (6)

Patient Information

Patient:	(b) (6)	Age: 8	years	Referring Veterinarian:	(b) (6)
Patient Number:	(b) (6)	Weight:(kg)	6.20	Cardiologist:	(b) (6) (Cardiology)
Breed:	Shih Tzu	Sex:	M	Client Number:	(b) (6)
Exam Date:	06/19/2017 17:26	BSA:	0.34		

History: (b)(6) was presented for evaluation of lethargy and progressive coughing. (b)(6) has had a progressive cough that started approximately 6 months ago. He was started on a cough suppressant (unknown dose/type) and Lasix (5 mg PO q24h) with no improvement. His respiratory rate/effort are normal at home. He has not had any episodes of weakness/collapse but has been lethargic over the past few weeks.

(b)(6) is on a limited ingredient diet with kangaroo as the sole protein source. He had a negative heartworm test in February and receives Sentinel monthly (1/2 of a 26-50# tablet?).

Physical Examination: T 100.8 P 128 R 30
Grade 3-4/6 left apical systolic murmur with radiation to the right base. Fair femoral pulses. Regular rhythm. Normal lung sounds. Eupneic. Normal abdominal palpation. PLNs WNL. Excessive bruising noted after jugular venipuncture (none from the first venipuncture). No other bruising/petechiation noted. Thin body condition. MM light pink/slightly tacky. CRTe< 2 sec. Fundic exam: Abnormal. Suspect partial retinal detachment on nasal aspect of retina OS with hyperreflectivity around the edge. No abnormalities identified OD.

Diagnostic Tests: Blood Pressure: 102 mmHg (#3 cuff, left forelimb)
Thoracic Radiographs: Generalized cardiomegaly (progressive as compared to previous films). No evidence of cardiogenic edema. Mild diffuse bronchointerstitial pattern.
CBC: Mild non/pre-regenerative anemia.
Chemistry Profile: Mild hypernatremia (154 mmol/L) with mild hypochloremia (107 mmol/L). Mild elevation in bicarb.
Taurine level pending
Echocardiogram: See below. Sinus rhythm on ECG.

Echocardiographic Report

2D ECHO

LA Systolic Diameter LX	3.3 cm	Aortic Root Diameter	1.2 cm

DOPPLER

AV Peak Velocity	60.7 cm/s	PV Peak Gradient	1.1 mmHg
AV Peak Gradient	1.5 mmHg	TR Peak Velocity	292 cm/s
MR Peak Velocity	545 cm/s	TR Peak Gradient	34.2 mmHg
PV Peak Velocity	51.8 cm/s		

M-MODE

LV Diastolic Diameter MM	4.3 cm	LVPW Diastolic Thickness MM	0.58 cm
LV Systolic Diameter MM	4 cm	LVPW Systolic Thickness MM	0.64 cm
LV Fractional Shortening MM	7.1 %	LVPW Percent Thickening MM	0.091
LV Diastolic Volume Cube	79 cm^3	IVS to PW Ratio MM	1
LV Systolic Volume Cube	63.2 cm^3	LV Mass MM	70.3 g
LV Ejection Fraction Cube	0.2	LV Mass Normalized MM	206 g/m^2
IVS Diastolic Thickness MM	0.58 cm	RV Diastolic Diameter MM	0.3 cm
IVS Systolic Thickness MM	0.63 cm	MV E Point Septal Separation	1.6 cm
IVS Percent Thickening MM	0.068		

Left Ventricle: Severe dilation (normalized LVIDd 1.5) with marked reduction in contractility (normalized LVIDs 2.25).

Left Atrium: Moderate dilation

Right Ventricle: Normal

Right Atrium: Normal

Mitral Valve: Mildly thickened valve leaflets. 3+ mitral regurgitation.

Aortic Valve: Normal

Tricuspid Valve: Mildly thickened valve leaflets. 1+ tricuspid regurgitation.

Pulmonic Valve: Normal valve morphology. Mild pulmonic insufficiency.

Aorta: Normal

Pericardium: Normal

Diagnosis

Dilated cardiomyopathy- This is a disease characterized by weakening of the heart muscle and dilation of the heart chambers. As the disease progresses, it can lead to congestive heart failure (fluid in the lungs causing shortness of breath and cough). Abnormal heart rhythms are common and can result in sudden death. Most commonly this is an inherited disease, though it can occur secondary to a deficiency in an amino acid called taurine. This is a relatively uncommon disease in small breed dogs so we generally recommend checking taurine levels in these cases.

Abnormal fundic exam - suspect partial retinal detachment of left eye - this change is not what I typically expect with taurine deficiency, but I strongly recommend having (b) (6) evaluated by a veterinary ophthalmologist to better characterize this change. As we discussed, it may be possible that this change is potentially linked with the heart disease and learning more about this may help us get a better idea of a reason for both conditions. Also, it may be important to initiate treatment to help protect his vision and decrease risk of further changes in the eye that could also eventually cause pain. I do not believe that he is in pain today from this.

Recommendations

Give all medications as directed:

Pimobendan (Vetmedin) 2.5 mg tablets- Give 1 tablet by mouth in the morning and 1/2 of a tablet in the evening. Give at 12 hour intervals.
This is a drug that is approved for the treatment of congestive heart failure secondary to dilated cardiomyopathy or chronic valve disease (endocardiosis). However, two studies of dogs with dilated cardiomyopathy, one in Doberman Pinschers (PROTECT) and one in Irish Wolfhounds, have shown a delay in the onset of heart failure in preclinical dogs treated with Vetmedin compared to placebo. Recently, another study (EPIC) has shown significant prolongation of the asymptomatic period in animals with progressive disease and heart enlargement from chronic valve disease, prior to the onset of congestive heart failure, as well. This is off-label use of this medication. In our experience, side effects are uncommon, but it is important that you advise us if you feel your pet is having any potential adverse effects from this medication. The reported potential side effects listed for this medication are increased heart rate, vomiting, diarrhea, inappetence, uneasiness, incoordination, convulsions, increased drinking and increase urinating.

Enalapril (Enacard, Vasotec) 2.5 mg tablets- Give 1/2 of a tablet by mouth every 12 hours.
This medication is a strong drug that dilates blood vessels, permitting the heart to pump blood more efficiently. It can lower blood pressure (hypotension) and cause changes in kidney function and electrolyte values. If your pet develops weakness or depression, decrease the drug dose by ½ and call. A kidney panel and blood pressure should be reevaluated 7-10 days after beginning this medication.

Taurine 500mg - Give 500mg orally every 12 hours. We will discontinue this if his taurine level comes back in the normal range.

You may discontinue the furosemide. The Cough-Tabs can be used as needed, especially at night, for the cough.

One thing that can be very helpful for home monitoring is checking sleeping or resting respiratory rates. A recent study showed that even pets with severe heart disease rarely have resting respiratory rates greater than 30 breaths per minute unless they are starting to decompensate for that disease. Elevated respiratory rates at home may be even more sensitive than chest radiographs at picking up early decompensation. Count your pet's respiratory rate when he/she is at rest or sleeping (not within 20 minutes of being active). If his/her respiratory rate is greater than 30 breaths per minute, recheck again in a couple of hours. If persistently elevated above this level, call.

With advanced heart disease, our biggest dietary concerns are adequate calorie content and low sodium content. We aim for less than 100mg sodium per 100 kilocalories (kcal) in patients with significant structural heart disease. We do not advise protein restriction unless there is concurrent kidney disease (i.e. kidney diets are not advised unless there is concurrent kidney disease). You had already investigated the sodium content of the kangaroo diet and it is within this range, but we may recommend a diet change if his taurine level were to come back abnormal.

We will make further recommendations for follow-up after we receive the taurine level and after we see what the opthalmologist determines with his eye. He should have a kidney panel and blood pressure rechecked after 7-10 days on the enalapril. This can be scheduled as a technician appointment. We will also want to hear about how his cough responds to the new cardiac medications when he comes for this recheck.

(b) (6) (Cardiology)

(Electronically Signed)

Final Date: 19 June 2017 19:42

Amended: 19sJunes2017s19:44

(b) (6)

Notes to our clients
-Please bring all medications to your pet's scheduled appointments.
-We require a 48 hour notice for all refills. When you call to request a refill, please leave the pharmacy phone number or clearly indicate if you plan on picking up the medication at our facility. PRESCRIPTION REFILLS ARE NOT AVAILABLE AFTER (b) (6) REGULAR BUSINESS HOURS (Evenings, Fridays, holidays and weekends).
-Check out WWW.GOODRX.COM and enter your local zip code to search for the best prices on your medications at your local pharmacies.
-If an emergency arises with your pet. (b) (6) is a 24 hour facility.

(b) (6)

(b) (6)

Client ID:	(b) (6)	Patient ID:	(b) (6)
Client Name:	(b) (6)	Name:	(b) (6)
Spouse/Other:	(b) (6)	Breed:	Shih Tzu Mix
Address:	(b) (6)	Sex:	Neutered Male
		Color:	White
Telephone:		Age:	8 Yrs. 6 Mos.
		DOB:	(b) (6)

Referring Veterinarian:	(b) (6)
Practice:	(b) (6)
Phone:	
FAX:	

Cardiology Reevaluation

Reevaluation of:
Dilated cardiomyopathy, Cough

Owner notes concern over significant increase in cough. They have been traveling frequently due to a recent death in the family and (b) (6) is not tolerating the car rides like he has in the past. Typically, (b) (6) is very calm in the car and will fall asleep right away for the trip but recently he is very anxious with respirations up into the 80s. His normal resting respirations have been averaging in the low 20s (22) when not coughing and not traveling. Owner describes the cough as being forceful but non-productive (does not sound congested). She does report an improved cough with the first two days of Vetmedin but it quickly returned to baseline and has continued to progress. Last night he had a bad night and was unable to sleep comfortably. No change in the cough with the cough tabs prescribed by (b)(6)' regular vet. Owner also reports that there was no improvement in the cough when (b)(6) was receiving his furosemide. (b)(6) has also had three urinary accidents in the house since starting the new medications.

Physical Exam:

	6/19/2017 1:44 PM	7/6/2017 11:38 AM
Vital Sign	ER	038
Weight	6.2 kilograms	6.08 kilograms
Temp	100.8	99.6
HR	128	164
RR	30	56
RQ		Panting

Grade 4/6 left apical systolic murmur with radiation to the right base. Adequate femoral pulses. Normal lung sounds. Eupneic. Normal abdominal palpation. PLNs WNL. MM pink/moist. CRT < 2 sec.

Diagnostics:
Chest radiographs: Unchanged cardiomegaly. No evidence of cardiogenic edema.
Renal panel: clinically unremarkable
Blood pressure: 138 mmHg (#3cm cuff, left forelimb)

Diagnosis:
Dilated cardiomyopathy
Cough - progressive
Urinary accidents - if (b)(6) continues to have accidents in the house a urinalysis would be recommended to rule out a urinary tract infection. This can be done through your regular vet.

Recommendations:

Please give the following medications as directed:

ITEM DESCRIPTION	DIRECTIONS
Enalapril 2.5mg tablets	Give 1/2 tablet by mouth every 12 hours
Vetmedin 2.5mg tablets	Give 1 tablet by mouth once daily in the mornings and 1/2 tablet by mouth once daily in the evenings
Cough tabs	Give 1/2 tablet by mouth every 12 hours as previously prescribed by your regular vet

ADD:

Doxycycline 100mg tablets Give 1/2 tablet by mouth once every 12 hours. Give with food or flush with water after medicating to avoid esophageal irritation.

(b)(6) does not have evidence of active heart failure on his x-rays. I suspect his cough is secondary to underlying primary airway disease. As we discussed, Lasix can have some anti-inflammatory effects which may account for the increase in cough after stopping this drug. Unfortunately, work up for primary airway disease usually involves general anesthesia to obtain an airway sample. (b)(6) is not a good candidate for this given the severity of his heart disease. We can try empirical therapy starting with doxycycline as it is an antibiotic that targets many respiratory pathogens but also has anti-inflammatory effects.

If his cough does not improve over the weekend, please call us on Monday. If you notice any respiratory concerns, you can always bring (b)(6) in through the emergency department. We will make further recommendations based on how he responds to the doxycycline.

(b) (6)

Notes to our clients

-Please bring all medications to your pet's scheduled appointments.

-We require a 48 hour notice for all refills. When you call to request a refill, please leave the pharmacy phone number or clearly indicate if you plan on picking up the medication at our facility. PRESCRIPTION REFILLS OUTSIDE OF (b) (6) REGULAR BUSINESS HOURS (Evenings, Fridays, holidays, and weekends) MAY BE ASSOCIATED WITH AN AFTER HOURS FILLING FEE.

-Check out **www.goodrx.com** and enter your local zip code to search for the best prices on your medications at your local pharmacies.

-If an emergency arises with your pet, (b) (6) is only a phone call away. (b) (6) is a 24 hour facility and the emergency veterinarians can always reach the cardiologist on-call.

-Please schedule your recommended recheck as soon as possible. Our schedule tends to book up quite quickly and we want to make sure that we see your pet in a timely manner.

Vet-LIRN Case Summary Document

Vet-LIRN Case Number:	
EON/CC #:	EON-350158
Owner LAST Name:	(b) (6)
Vet LAST Name:	(b) (6)
Vet-LIRN Initiation Date:	3/28/2018
MedRec: Requested:	Received with Complaint
MedRec: Received:	
MedRec: Significant finding:	
Vet-LIRN Tests (planned):	
Vet-LIRN Test Results:	
Result Interpretation:	
IF NFA, justification:	

COMPLAINT Narrative: At the time of diagnosis (b) (6), (b) (6) was a 13 year old female spayed Labrador retriever who had been maintained on a Zignature Kangaroo formula. She presented with a history of a progressive cough which, prior to presentation, became productive and she coughed up a small volume of pink foam (possible pulmonary edema). On examination she had a 2/6 left apical systolic heart murmur and on echo diagnosed with advanced dilated cardiomyopathy with severe left ventricular dilation, moderate to severe left ventricular systolic dysfunction, and moderate to severe left atrial dilation. Thoracic radiographs were suspicious for early congestive heart failure. A whole blood taurine level was submitted and was low at 168. She was treatment with furosemide, benazepril, pimobendan, spironolactone, taurine and l-carnitine and her diet was changed to Royal Canin Early Cardiac. At her recheck in 2/26/18, (b) (6) heart had improved significantly with now mild dilated cardiomyopathy with normalized left atrial dimensions, mild left ventricular dilation and low normal left ventricular systolic function. The furosemide was able to be discontinued at this time.

Signalment: (b) (6) -13 yr FS Lab

Signs: productive, progressive cough

Food Product: Zignature Kangaroo Formula

Plan:

- MRx
- Open product for Tau, Cysteine, Methionine, +/- Beta-Alanine

MRx summary:
Presenting complaint 10/31/2017: developed a cough on 10/25, Rads and labwork at the vet showed ALP 440, GGT 30, mildly low Lymph, cardiomegaly → treated with hydroxyzine, doxycycline, hydrocodone → stopped drugs Monday b/c cough worsened → to ER on (b) (6) after coughing up pink tinged foam; no lethargy, continues to eat and drink; UTD on vaccines and HWP, no drugs → treat with Lasix, benazepril, vetmedin, spironolactone, Tau, L-carnitine and **vet recommended a diet change** → recheck 2/26/18: intermittent cough, related to excitement, change diet to RC Early Cardiac → on

recheck improved → suspect Tau responsive DCM-mild, suspect cough secondary to bronchial or primary respiratory disease

PE (b) (6)**:** LS-OU, HR 132, mild periodontal disease, Gr II/VI, left apical protosystolic murmur, questionable mild inc bronchovesicular sounds bilaterally, SC mass left ventrum;

PE 2/26: Gr III/VI pansystolic, PMI MV, reg rhythm with S3 gallop, HR 130, BCS 6/9, hepatomegaly

Labs: (b) (6) BP 100 (based on Echo)

-2/26:155 mg Hg, direct measurement

11/3: Tau-blood: 168 (200-350)

Rads 10/27: generalized cardiomegaly, left atrial enlargement, slight left auricular bulge, increased sternal contact & rounded heart, dorsal tracheal deviation, prominent pulmonary vasculature with questionably mild inc interstitial opacity in caudal-dorsal lungs, suggesting early CHF/PE

(b) (6) **Echo:** severe LV hypertrophy, mild-mod MV regurgitation, mod-sev LA dilation, mild TV regurg, mild RV & RA dilation, mod-sev lower systolic function values

-2/26: mild LV dilation, mild MV regurg, normal LA, mild TV regurg, normal RV & RA, low normal systolic functional indices of LV

(b) (6) **ECG:** normal sinus rhythm

An article about beta-alanine: https://academic.oup.com/alcalc/article/36/1/29/138000

If Tau & Cys/Met are normal, we may need to reconsider other MOA's causing this, unrelated to the food.

I emailed the vet to request the full MRx and see if lot/best by information available for the leftover food.

4/4/2018

JJ-Vet sent the full MRx available and does not have any leftover food. We will purchase the food for testing. A dog from a previous case without food (800.218- (b) (6) Cocker Spaniel with Low Tau and also eating Zignature Essentials Kangaroo.

MRx added to above summary.

Vet-LIRN Case Summary Document

Vet-LIRN Case Number:	800.261
EON/CC #:	EON-350158
Owner LAST Name:	(b) (6)
Vet LAST Name:	(b) (6)
Vet-LIRN Initiation Date:	3/28/2018
MedRec: Requested:	Received with Complaint
MedRec: Received:	
MedRec: Significant finding:	

Vet-LIRN Tests (planned):	• MSU
	  ○ Iodine
	• (b) (4)
	  ○ Cys-Met-Tau

Vet-LIRN Test Results:	
Result Interpretation:	
IF NFA, justification:	

COMPLAINT Narrative: At the time of diagnosis (10/31/17), (b) (6) was a 13 year old female spayed Labrador retriever who had been maintained on a Zignature Kangaroo formula. She presented with a history of a progressive cough which, prior to presentation, became productive and she coughed up a small volume of pink foam (possible pulmonary edema). On examination she had a 2/6 left apical systolic heart murmur and on echo diagnosed with advanced dilated cardiomyopathy with severe left ventricular dilation, moderate to severe left ventricular systolic dysfunction, and moderate to severe left atrial dilation. Thoracic radiographs were suspicious for early congestive heart failure. A whole blood taurine level was submitted and was low at 168. She was treatment with furosemide, benazepril, pimobendan, spironolactone, taurine and l-carnitine and her diet was changed to Royal Canin Early Cardiac. At her recheck in 2/26/18, (b) (6) heart had improved significantly with now mild dilated cardiomyopathy with normalized left atrial dimensions, mild left ventricular dilation and low normal left ventricular systolic function. The furosemide was able to be discontinued at this time.

Signalment: (b) (6) -13 yr FS Lab

Signs: productive, progressive cough

Food Product: Zignature Kangaroo Formula

Plan:

- MRx
- Open product for Tau, Cysteine, Methionine, +/- Beta-Alanine

MRx summary:
Presenting complaint 10/27 to rDVM: developed a cough on 10/25, cough for 3-4 days, not lethargic, normal eating/drinking, no vomiting or diarrhea, worse when lying down, dog didn't cough while in clinic except for a tracheal cough when pulling on the leash→ treated with hydroxyzine, doxycycline, hydrocodone → stopped all 3 drugs Monday b/c cough worsened → to ER on (b) (6) after coughing up

pink tinged foam; no lethargy, continues to eat and drink; UTD on vaccines and HWP, no drugs → treat with Lasix, benazepril, vetmedin, spironolactone, Tau, L-carnitine and **vet recommended a diet change** →labwork done 11/14 → to rDVM 11/16: doing well → recheck 2/26/18: intermittent cough, related to excitement, change diet to RC Early Cardiac → on recheck improved → suspect Tau responsive DCM-mild, suspect cough secondary to bronchial or primary respiratory disease → recheck 3/13: resting RR 16 rpm, minimal coughing only when excited, since switching to cardiac food BMs are dense and tenesmus, owner is weaning dog off lasix

PE 10/27 @ rDVM: numerous lipomatous & dermal masses, no audible murmur or arrhythmia, shallow breathing

PE (b) (6) @ specialist: LS-OU, HR 100 bpm, mild periodontal disease, Gr II/VI, left apical protosystolic murmur, questionable mild inc bronchovesicular sounds bilaterally, SC mass left ventrum, mildly tense cranial abdominal palpation

PE 11/16 @ (b) (6): mild underbite, H/L wnl

PE 2/26: Gr III/VI pansystolic, PMI MV, reg rhythm with S3 gallop, HR 130, BCS 6/9, hepatomegaly

PE 3/13: T 99.9F, RR 56, HR 124 bpm, Gr III/VI murmur, rest nsf

Labs:

10/27	CBC: Lym 1.01 (1.05-5.1)
	-3/13: Lym 1044 (1060-4950), Plt 615 (143-448), Plt inc on direct
10/27	Chem: ALP 440 (23-212), GGT 30 (0-11), rest nsf
	-11/14: Glu 51 (70-143), Glob 4.7 (2.5-4.5), ALP 621, GGT 31
	-3/13: Na:K 27, ALP 2243 (5-180), GGT 117 (0-13)
(b) (6)	BP 100 (based on Echo)
	-2/26:155 mg Hg, direct measurement
	-3/13: 130-140 mmHg, direct measurement
11/3	Tau-blood: 168 (200-350)
3/13	UA: 1.010, pH 5
3/13	TT4: 0.8 (1-4)

Rads 10/27: generalized cardiomegaly, left atrial enlargement, slight left auricular bulge, increased sternal contact & rounded heart, dorsal tracheal deviation, prominent pulmonary vasculature with questionably mild inc interstitial opacity in caudal-dorsal lungs, suggesting early CHF/PE

(b) (6) **Echo:** severe LV hypertrophy, mild-mod MV regurgitation, mod-sev LA dilation, mild TV regurg, mild RV & RA dilation, mod-sev lower systolic function values

-2/26: mild LV dilation, mild MV regurg, normal LA, mild TV regurg, normal RV & RA, low normal systolic functional indices of LV

(b) (6) **ECG:** normal sinus rhythm

Prior MHx: 7/2017: doing well at home-occasionally coughs, several SQ masses, no murmur or cough on tracheal palpation; 10/23/2017-vaccines, doing well per O, no murmur ausculted, not been getting HWP consistently,

An article about beta-alanine: https://academic.oup.com/alcalc/article/36/1/29/138000
If Tau & Cys/Met are normal, we may need to reconsider other MOA's causing this, unrelated to the food.

I emailed the vet to request the full MRx and see if lot/best by information available for the leftover food.

4/4/2018

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MRx added to above summary.

4/11/2018
JJ-JG received the sample. I prepared the lab submission forms and will aliquot the sample today for testing.

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Vet LAST Name:	(b) (6)
Vet-LIRN Initiation Date:	3/28/2018
MedRec: Requested:	Received with Complaint
MedRec: Received:	
MedRec: Significant finding:	

Vet-LIRN Tests (planned):	• MSU
	  ○ Iodine
	• (b) (4)
	  ○ Cys-Met-Tau

Vet-LIRN Test Results:	• Iodine < 10 ppm-no suspicion of exogenous thyroid tissue • Tau
Result Interpretation:	
IF NFA, justification:	

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MRx added to above summary.

4/10/18
JG – Received the sample. Treat-sub1 (Zignature, Kangaroo formula)

4/11/2018
JJ-JG received the sample. I prepared the lab submission forms and will aliquot the sample today for testing.

4/12/2018
JJ-I prepared the samples and sent them to MSU for iodine screening and (b) (6) for Tau/Cys/Met screening.

5/4/2018
JJ-The MSU iodine results were < 10 ppm and not suspicious for exogenous thyroid tissue.

The (b) (4) results came back for Taurine, Cystine, and Methionine.

- Taurine = 45.5 mg/100g = 0.0455g/100g = 0.046% As Is Basis
  If we assume a max of 10% moisture per the label (= 90% DMB),
  then 0.0455 / 0.90 = 0.05% DMB, which is less than the AAFCO minimum for cats eating extruded foods (0.1% DMB.)
- Cystine = 293 mg/100g = 0.293 g/100g = 0.29% As Is Basis
  If we assume a max of 10% moisture per the label (= 90% DMB), then 0.293 / 0.90 = 0.33% DMB
- Methionine = 358mg/100g = 0.358 g/100g = 0.36% As Is Basis
  If we assume a max of 10% moisture per the label (= 90% DMB),
  then 0.358 / 0.90 = 0.4% DMB, which is greater than the AAFCO minimum for growth & reproduction of 0.35% DMB.
  The Methionine-cystine % = 0.4% + 0.33% = 0.73% DMB, which is greater than the AAFCO minimum for growth & reproduction of 0.7% DMB.

BLUF: Taurine was low based on the AAFCO minimum for feline extruded foods.

Patient Demographics

(b) (6) **Study Date: 11/01/2017**

Patient ID: (b) (6) Accession #: Alt ID:

DOB: Age: Gender: Ht: Wt: 67lb 4oz BSA:

Institution: CVCA (b) (6)

Referring Physician:

Physician of Record: Performed By:

Comments:

Adult Echo: Measurements and Calculations

2D

LVIDd (2D)	6.23 cm	LVAd (A4C)	34.40 cm²	IVSd (2D)	0.932 cm
LVPWd (2D)	0.791 cm	LVAs (A4C)	25.70 cm²	RVIDd/LVIDd	0.139
EDV (2D-Teich)	196 ml	EDV (A4C)	141 ml	RVIDd (2D)	0.866 cm
EDV (2D-Cubed)	242 ml	ESV (A4C)	88.8 ml	LA Area	24.1 cm²
A4Cd		LV Mass (Cubed)	239 g	LA Dimen (2D)	4.2 cm
LV Vol	141 ml				
LV Length	6.89 cm				
LV Area	34.4 cm²				
A4Cs		IVS/LVPW (2D)	1.18	LA/Ao (2D)	1.75
LV Vol	88.8 ml				
LV Length	6.13 cm				
LV Area	25.7 cm²				
LVLd (A4C)	6.9 cm	SV (A4C)	52.2 ml	AoR Diam (2D)	2.4 cm
LVLs (A4C)	6.1 cm	EF (A4C)	37.0 %		

MMode

IVSd (MM)	0.966 cm	SV (MM-Teich)	78.0 ml	LVPW % (MM)	21.1 %
LVIDd (MM)	6.30 cm	FS (MM-Teich)	19.4 %	RVIDd (MM)	0.322 cm
LVPWd (MM)	0.859 cm	EF (MM-Teich)	38.8 %	LA Dimen (MM)	3.7 cm
IVSs (MM)	1.11 cm	EDV (MM-Cubed)	250 ml	AoR Diam (MM)	2.3 cm
LVIDs (MM)	5.08 cm	ESV (MM-Cubed)	131 ml	LA/Ao (MM)	1.61
LVPWs (MM)	1.04 cm	SV (MM-Cubed)	119 ml	MV D-E Exc Dist	1.4 cm
IVS/LVPW (MM)	1.12	EF (MM-Cubed)	47.6 %	MV D-E Slope	43.6 cm/s

EDV (MM-Teich)	201 ml	FS (MM-Cubed)	19.4 %	MV E-F Slope	19.1 cm/s
ESV (MM-Teich)	123 ml	IVS % (MM)	14.9 %	MV EPSS	1.4 cm

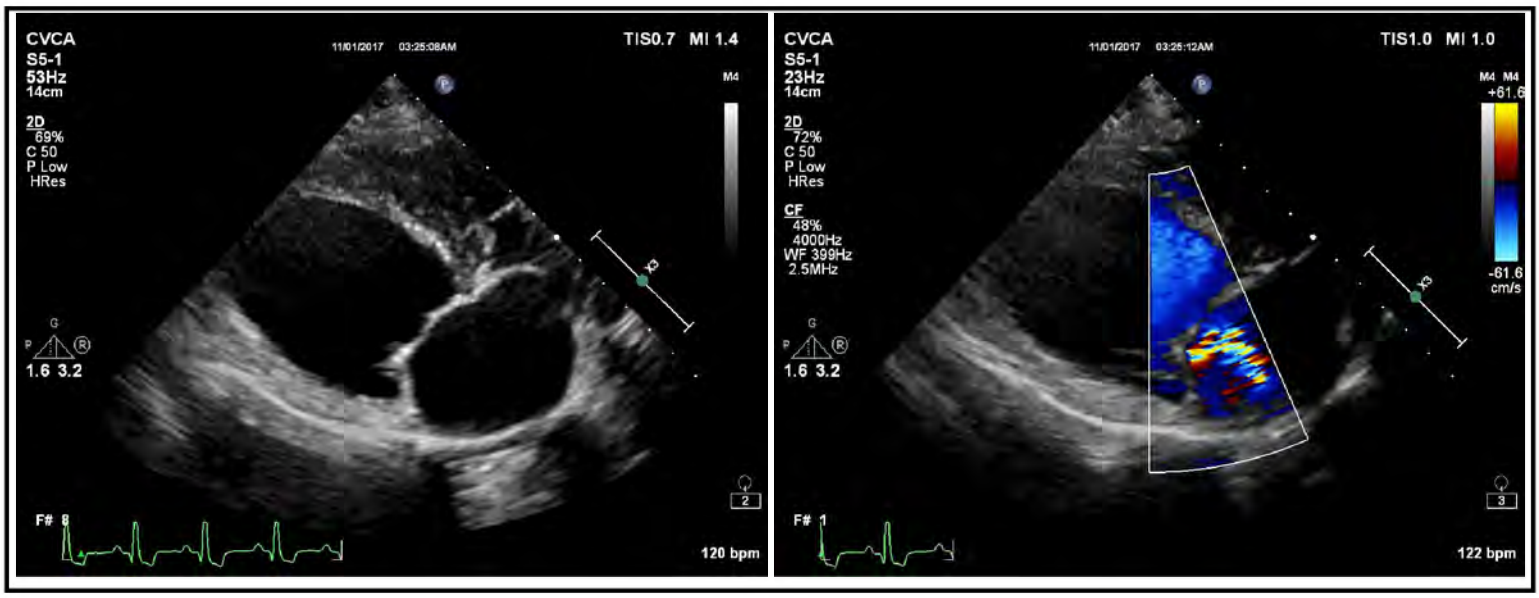
Doppler

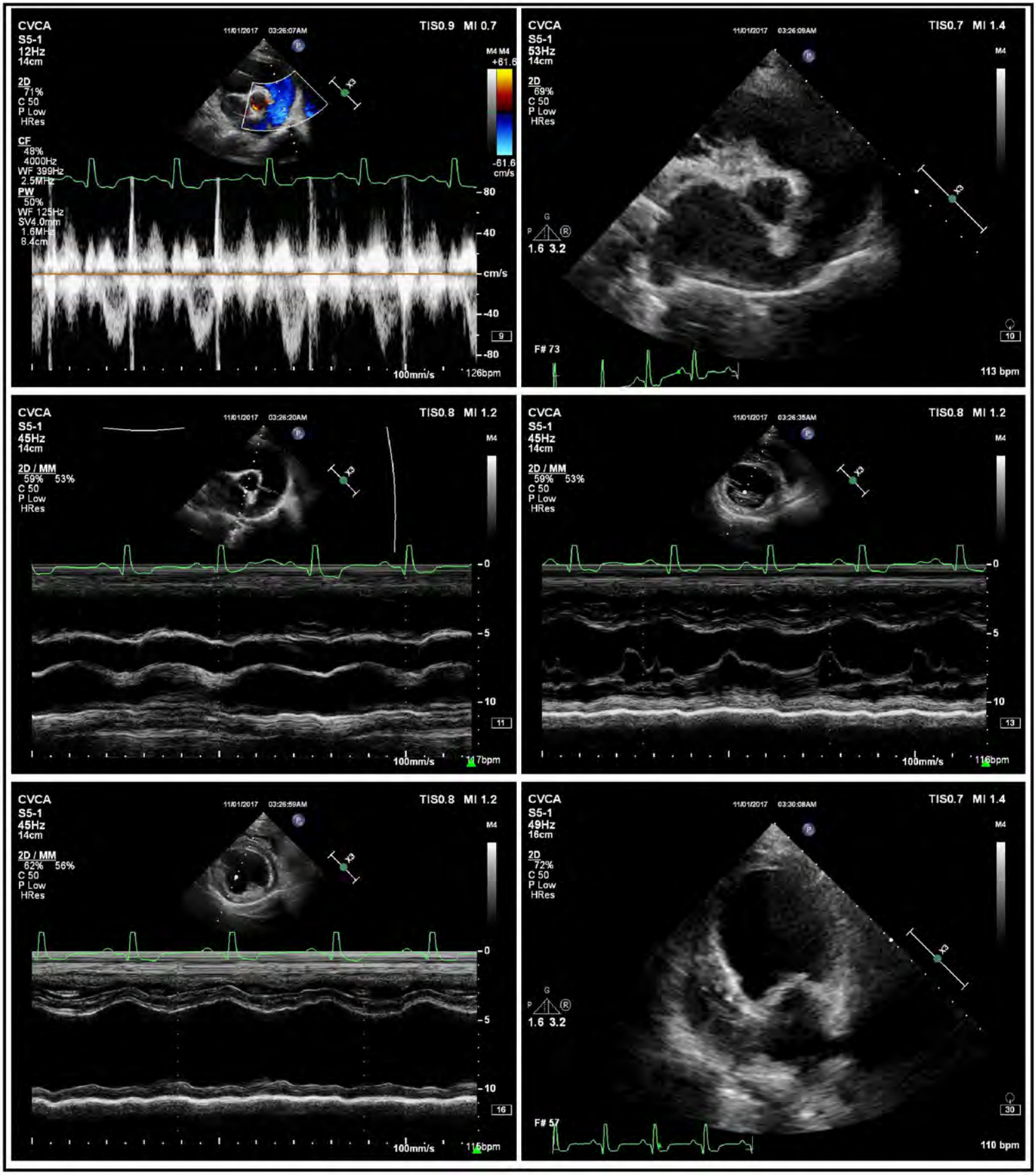
LVOT Vmax		MV Peak A Vel		Lat A` Vel	10.7 cm/s
Max PG	7 mmHg	Vel	75.2 cm/s		
Vmax	134 cm/s	PG	2 mmHg		
RVOT Vmax		MV E/A	1.6	E`/A` Lateral	1.2
Max PG	2 mmHg				
Vmax	77.1 cm/s				
MR Vmax		Lat E` Vel	12.7 cm/s	TR Vmax	
Max PG	100 mmHg			Max PG	40 mmHg
Vmax	501 cm/s			Vmax	315 cm/s
MV Peak E Vel		E/Lat E`	9.8		
Vel	1.24 m/s				
PG	6 mmHg				

Other Measurements

Dimensions: 2D LAX	
LA lax (2D)	5.41 cm
Dimensions: Diameters	
LVID/Ao (2D)	2.60
EF & Volume: Simpson's	
Sphericity Id	1.1
Dimensions: Diameters	
LVEDDN	2.31
LVID/Ao (2D)	2.60

Images

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12Hz
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2D
71%
C 50
P Low
HRes
CF
48%
4000Hz
WF 399Hz
2.5MHz
PW
50%
WF 125Hz
SV4.0mm
1.6MHz
8.4cm
M4 M4
+61.6
-61.6
cm/s
-80
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126bpm
CVCA
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53Hz
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2D
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113 bpm
CVCA
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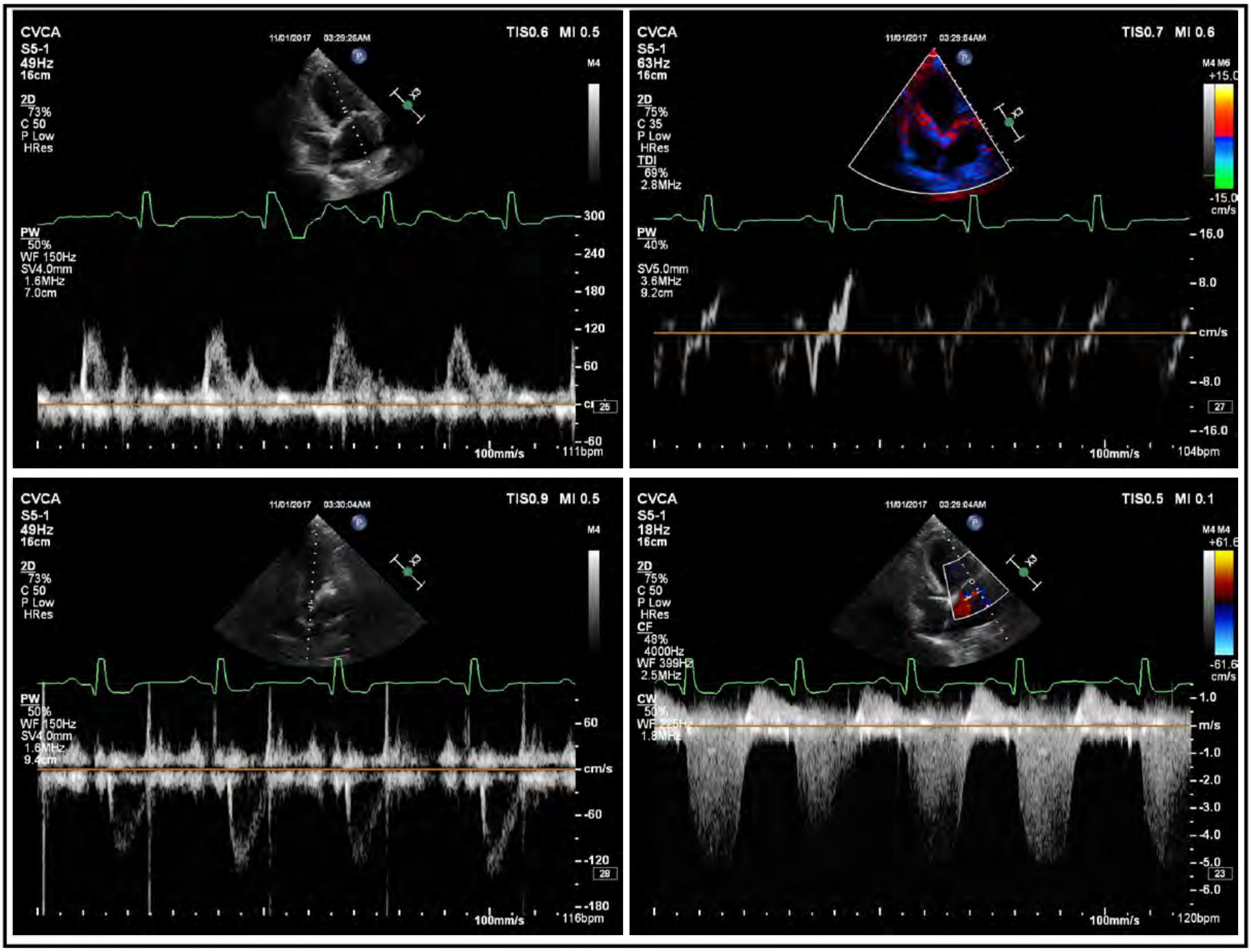


Signature

Signature:

Name(Print): Date:

11-25-13	64.00
09-16-13	69.00
07-10-13	59.30
07-25-12	68.30
01-09-12	71.00

MEDICAL HISTORY

Date	By	Code	Description	Qty (Variance)	Photo
03-13-18	JO2	(b) (4)	(b) (4) Requisition (b) (6)		
		865	Senior Screen		
			Attachments\8546 (b) (6) (b) (6) 3.14.18 Lab.pdf		
		C153	Office Visit- Recheck		
		P183	Blood Pressure		
		CHECK-IN	Patient check-in		

SMT: 11-14-17 at 10:51a: recheck blood chemistry proile w/ electrolytes O wants AB
CMO: 02-12-18 at 4:59p: called o to r/s - ok with JO
AB2: 02-27-18 at 11:15a: exam, BP, sr screen per last CVCA report
SMT: 03-12-18 at 2:09p: LMOM

Age: 12y **Weight:** 71.50 **Temp:** 99.90 **Respiration:** 56.00 **Pulse:** 124.00
CRT: pink 1-2 secs.

SUBJECTIVE SECTION

exam, BP, sr screen per last CVCA report

resting resp around 16 per mom, doing well at home, eating/drinking normal, bathroom normal, minimal coughing only when excited, since o switched to cardiac food BMs are very dense and sometimes has trouble passing stool, no vomiting, no other concerns, per o is weaning p off lasix

OBJECTIVE SECTION

ABNORMALITIES

Oral Cavity
mm pink

Cardiovascular
III/VI murmur as previously described

Respiratory
Respiratory rate normal; lungs eupneic

Lymphatic
All palpable LN's WNL

Other
euhydrated, BAR

PLAN SECTION

NOTES

BP 130-140 (LHL, size 5 cuff)

Date	By	Code	Description	Qty (Variance)	Photo

Senior screen to (b) (4) UA free catch

Disc firm stools and mild tenesmus- adv can trial metamucil but rec confirm with cardiologist ok to add in.

121217 B

(b) (6)

CVCA CONSULTATION REQUEST FORM

Date: (b) (6)

Client Id #: (b) (6) **Client Name:** (b) (6)

Address: (b) (6) **City:** (b) (6) **State:** (b)(6) **Zip:** (b) (6)

Telephone:

Cellular:	:	(b) (6)
Cellular:	:	(b) (6)

Animal Name: (b) (6) **Species:** Canine **Breed:** Labrador Retriever

Color: Yellow **Sex:** spayed female **Weight:** 0Kg.

Date of Birth: (b) (6) **Age:** 13 Yrs. 0 Mos.

Referring Veterinary Hospital: **No Vet**
Doctor's Name: No Vet
Referring Veterinary Hospital Phone #: (b) (6)

(b) (6) **Requesting Consult:** (b) (6)

Relevant History / Physical Findings:
Cough started last Wednesday. Radiographs and blood work were performed. Radiographs revealed suspected cardiomegaly. Blood work showed mild ALP and GGT elevations.
The owner made cardio-consultation on Friday however her cough got worse with pink tinged foam so (b) (6) was brought to (b) (6) for a cardiology consultation.
(b) (6) has been a healthy dog with no current medications. She is up to date on vaccination and heartworm preventative.

Current Medications:
Hydroxyzine, Doxycycline, and hydrocodone, which was stopped because her coughing got worse with those medications.

Radiographs performed at:

☒ RDVM
☐ (b) (6)

Consulting Cardiologist:

(b) (6) (6)
(b) (6)

CVCA, Cardiac Care for Pets
(b) (6)
Phone: (b) (6)
Email: (b) (6)@cvcavets.com
www.cvcavets.com

CVCA
Cardiac Care for Pets

Client: (b) (6)
Co-owner:
Patient name (b) (6)
Species: Canine
Breed: Labrador Retriever
Sex: FS
Age: 13 years and 5 months old
Weight: 33.18kg. / 73.15 lbs

(b)(6)
Email:

Cardiac Evaluation Report
Exam Date: 02/26/2018

Diagnosis

- Mild, improved dilated cardiomyopathy - suspect taurine-responsive
- Mild, improved mitral and very mild tricuspid valve regurgitation as cause of heart murmur
- Normal, improved left atrial chamber dilation
- Mild, improved eccentric left ventricular chamber dilation
- Low normal, improved left ventricular contractility/heart muscle function
- Cough - suspect bronchial/primary respiratory disease

Medications

- Decrease Lasix/Furosemide 40 mg tablets - Give 1 and 1/2 tablets twice daily for 1 week then decrease to 1 tablet twice daily for 1 week then decrease to 1/2 tablet twice a day for 1 week then discontinue. Please call if you note an increase respiratory rate while decreasing the Lasix. If there is an increase in cough (but normal respiratory rate), we will consider adding in a bronchodilator.
- Continue Benazapril 10 mg tablets - Give 1 and 1/2 tablets twice daily
  Continue Vetmedin/Pimobendan 7.5 mg EZ tablets - Give 1 tablet twice daily.
- Continue Spironolactone 25 mg tablets - Give 1 tablet twice daily.
- Continue Taurine 1500 mg twice daily.
- Continue L-carnitine 1500 mg three times daily.
- You may purchase the taurine and L-carnitine at any health food or nutrition store or www.puritanspride.com. You may also obtain the L-carnitine in bulk powder form from North Carolina State University by calling 919-513-6325.
- Continue with monthly heartworm and flea/tick control as prescribed by (b) (6)

Please allow 24-48 hours for CVCA to process prescription refill requests.
Refill all medications indefinitely unless directed by CVCA or your primary care veterinarian.

- **Please check all medications and dosages on your discharge report against the pharmacy labels.**

Please Note

- Please see our website www.cvcavets.com for more information about (b) (6) dilated cardiomyopathy.

Nutrition Recommendations:

• Continue the Royal Canin Early Cardiac diet.

• Consider fish oil supplements (omega-3 fatty acids). Her dose is approximately EPA 1220 mg and DHA 760 mg total per day. Please start at 1/2 the dose for one week, then increase to the full dose if tolerating well thereafter. Please avoid Cod liver oil and flax seed as well as products with Vit A and/or D.
For more information about fish oils, please visit --http://vet.tufts.edu/heartsmart/diet/important-nutrients-for-pets-with-heart-disease/

• In addition to the supplements approved by Tuft's Veterinary Nutrition Service, other reputable brands include Welactin and Nordic Naturals. (b) (6) may have additional brand recommendations.

Activity Recommendations:

• Continue normal activity as she wants and is able to do. Please allow (b) (6) to take more breaks and rest during activity.

• Please avoid exercise in the hot/humid weather.

At Home Monitoring:

• In order to monitor for the development of early congestive heart failure in the out-patient setting, we recommend monitoring your pet's resting respiratory rate several times a week. Normal resting respiratory rates should be less than 30 breaths per minute. Consider using a respiratory rate monitoring application to track (b) (6) respiratory rate - Cardalis or BI Pharma have reliable phone applications. Please contact us if you note a persitent or progressive increase.

Future Anesthesia/Fluid Recommendations

• We expect (b) (6) to tolerate carefully monitored general anesthesia with normal preoperative bloodwork and a balanced anesthetic regimen. During anesthesia, we recommend careful monitoring of ECG, BP and pulse ox and ½ usual surgical fluid rate (ie: 2-4 ml/kg/hr). Carefully monitor for several hours post-operatively for signs of respiratory congestion and consider chest radiographs if these signs occur. There is some risk associated with all anesthetic events.

• Avoid medications with tachycardia as a side effect, such as ketamine, telazol and glycopyrrolate. Cleared for low dose atropine if needed for intraprocedure bradycardia. Avoid medications that significantly alter blood pressure such as acepromazine and Domitor.

• (b) (6) should not receive corticosteroids (prednisone) in the future please contact CVCA for recommendations, if corticosteroids are indicated.

Reevaluation

• Recheck with (b) (6) in the next 2-4 weeks and every 6 months for wellness care as directed, close auscultation, blood pressure and complete lab tests including blood and urine testing (CBC/Chemistry/Urinalysis/ Thyroid evaluation). Please forward these results when available.

• Please recheck with CVCA in 6 months for a follow up consultation/examination, blood pressure, and echocardiogram. Please contact us or schedule an earlier appointment if (b) (6) has any problems or symptoms indicative of worsening heart disease or if recommended by (b) (6)

We thank you for trusting in CVCA to care for (b) (6) today. Please do not hesitate to call us with any questions or concerns.

Sincerely,

(b) (6)

Visit Summary

Heart Rate: 130 **BP**: 155 mmHg **Cuff Size/Location:** 6 cuff/LF

History: Recheck DCM, suspected early CHF; doing well; RRR - 16 bpm, increased Lasix in January due to increased cough; cough seems to be intermittent and related to excitement; good appetite; 3 kg weight gain since 10/2017; walks 30-45 minutes per dayl- slow pace, at times winded but recovers very quickly.

(b)(6) developed a cough last Wednesday (10/25/17). Radiographs and blood work were performed by (b) (6) The lab work (which is unavailable for review) reportedly showed an elevated ALP 440 and GGT 30 and mild lymphopenia. Thoracic radiographs were performed which revealed cardiomegaly. (b) (6) was treated with hydroxyzine 50mg BID, doxycycline 200mg AM and 100mg PM, and hydrocodone 5mg q8-12h. All medications were stopped on Monday as her cough had worsened and she was presented to the (b) (6) for a cardiac evaluation as her coughing had worsened and she had brought up a small volume of pink-tinged foam after a coughing fit. During this time there has been no evidence of lethargy and she continues to eat and drink normally at home.

PPHx: None
Meds: None
Other: UTD on vaccinations, On HW preventative
Diet: changed from Zignature (Kangaroo) to Royal Canin Early Cardiac

Physical Exam Findings: 3/6 pansystolic murmur, PMI - mitral valve, regular rhythm with S3 gallop; LUNGS - clear all fields, panting, normal effort; Sl. overweight body condition (BCS - 6/9); Pink mm; PP - SS; PLN - WNL; ABD - hepatomegaly; BAR

Echocardiographic Findings

Mild left ventricular eccentric dilation - significant improvement compared to previous exam; mild, improved centrally located mitral regurgitant jet, normal, improved left atrial dimensions on 2D imaging and on M-mode imaging, mild, low velocity eccentric low velocity tricuspid regurgitation, subjectively normal right ventricular and right atrial dimensions, normal left and right ventricular outflow velocities, low normal, improved indices of systolic function (FS% and EF% by modified Simpson's, normal EPSS, normal transmitral inflow velocities and E:A wave ratio on spectral Doppler tracings, normal TDI E':A' ratio of the lateral mitral annulus, no masses, effusions or heartworms observed.

Comments

Dear (b) (6),

Thank you for sending (b) (6) to see us with (b) (6) today. I am quite pleased with (b) (6) exam today. She has had remarkable improvement in her echocardiogram with the cardiac medications, change in diet and supplementation with Taurine and L-carnitine. Her risk for congestive heart failure at this point is very low so we will be weaning (b) (6) off the Lasix/furosemide while (b) (6) monitors (b) (6) respiratory rate. Her current cough is likely due to respiratory disease and if the cough progresses/worsens, we will consider adding in a bronchodilator, such as Theophylline. Right now, with the marked improvement, (b) (6) long-term prognosis has improved considerably. I suspect we will be able to further discontinue cardiac medications if her heart remains stable. We will continue to closely monitor (b) (6) heart disease via serial echocardiography and institute further therapy when progression is noted. While on this course of medication, it is important to monitor the chemistry profiles and blood pressures. Hopefully, (b) (6) will continue to do so well - she's a sweety!

We appreciate your continued referrals and the trust you place in CVCA to co-manage your cardiac patients. We look forward to working with you on this case and others. In an effort to continue to improve CVCA's service to both you and your clients, please visit our website at www.cvcavets.com and complete our online referring veterinarian survey.

Sincerely,

(b) (6)

Patient Demographics

(b) (6)					**Study Date: 02/26/2018**
Patient ID: (b) (6)		Accession #:			Alt ID:
DOB:	Age:	Gender:	Ht:	Wt: 73lb 0oz	BSA:
Institution: Philips Medical					
Referring Physician:					
Physician of Record:				Performed By: (b) (6)	
Comments:					

Adult Echo: Measurements and Calculations

2D

LVIDd (2D)	5.01 cm	LVAd (A4C)	21.30 cm²	IVSd (2D)	1.24 cm
LVPWd (2D)	1.20 cm	LVAs (A4C)	13.90 cm²	RVIDd/LVIDd	0.139
EDV (2D-Teich)	119 ml	EDV (A4C)	61.9 ml	RVIDd (2D)	0.695 cm
EDV (2D-Cubed)	126 ml	ESV (A4C)	33.3 ml	LA Area	15.8 cm²
A4Cd		LV Mass (Cubed)	186 g	LA Dimen (2D)	2.9 cm
LV Vol	61.9 ml				
LV Length	5.90 cm				
LV Area	21.3 cm²				
A4Cs		IVS/LVPW (2D)	1.03	LA/Ao (2D)	1.21
LV Vol	33.3 ml				
LV Length	4.79 cm				
LV Area	13.9 cm²				
LVLd (A4C)	5.9 cm	SV (A4C)	28.6 ml	AoR Diam (2D)	2.4 cm
LVLs (A4C)	4.8 cm	EF (A4C)	46.2 %	HR - AV	82 bpm

MMode

IVSd (MM)	1.09 cm	SV (MM-Teich)	52.1 ml	LVPW % (MM)	40.9 %
LVIDd (MM)	4.96 cm	FS (MM-Teich)	22.4 %	RVIDd (MM)	0.806 cm
LVPWd (MM)	0.965 cm	EF (MM-Teich)	44.9 %	LA Dimen (MM)	3.1 cm
IVSs (MM)	1.58 cm	EDV (MM-Cubed)	122 ml	AoR Diam (MM)	2.4 cm
LVIDs (MM)	3.85 cm	ESV (MM-Cubed)	57.1 ml	LA/Ao (MM)	1.29
LVPWs (MM)	1.36 cm	SV (MM-Cubed)	64.9 ml	MV D-E Slope	25.7 cm/s
IVS/LVPW (MM)	1.13	EF (MM-Cubed)	53.2 %	MV E-F Slope	13.6 cm/s

EDV (MM-Teich)	116 ml	FS (MM-Cubed)	22.4 %	MV EPSS	0.3 cm
ESV (MM-Teich)	63.9 ml	IVS % (MM)	45.0 %		

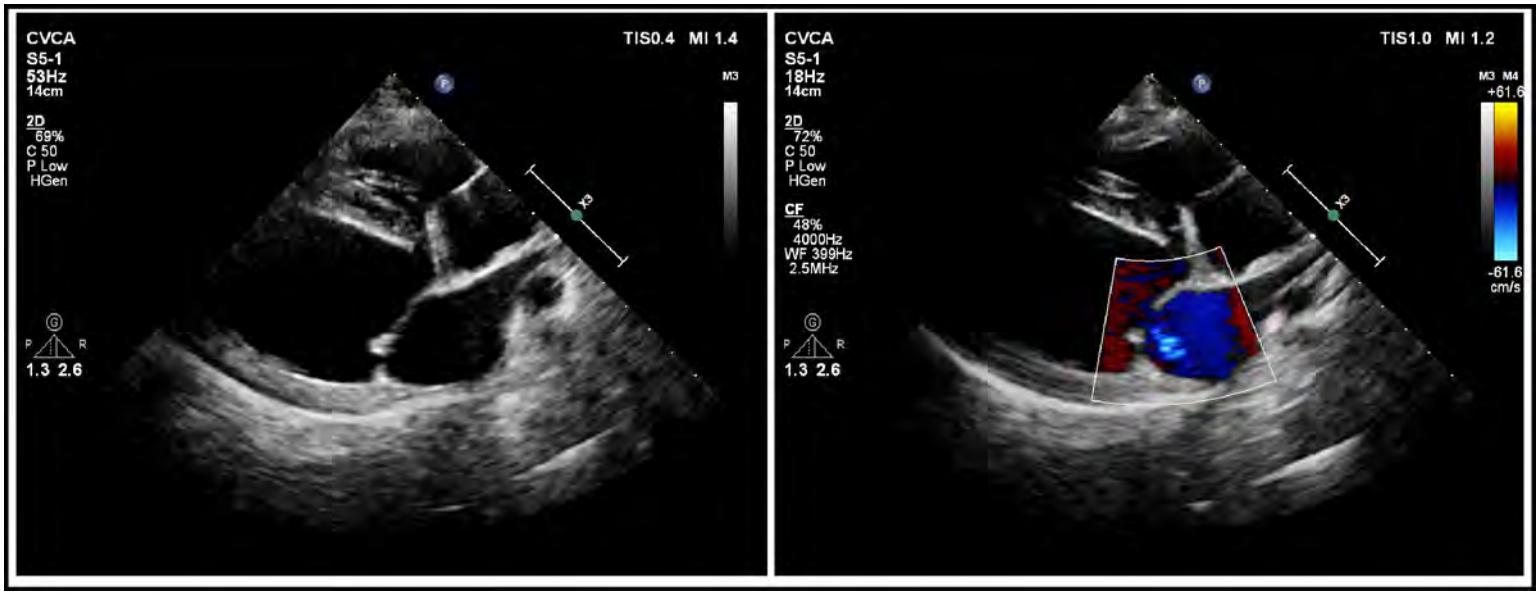
Doppler

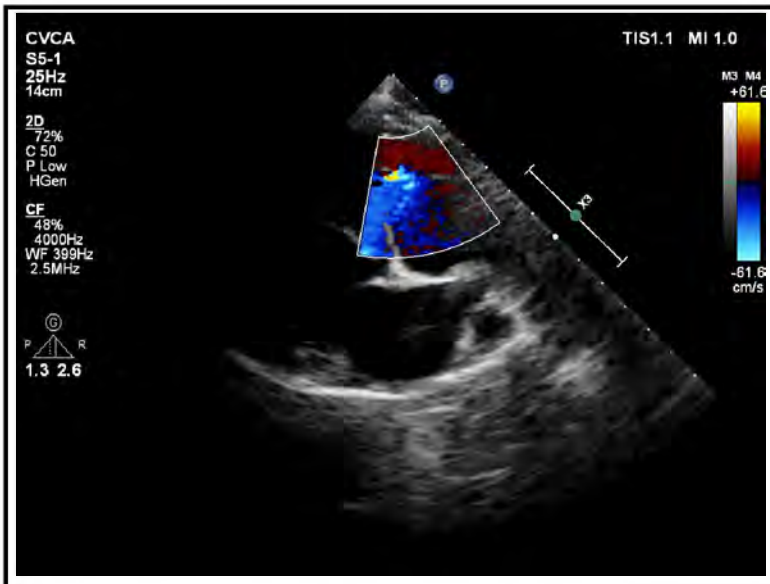
LVOT Vmax		MV E/A	1.6	E`/A` Medial	1.3
Max PG	18 mmHg				
Vmax	211 cm/s				
RVOT Vmax		Med E` Vel	5.71 cm/s	TR Vmax	
Max PG	3 mmHg			Max PG	6 mmHg
Vmax	91.2 cm/s			Vmax	125 cm/s
MV Peak E Vel		E/Med E`	8.5		
Vel	0.488 m/s				
PG	1 mmHg				
MV Peak A Vel		Med A` Vel	4.54 cm/s		
Vel	30.8 cm/s				
PG	0 mmHg				

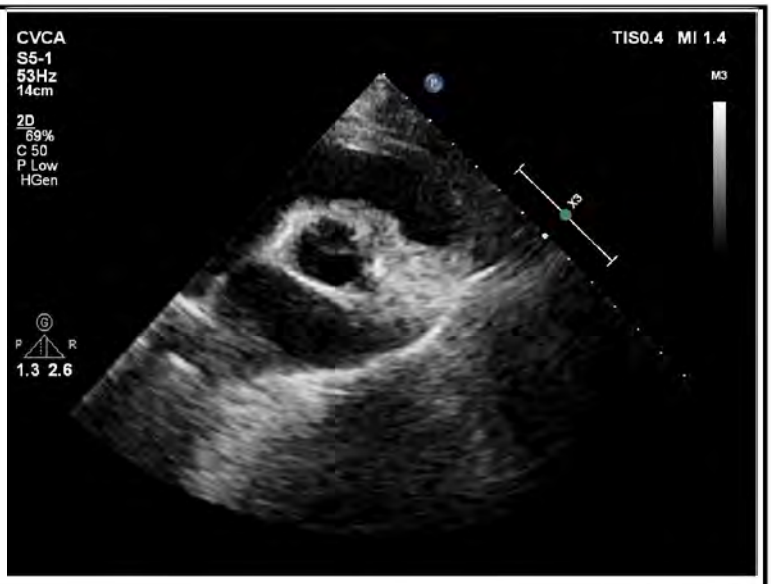
Other Measurements

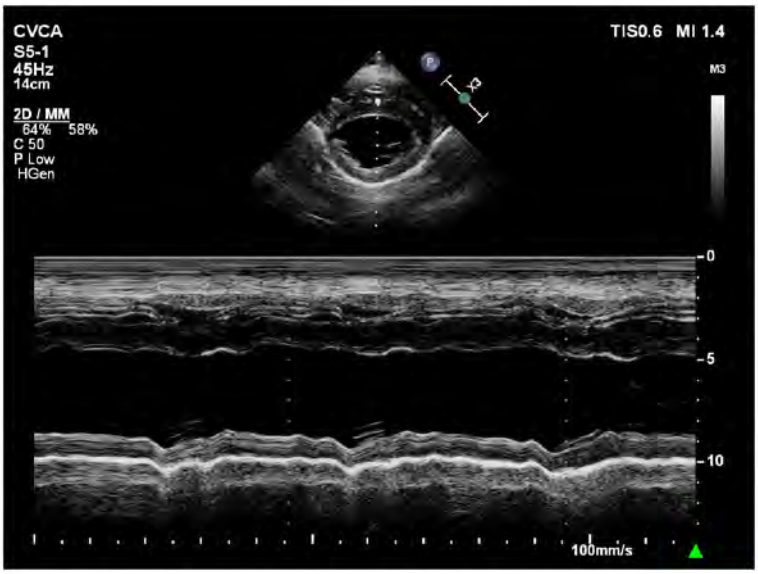
Dimensions: Diameters	
LVID/Ao (2D)	2.09
EDVI	57.4 ml/m²
ESVI	30.9 ml/m²
EF & Volume: Simpson's	
Sphericity Id	1.2
Dimensions: Diameters	
LVEDDN	1.77
LVID/Ao (2D)	2.09

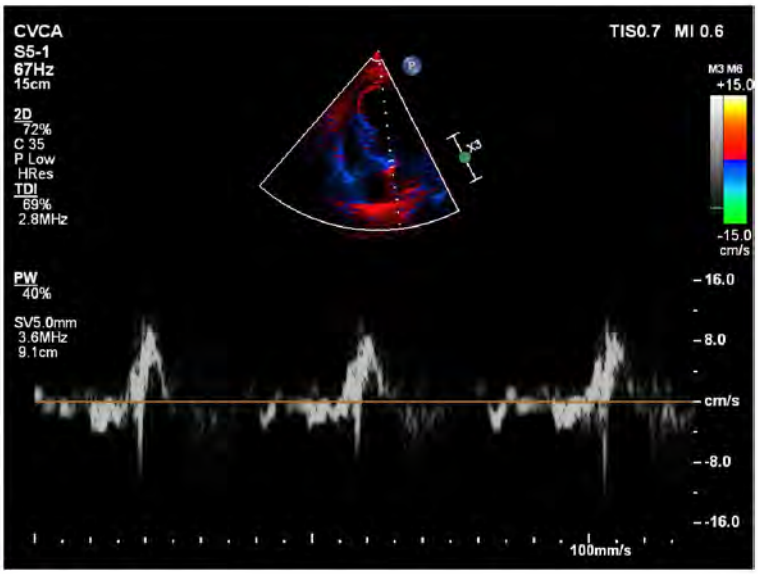
Images

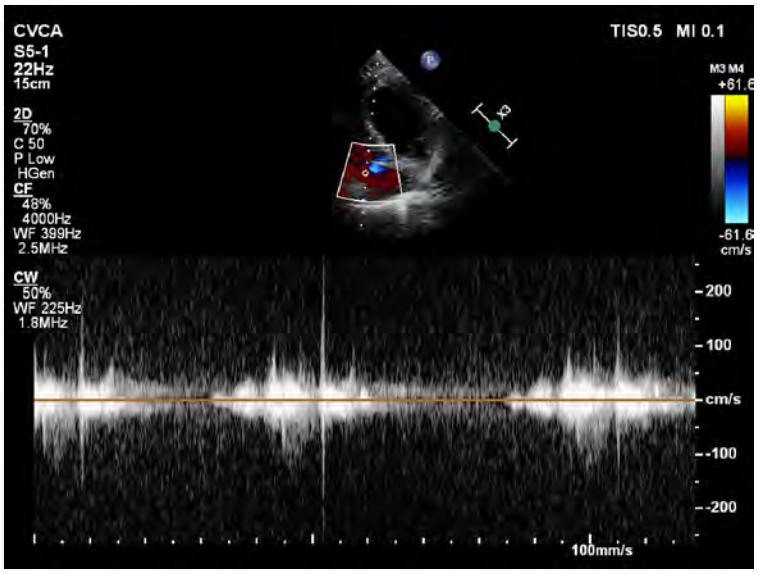












Signature

Signature:

Name(Print): Date:

CVCA, Cardiac Care for Pets
(b) (6)
Phone: (b) (6)
Email: (b) (6)@cvcavets.com
www.cvcavets.com

CVCA
Cardiac Care for Pets

Client: (b) (6)
Co-owner:
Patient name: (b) (6)
Species: Canine
Breed: Labrador Retriever
Sex: FS
Age: 13 years and 5 months old
Weight: 33.18kg. / 73.15 lbs

(b) (6)

Cardiac Evaluation Report
Exam Date: 10/31/2017

Diagnosis

- Advanced dilated cardiomyopathy - ruleout idiopathic vs. taurine-responsive
- Mild to moderate mitral valve regurgitation as cause of heart murmur
- Trace tricuspid valve regurgitation
- Moderate to severe left atrial chamber dilation
- Severe eccentric left ventricular chamber dilation
- Moderate to severe decrease in contractility/heart muscle function
- Mild left ventricular wall thinning
- Mild right atrial and right ventricular chamber dilation
- Progressive cough - rule out: early left sided congestive heart failure vs. mainstem bronchial compression

Medications

- Begin Lasix/Furosemide 40 mg tablets - Give 1 tablet twice daily.
  > For mild increases in respiratory rate/effort, you may give an additional dose of Lasix.
  > If you are consistently giving an additional dose of Lasix, please contact our office so we may help adjust medications long-term.
  > We may increase this dose in the future based on at home monitoring of breathing and recheck blood work.
- Begin Benazapril 10 mg tablets - Give 1 tablet twice daily for 4 days then increase to 1 and 1/2 tablet twice daily thereafter.
- Begin Vetmedin/Pimobendan 5mg tablets - Give 1 and 1/2 tablets twice daily. Will switch to 7.5 mg EZ tablets at 1 tablet twice daily. The 7.5mg tablet will be compounded through (b) (6), please call them to set up shipping and billing (b) (6)

- Please call if you notice a decrease in appetite, vomiting, lethargy, weakness or any other signs of illness while beginning/adjusting the medications.
- Continue with monthly heartworm and flea/tick control as prescribed by (b) (6)

In 2 weeks, if (b) (6) is eating and feeling well:

- Begin Spironolactone 25 mg tablets - Give 1 tablet once daily for 4 days then increase to 1 tablet twice daily thereafter.

- Begin Taurine 1500 mg twice daily.
- Begin L-carnitine 1500 mg three times daily.
- You may purchase the taurine and L-carnitine at any health food or nutrition store or www.puritanspride.com. You may also obtain the L-carnitine in bulk powder form from North Carolina State University by calling 919-513-6325.

Please allow 24-48 hours for CVCA to process prescription refill requests.
Refill all medications indefinitely unless directed by CVCA or your primary care veterinarian.

- **Please check all medications and dosages on your discharge report against the pharmacy labels.**

Please Note

- Please see our website www.cvcavets.com for more information about (b) (6) dilated cardiomyopathy.

Nutrition Recommendations:

- (b) (6) is on a specialized diet which could be contributing to taurine deficiency. Please change her to a new diet, as her housemate is on a novel protein diet - consider prescription diets such as Royal Canin or Science Diet. Please discuss diet options with (b) (6)
- In patients with early/mild heart failure, CVCA recommends feeding a diet with less than 80 mg of sodium per 100 kCal of food (50-80 mg/100 kCal). In patients with refractory heart failure signs, further sodium restriction may be beneficial.
- For more information about sodium content of various foods, please visit:
  - Dog: http://vet.tufts.edu/wp-content/uploads/reduced_sodium_diet_for_dogs.pdf
  - Treats: http://vet.tufts.edu/wp-content/uploads/treats_for_dogs_with_heart_disease.pdf

- CVCA recommends avoiding kidney diets unless (b) (6) has kidney disease that warrants protein restriction.
- Diet changes should be done gradually (ie. over ~1 month) to avoid GI upset and avoided until (b) (6) is stable and eating well on the cardiac medications, usually about 2 weeks after starting or adjusting therapy.
- If you are interested in a consultation with a veterinary nutritionist, please visit -http://vetnutrition.tufts.edu/make-an-appointment/
- CVCA recommends fish oil supplements (omega-3 fatty acids) in many dogs with cardiac disease. Her dose should be approximately EPA 1220 mg and DHA 760 mg total per day. Please start at 1/2 the dose for one week, then increase to the full dose if tolerating well thereafter. Please avoid Cod liver oil and flax seed as well as products with Vit A and/or D.
  For more information about fish oils, please visit --http://vet.tufts.edu/heartsmart/diet/important-nutrients-for-pets-with-heart-disease/
- In addition to the supplements approved by Tuft's Veterinary Nutrition Service, other reputable brands include Welactin and Nordic Naturals. (b) (6) may have additional brand recommendations.

Activity Recommendations:

- Keep (b) (6) very quiet for the next 3-4 days with only brief leash walks to eliminate.
- Once her coughing has resolved, (b) (6) may gradually resume activity as she wants and is able to do. Please allow (b) (6) to take more breaks and rest during activity.
- Please try avoid burst type activity, as this increases the arrhythmia risk and avoid exercise in the hot/humid weather.
- Please try to warm (b) (6) up for 5-10 minutes with walking prior to moderate activity and take more rests during more vigorous activity.

At Home Monitoring:

- Monitor for signs of cough, respiratory difficulty, exercise intolerance, abdominal swelling, weakness, lethargy, etc. If you note any of these symptoms, please notify CVCA or (b) (6) as these symptoms may indicate recurrent congestive heart failure. If you note an increase in cough, respiratory rate or effort, please feel free to give an additional dose of Lasix/Furosemide, while contacting CVCA.
- In order to monitor for the development of early congestive heart failure in the out-patient setting, we recommend monitoring your pet's resting respiratory rate several times a week. Normal resting respiratory rates should be less than 30 breaths per minute. Consider using a respiratory rate monitoring application to track (b) (6) respiratory rate - Cardalis or BI Pharma have reliable phone applications. Please contact us if you note a persitent or progressive increase.
- In addition, (b) (6) is sadly at increased risk for sudden cardiac death due to her cardiac disease. Dobermans are particularly at risk for development of severe, sudden malignant arrhythmias that sadly may result in sudden death. However, we hope to minimize these risks with our treatment plan.

Future Anesthesia/Fluid Recommendations

- Avoid intravenous or subcutaneous fluid therapy in the future, if possible. If fluid therapy is indicated, please contact CVCA.
- (b)(6) should not receive corticosteroids (prednisone) in the future please contact CVCA for recommendations, if corticosteroids are indicated.
- Avoid elective anesthesia, as (b)(6) is at high risk for complications due to the degree of cardiac disease. If anesthesia is necessary in the future, please contact CVCA for recommendations for monitoring and anesthetics.

Reevaluation

- Please recheck with (b) (6) in the next day or two to obtain taurine levels. Please forward these results when available.
- Please recheck with (b) (6) in 2 weeks for a follow up examination and blood chemistry profile with electrolytes and as recommended by (b) (6) Please forward these results when available.
- Please recheck with (b) (6) every 4-6 months for a follow up examination and blood chemistry profile with electrolytes and as recommended by (b) (6) Please forward these results when available.
- Please recheck with CVCA in 5 months for a follow up consultation/examination, blood pressure, and echocardiogram. Please contact us or schedule an earlier appointment if (b)(6) has any problems or symptoms indicative of worsening heart disease or if recommended by (b) (6)

Visit Summary

Heart Rate: 132 bpm **BP**: 100mmHg (based on MR gradient)

History:

(b)(6) developed a cough last Wednesday (10/25/17). Radiographs and blood work were performed by (b) (6) The lab work (which is unavailable for review) reportedly showed an elevated ALP 440 and GGT 30 and mild lymphopenia. Thoracic radiographs were performed which revealed cardiomegaly. (b)(6) was treated with hydroxyzine 50mg BID, doxycycline 200mg AM and 100mg PM, and hydrocodone 5mg q8-12h. All medications were stopped on Monday as her cough had worsened and she was presented to the (b) (6) for a cardiac evaluation as her coughing had worsened and she had brought up a small volume of pink-tinged foam after a coughing fit. During this time there has been no evidence of lethargy and she continues to eat and drink normally at home.

PPHx: None
Meds: None
Other: UTD on vaccinations, On HW preventative
Diet: Zignature (Kangaroo)

Physical Exam Findings:

BAR, sweet but nervous
OP/EENT: Pink, moist mucous membranes, CRT <2s, mild periodontal disease, LS OU, clear AU, No nasal or ocular discharge, no cough on tracheal palpation
PLN: WNL
H/L: Grade 2/6 left apical protosystolic heart murmur, regular rhythm, strong synchronous femoral pulses, RR: 36 breaths/min, questionable mild increase in bronchovesicular sounds bilaterally, no crackles or wheezes ausculted, eupneic
Abd: Soft non-painful abdominal palpation, no palpable masses or fluid wave
MS/Neuro: BCS 5/9, Amb x 4, Mentally alert and appropriate
Integ: Normal turgor, subcutaneous mass left ventrum

Other Diagnostics:

10/27/17 pDVM CXR: Generalized cardiomegaly characterized by widening of the cardiac silhouette and loss of the caudal cardiac waist consistent with left atrial enlargement. Slight left auricular bulge. Increased sternal contact and rounding of the right heart on the VD radiograph. Dorsal deviation of the trachea. Prominent pulmonary vasculature with a questionable mild increase in interstitial opacity in the caudodorsal lung fields which may suggest early congestive heart failure/pulmonary edema.

Echocardiographic Findings

Severe left ventricular eccentric hypertrophy with apical rounding and increased spherocity, mild-moderate centrally

located mitral regurgitant jet, moderate-severe secondary left atrial dilation on 2D imaging and moderately-severely increased LA:Ao ratio on M-mode imaging, mild eccentric low velocity tricuspid regurgitation with mildly elevated estimated right ventricular pressures consistent with mild pulmonary hypertension, mild right ventricular and right atrial dilation, normal left and right ventricular outflow velocities, moderately to severely depressed indices of systolic function (FS% and EF% by modified Simpson's - LVDI 144ml/m^2, LVSI 90ml/m^2), increased EPSS, elevated transmitral inflow velocities and E:A wave ratio on spectral Doppler tracings, normal TDI E':A' ratio of the lateral mitral annulus, no masses, effusions or heartworms observed.
ECG during echocardiogram: Normal sinus rhythm. No ventricular ectopy noted.

Comments

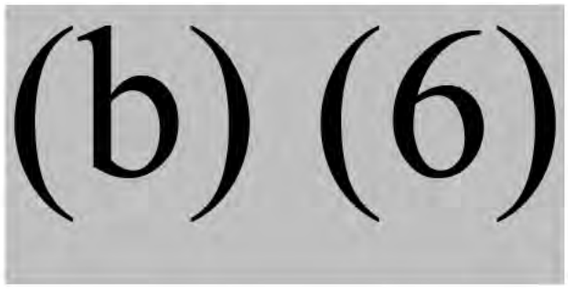
Dear (b) (6)

Thank you for sending (b) (6) to see us with (b) (6) today. Sadly, (b) (6) has dilated cardiomyopathy with moderate to severe systolic dysfunction and moderate to severe left atrial dilation. This places her at a high risk of developing congestive heart failure and with the progression in her cough I am concerned that we may be dealing with congestive heart failure at this time. We have begun therapy to control congestive heart failure, support cardiac function, slow down the progression of the heart disease and improve survival. We are now seeing more dogs on specialized diets that are developing taurine deficiency and we have discussed submission of taurine levels to evaluate whether this may be a contributing factor to (b) (6) condition. (b) (6) is interested in pursuing this test at your clinic, taurine levels should be drawn and placed in a heparinized tube (green top) and should be frozen and submitted to (b) (4) (who sends it to UC Davis). It will be interesting to see if this is a contributing factor to (b) (6) condition.

We will continue to closely monitor (b) (6) heart disease via serial echocardiography and institute further therapy when progression is noted. While on this course of medication, it is important to monitor the chemistry profiles and blood pressures. Dogs with dilated cardiomyopathy are at a higher risk of developing ventricular arrhythmias. None were noted today; however, it will be important to monitor for arrhythmias periodically in the future. Unfortunately, the prognosis is guarded after the onset of congestive heart failure, and we discussed with the (b) (6) family that the average survival is ~ 6-12 months.[1,2] Survival time is highly individually variable depending on response to therapy.

We appreciate your continued referrals and the trust you place in CVCA to co-manage your cardiac patients. We look forward to working with you on this case and others. In an effort to continue to improve CVCA's service to both you and your clients, please visit our website at www.cvcavets.com and complete our online referring veterinarian survey.

Sincerely,
(b) (6)



Case Summary:

(b) (6) a 13 Yrs. 0 Mos. old, spayed female, Labrador Retriever presented on (b) (6) to the (b) (6) for a coughing.

History: (b) (6) started coughing last Wednesday. She was brought to a primary veterinarian. Radiographs and blood work were performed. Radiographs revealed suspected cardiomegaly. Blood work showed mild ALP and GGT elevations. Prescribed hydroxyzine, doxycycline, and hydrocodone, which was stopped on Monday because her coughing got worse with those medications.
The owner made an appointment with a CVCA on Friday(11-1-2017). However her cough got worse with pink tinged foam so (b) (6) was brought to (b) (6) for a cardiology consultation.
(b) (6) has been a healthy dog with no current medications. She is up to date on vaccination and heartworm preventative.

CBC (10-27-2017) WNL
Chem (10-27-2017) ALP 440, GGT 30, other values were WNL
OVA & Parasites (7-17-2017) Negative

Physical Exam:

	(b)(6)
	1:47 PM
Vital Sign	656
Weight	30.5 kilograms
Temp	100.5
HR	100
Resp	42
Muc_Membrane	Pink/Healthy
CRT	<2 sec
Mentation	QAR
Pain Scale	0 - No visible Pain

BCS: 5/9
EENT: MM- pink. mild calculus and gingivitis, CRT <2 sec. Oral exam- no significant findings (NSF), Lenticular sclerosis on OU, throat -NSF.
Hydration appears: within normal limits (WNL)
Peripheral lymph nodes: Palpate WNL.
Airway: RR= 30 BPM, no upper respiratory noise, airway not compromised.
Respiration: RR= 24 RPM. Eupneic with no crackles or wheezes. Bilateral breath sounds ausculted, normal bronchovesicular sounds.
Cardiovascular: HR = 100 BPM, Heart auscults with NSF. No murmurs noted. Femoral pulses are adequate and synchronous.
Abdomen: Mildly tensed cranial abdomen on palpation, no organomegaly was noticed.
Neurologic: Alert and responsive. Ambulatory with no CP deficits noted. Full neurologic examination was not performed.

Integument: Hair coat has NSF. A 3cm x 3 cm soft subcutaneous mass was palpated on left caudal abdomen.
Musculoskeletal: Musculature is WNL.No obvious lameness or gait disturbance.
Urogenital: WNL
Rectal: Normal stool was palpated on rectal examination.

Initial Diagnostics:
Echocardiogram

Differential Diagnosis:
Coughs -R/O heart vs lung

Client Communication:

Plan:

Please call if you have any questions or concerns.

Thank you,

(b) (6)

(b) (6)

10/31/2017 Initial PE
(b) (6)

(b) (6)

(b) (6)	Name: (b) (6)	Species: Canine	Breed: Lab Retx	Color: Yellow	DOB: (b) (6)	SEX: F(S)

Date: 7/10/17 — 72 lbs Ivrab 3TF, 3yr, Tag #1520 (b) (6)
SNAP HW ⊖ lyme ⊖ ehr ⊖ ana ⊖
Fecal to (b) (6) (A) NPS
DW @ home occasionally coughs. Several SQ masses - no changes noted per O.
PE: BAR. H/L NSF - no audible murmurs, no cough elicited on tracheal palp. Abd NSF on palp. Min tartar. Several SQ masses - palpate lipomatous
P: Due 10/12/17 lyme & DHL vaccines (b) (6)
#305581 22.6^50 22.6^50 (b) (6)

7/12/17 — Disp: Advantix II Navy (>55 lbs) (#1) + 2 free doses
Heartgard ⊕ Brown Lepk (#1)
#305994 28.6^74 28.6^74 (b) (6)

10/23/17 — Disp: Advantix II Navy (>55 lb) 6pk (#1)
H/G to share w/ Bob
(b) (6)

10/27/17 — ~65.5 lbs ✓ Cough = x3-4d, not lethargic
T 100.7° — o/d ↓, no V/D, worse when lays down
PE: BAR. Numerous lipomatous & dermal masses. MM pink, euhydrated, min tartar. Abd nonpainful on palp. H/L - no audible murmurs or arrhythmia, no abn lung sounds. Breathing very shallow - thorax doesn't expand fully/normally - not dyspneic, no visible abd component to breathing
P: CBC/Chem ALP 440, ALT 30, lymphs very ↓, NS Fecal
R Lat thoracic X-ray: heart appears sl large

(b) (6)

(b) (6)	Name:	Species:	Breed:	Color:	DOB:	SEX:
	(b) (6)	Canine	Lab Ret	Yellow	(b) (6)	F(S)

Date: 10/27/17

Some ↑opacity in cd-dorsal lung fields
CONT: Trachea NSF. VHS ~ 13
VD thorax xray: R side of heart rounded, lung pattern less prominent on this view.
Reviewed xrays w/ D-discussion chronic lung fibrosis d/t age, cardiac, open.
DISC R side of heart looks ↑, DISCHNDz (⊖ test 3 mos ago & on HWP), DCM (heart not globoid), pericardial effusion (heart not globoid), etc
Rec await lab results, consider tx for allergic bronchitis, but rec cardiac workup if not improving.
Dog did not cough while in clinic except for tracheal cough when pulling on leash.
Called D-discuss GI HPI, mild ↑ ALP - not likely a concern at this time.
Rec meds below, call in 3-5d (b) (6) update.
DISP: Hydroxyzine 50mg #30, 1PO BID PRN
Hydrocodone 5mg #20, 1PO Q8-12H PRN
Doxycycline 100mg #40, 2PO am, 1PO pm

(b) (6)
(b) (6)
(b) (6)

(b) (4) (b) (6)

(b) (6)

Account: (b) (6)

Owner: (b) (6)
Patient:
Species: CANINE
Breed: LABRADOR_RETRIE
Age: 11Y
Gender: FS

Requisition #: (b) (6)
Accession #:
Order recv'd: 11/03/2017
Ordered by: (b)(6)
Reported: 11/10/2017

TAURINE (WHOLE BLOOD)

Test	Result			
TAURINE	168	(200 - 350)	L	

Testing performed at University of California, Davis

(b) (6)
11/10/2017

FINAL REPORT

CVCA, Cardiac Care for Pets
(b) (6)
Phone: (b) (6) Fax: (b) (6)
Email: (b) (6)@cvcavets.com
www.cvcavets.com

CVCA
Cardiac Care for Pets

Client: (b) (6)
Co-owner:
Patient name: (b) (6)
Species: Canine
Breed: Labrador Retriever
Sex: FS
Age: 13 years and 5 months old
Weight: 33.18kg. / 73.15 lbs

Primary Care Veterinarian: (b) (6)
Primary Care Hospital: (b) (6)
Phone (b) (6) ext:
Fax: (b) (6)
Email:

Cardiac Evaluation Report
Exam Date: 10/31/2017

Diagnosis

- Advanced dilated cardiomyopathy - ruleout idiopathic vs. taurine-responsive
- Mild to moderate mitral valve regurgitation as cause of heart murmur
- Trace tricuspid valve regurgitation
- Moderate to severe left atrial chamber dilation
- Severe eccentric left ventricular chamber dilation
- Moderate to severe decrease in contractility/heart muscle function
- Mild left ventricular wall thinning
- Mild right atrial and right ventricular chamber dilation
- Progressive cough - rule out: early left sided congestive heart failure vs. mainstem bronchial compression

Medications

- Begin Lasix/Furosemide 40 mg tablets - Give 1 tablet twice daily.
  > For mild increases in respiratory rate/effort, you may give an additional dose of Lasix.
  > If you are consistently giving an additional dose of Lasix, please contact our office so we may help adjust medications long-term.
  > We may increase this dose in the future based on at home monitoring of breathing and recheck blood work.
- Begin Benazapril 10 mg tablets - Give 1 tablet twice daily for 4 days then increase to 1 and 1/2 tablet twice daily thereafter.
- Begin Vetmedin/Pimobendan 5mg tablets - Give 1 and 1/2 tablets twice daily. Will switch to 7.5 mg EZ tablets at 1 tablet twice daily. The 7.5mg tablet will be compounded through (b) (6), please call them to set up shipping and billing (b) (6)

- Please call if you notice a decrease in appetite, vomiting, lethargy, weakness or any other signs of illness while beginning/adjusting the medications.
- Continue with monthly heartworm and flea/tick control as prescribed by (b) (6)

In 2 weeks, if (b) (6) is eating and feeling well:

- Begin Spironolactone 25 mg tablets - Give 1 tablet once daily for 4 days then increase to 1 tablet twice daily thereafter.

- Begin Taurine 1500 mg twice daily.
- Begin L-carnitine 1500 mg three times daily.
- You may purchase the taurine and L-carnitine at any health food or nutrition store or www.puritanspride.com. You may also obtain the L-carnitine in bulk powder form from North Carolina State University by calling 919-513-6325.

Please allow 24-48 hours for CVCA to process prescription refill requests.
Refill all medications indefinitely unless directed by CVCA or your primary care veterinarian.

- **Please check all medications and dosages on your discharge report against the pharmacy labels.**

Please Note

- Please see our website www.cvcavets.com for more information about (b) (6) dilated cardiomyopathy.

Nutrition Recommendations:

- (b) (6) is on a specialized diet which could be contributing to taurine deficiency. Please change her to a new diet, as her housemate is on a novel protein diet - consider prescription diets such as Royal Canin or Science Diet. Please discuss diet options with (b) (6)
- In patients with early/mild heart failure, CVCA recommends feeding a diet with less than 80 mg of sodium per 100 kCal of food (50-80 mg/100 kCal). In patients with refractory heart failure signs, further sodium restriction may be beneficial.
- For more information about sodium content of various foods, please visit:
  - Dog: http://vet.tufts.edu/wp-content/uploads/reduced_sodium_diet_for_dogs.pdf
  - Treats: http://vet.tufts.edu/wp-content/uploads/treats_for_dogs_with_heart_disease.pdf

- CVCA recommends avoiding kidney diets unless (b) (6) has kidney disease that warrants protein restriction.
- Diet changes should be done gradually (ie. over ~1 month) to avoid GI upset and avoided until (b) (6) is stable and eating well on the cardiac medications, usually about 2 weeks after starting or adjusting therapy.
- If you are interested in a consultation with a veterinary nutritionist, please visit -http://vetnutrition.tufts.edu/make-an-appointment/
- CVCA recommends fish oil supplements (omega-3 fatty acids) in many dogs with cardiac disease. Her dose should be approximately EPA 1220 mg and DHA 760 mg total per day. Please start at 1/2 the dose for one week, then increase to the full dose if tolerating well thereafter. Please avoid Cod liver oil and flax seed as well as products with Vit A and/or D.
  For more information about fish oils, please visit --http://vet.tufts.edu/heartsmart/diet/important-nutrients-for-pets-with-heart-disease/
- In addition to the supplements approved by Tuft's Veterinary Nutrition Service, other reputable brands include Welactin and Nordic Naturals. (b) (6) may have additional brand recommendations.

Activity Recommendations:

- Keep (b) (6) very quiet for the next 3-4 days with only brief leash walks to eliminate.
- Once her coughing has resolved, (b) (6) may gradually resume activity as she wants and is able to do. Please allow (b) (6) to take more breaks and rest during activity.
- Please try avoid burst type activity, as this increases the arrhythmia risk and avoid exercise in the hot/humid weather.
- Please try to warm (b) (6) up for 5-10 minutes with walking prior to moderate activity and take more rests during more vigorous activity.

At Home Monitoring:

- Monitor for signs of cough, respiratory difficulty, exercise intolerance, abdominal swelling, weakness, lethargy, etc. If you note any of these symptoms, please notify CVCA or (b) (6) as these symptoms may indicate recurrent congestive heart failure. If you note an increase in cough, respiratory rate or effort, please feel free to give an additional dose of Lasix/Furosemide, while contacting CVCA.
- In order to monitor for the development of early congestive heart failure in the out-patient setting, we recommend monitoring your pet's resting respiratory rate several times a week. Normal resting respiratory rates should be less than 30 breaths per minute. Consider using a respiratory rate monitoring application to track (b) (6) respiratory rate - Cardalis or BI Pharma have reliable phone applications. Please contact us if you note a persitent or progressive increase.
- In addition, (b) (6) is sadly at increased risk for sudden cardiac death due to her cardiac disease. Dobermans are particularly at risk for development of severe, sudden malignant arrhythmias that sadly may result in sudden death. However, we hope to minimize these risks with our treatment plan.

Future Anesthesia/Fluid Recommendations:

- Avoid intravenous or subcutaneous fluid therapy in the future, if possible. If fluid therapy is indicated, please contact CVCA.
- (b) (6) should not receive corticosteroids (prednisone) in the future please contact CVCA for recommendations, if corticosteroids are indicated.
- Avoid elective anesthesia, as (b) (6) is at high risk for complications due to the degree of cardiac disease. If anesthesia is necessary in the future, please contact CVCA for recommendations for monitoring and anesthetics.

Reevaluation

- Please recheck with (b) (6) in the next day or two to obtain taurine levels. Please forward these results when available.
- Please recheck with (b) (6) in 2 weeks for a follow up examination and blood chemistry profile with electrolytes and as recommended by (b) (6) Please forward these results when available.
- Please recheck with (b) (6) every 4-6 months for a follow up examination and blood chemistry profile with electrolytes and as recommended by (b) (6) Please forward these results when available.
- Please recheck with CVCA in 5 months for a follow up consultation/examination, blood pressure, and echocardiogram. Please contact us or schedule an earlier appointment if (b) (6) has any problems or symptoms indicative of worsening heart disease or if recommended by (b) (6)

Visit Summary

Heart Rate: 132 bpm **BP**: 100mmHg (based on MR gradient)

History:

(b) (6) developed a cough last Wednesday (10/25/17). Radiographs and blood work were performed by (b) (6) The lab work (which is unavailable for review) reportedly showed an elevated ALP 440 and GGT 30 and mild lymphopenia. Thoracic radiographs were performed which revealed cardiomegaly. (b) (6) was treated with hydroxyzine 50mg BID, doxycycline 200mg AM and 100mg PM, and hydrocodone 5mg q8-12h. All medications were stopped on Monday as her cough had worsened and she was presented to the (b) (6) for a cardiac evaluation as her coughing had worsened and she had brought up a small volume of pink-tinged foam after a coughing fit. During this time there has been no evidence of lethargy and she continues to eat and drink normally at home.

PPHx: None
Meds: None
Other: UTD on vaccinations, On HW preventative
Diet: Zignature (Kangaroo)

Physical Exam Findings:

BAR, sweet but nervous
OP/EENT: Pink, moist mucous membranes, CRT <2s, mild periodontal disease, LS OU, clear AU, No nasal or ocular discharge, no cough on tracheal palpation
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Abd: Soft non-painful abdominal palpation, no palpable masses or fluid wave
MS/Neuro: BCS 5/9, Amb x 4, Mentally alert and appropriate
Integ: Normal turgor, subcutaneous mass left ventrum

Other Diagnostics:

10/27/17 pDVM CXR: Generalized cardiomegaly characterized by widening of the cardiac silhouette and loss of the caudal cardiac waist consistent with left atrial enlargement. Slight left auricular bulge. Increased sternal contact and rounding of the right heart on the VD radiograph. Dorsal deviation of the trachea. Prominent pulmonary vasculature with a questionable mild increase in interstitial opacity in the caudodorsal lung fields which may suggest early congestive heart failure/pulmonary edema.

Echocardiographic Findings

Severe left ventricular eccentric hypertrophy with apical rounding and increased spherocity, mild-moderate centrally

located mitral regurgitant jet, moderate-severe secondary left atrial dilation on 2D imaging and moderately-severely increased LA:Ao ratio on M-mode imaging, mild eccentric low velocity tricuspid regurgitation with mildly elevated estimated right ventricular pressures consistent with mild pulmonary hypertension, mild right ventricular and right atrial dilation, normal left and right ventricular outflow velocities, moderately to severely depressed indices of systolic function (FS% and EF% by modified Simpson's - LVDI 144ml/m^2, LVSI 90ml/m^2), increased EPSS, elevated transmitral inflow velocities and E:A wave ratio on spectral Doppler tracings, normal TDI E':A' ratio of the lateral mitral annulus, no masses, effusions or heartworms observed.
ECG during echocardiogram: Normal sinus rhythm. No ventricular ectopy noted.

Comments

Dear (b) (6),

Thank you for sending (b) (6) to see us with (b) (6) today. Sadly (b) (6) has dilated cardiomyopathy with moderate to severe systolic dysfunction and moderate to severe left atrial dilation. This places her at a high risk of developing congestive heart failure and with the progression in her cough I am concerned that we may be dealing with congestive heart failure at this time. We have begun therapy to control congestive heart failure, support cardiac function, slow down the progression of the heart disease and improve survival. We are now seeing more dogs on specialized diets that are developing taurine deficiency and we have discussed submission of taurine levels to evaluate whether this may be a contributing factor to (b) (6) condition. (b) (6) is interested in pursuing this test at your clinic, taurine levels should be drawn and placed in a heparinized tube (green top) and should be frozen and submitted to (b) (4) (who sends it to UC Davis). It will be interesting to see if this is a contributing factor to (b) (6) condition.

We will continue to closely monitor (b) (6) heart disease via serial echocardiography and institute further therapy when progression is noted. While on this course of medication, it is important to monitor the chemistry profiles and blood pressures. Dogs with dilated cardiomyopathy are at a higher risk of developing ventricular arrhythmias. None were noted today; however, it will be important to monitor for arrhythmias periodically in the future. Unfortunately, the prognosis is guarded after the onset of congestive heart failure, and we discussed with the (b) (6) family that the average survival is ~ 6-12 months.[1,2] Survival time is highly individually variable depending on response to therapy.

We appreciate your continued referrals and the trust you place in CVCA to co-manage your cardiac patients. We look forward to working with you on this case and others. In an effort to continue to improve CVCA's service to both you and your clients, please visit our website at www.cvcavets.com and complete our online referring veterinarian survey.

Sincerely,

(b) (6)

CVCA, Cardiac Care for Pets
(b) (6)
Phone: (b) (6) Fax: (b) (6)
Email: (b) (6)@cvcavets.com
www.cvcavets.com

Client: (b) (6)
Co-owner:
Patient name: (b) (6)
Species: Canine
Breed: Labrador Retriever
Sex: FS
Age: 13 years and 5 months old
Weight: 33.18kg. / 73.15 lbs

Primary Care Veterinarian: (b) (6)
Primary Care Hospital: (b) (6)
Phone: (b) (6) ext:
Fax: (b) (6)
Email:

Cardiac Evaluation Report
Exam Date: 02/26/2018

Diagnosis
- Mild, improved dilated cardiomyopathy - suspect taurine-responsive
- Mild, improved mitral and very mild tricuspid valve regurgitation as cause of heart murmur
- Normal, improved left atrial chamber dilation
- Mild, improved eccentric left ventricular chamber dilation
- Low normal, improved left ventricular contractility/heart muscle function
- Cough - suspect bronchial/primary respiratory disease

Medications
- Decrease Lasix/Furosemide 40 mg tablets - Give 1 and 1/2 tablets twice daily for 1 week then decrease to 1 tablet twice daily for 1 week then decrease to 1/2 tablet twice a day for 1 week then discontinue. Please call if you note an increase respiratory rate while decreasing the Lasix. If there is an increase in cough (but normal respiratory rate), we will consider adding in a bronchodilator.
- Continue Benazapril 10 mg tablets - Give 1 and 1/2 tablets twice daily
  Continue Vetmedin/Pimobendan 7.5 mg EZ tablets - Give 1 tablet twice daily.
- Continue Spironolactone 25 mg tablets - Give 1 tablet twice daily.
- Continue Taurine 1500 mg twice daily.
- Continue L-carnitine 1500 mg three times daily.
- You may purchase the taurine and L-carnitine at any health food or nutrition store or www.puritanspride.com. You may also obtain the L-carnitine in bulk powder form from North Carolina State University by calling 919-513-6325.
- Continue with monthly heartworm and flea/tick control as prescribed by (b) (6)

Please allow 24-48 hours for CVCA to process prescription refill requests.
Refill all medications indefinitely unless directed by CVCA or your primary care veterinarian.
- **Please check all medications and dosages on your discharge report against the pharmacy labels.**

Please Note
- Please see our website www.cvcavets.com for more information about (b) (6) dilated cardiomyopathy.

Nutrition Recommendations:

- Continue the Royal Canin Early Cardiac diet.
- Consider fish oil supplements (omega-3 fatty acids). Her dose is approximately EPA 1220 mg and DHA 760 mg total per day. Please start at 1/2 the dose for one week, then increase to the full dose if tolerating well thereafter. Please avoid Cod liver oil and flax seed as well as products with Vit A and/orD.

For more information about fish oils, please visit -- http://vet.tufts.edu/heartsmart/diet/important-nutrients-for-pets-with-heart-disease/

- In addition to the supplements approved by Tuft's Veterinary Nutrition Service, other reputable brands include Welactin and Nordic Naturals. (b) (6) may have additional brand recommendations.

Activity Recommendations:

- Continue normal activity as she wants and is able to do. Please allow (b) (6) to take more breaks and rest during activity.
- Please avoid exercise in the hot/humid weather.

At Home Monitoring:

- In order to monitor for the development of early congestive heart failure in the out-patient setting, we recommend monitoring your pet's resting respiratory rate several times a week. Normal resting respiratory rates should be less than 30 breaths per minute. Consider using a respiratory rate monitoring application to track (b) (6) respiratory rate - Cardalis or BI Pharma have reliable phone applications. Please contact us if you note a persitent or progressive increase.

Future Anesthesia/Fluid Recommendations:

- We expect (b) (6) to tolerate carefully monitored general anesthesia with normal preoperative bloodwork and a balanced anesthetic regimen. During anesthesia, we recommend careful monitoring of ECG, BP and pulse ox and½ usual surgical fluid rate (ie: 2-4 ml/kg/hr). Carefully monitor for several hours post-operatively for signs of respiratory congestion and consider chest radiographs if these signs occur. There is some risk associated with all anesthetic events.
- Avoid medications with tachycardia as a side effect, such as ketamine, telazol and glycopyrrolate. Cleared for low dose atropine if needed for intraprocedure bradycardia. Avoid medications that significantly alter blood pressure such as acepromazine and Domitor.
- (b) (6) should not receive corticosteroids (prednisone) in the future please contact CVCA for recommendations, if corticosteroids are indicated.

Reevaluation

- Recheck with (b) (6) in the next 2-4 weeks and every 6 months for wellness care as directed, close auscultation, blood pressure and complete lab tests including blood and urine testing (CBC/Chemistry/Urinalysis/ Thyroid evaluation). Please forward these results when available.
- Please recheck with CVCA in 6 months for a follow up consultation/examination, blood pressure, and echocardiogram. Please contact us or schedule an earlier appointment if (b) (6) has any problems or symptoms indicative of worsening heart disease or if recommended by (b) (6)

We thank you for trusting in CVCA to care for (b) (6) today. Please do not hesitate to call us with any questions or concerns.

Sincerely,

(b) (6)

Visit Summary

Heart Rate: 130 **BP**: 155 mmHg **Cuff Size/Location:** 6 cuff/LF

History: Recheck DCM, suspected early CHF; doing well; RRR - 16 bpm, increased Lasix in January due to increased cough; cough seems to be intermittent and related to excitement; good appetite; 3 kg weight gain since 10/2017; walks 30-45 minutes per day - slow pace, at times winded but recovers very quickly.

(b)(6) developed a cough last Wednesday (10/25/17). Radiographs and blood work were performed by (b) (6) The lab work (which is unavailable for review) reportedly showed an elevated ALP 440 and GGT 30 and mild lymphopenia. Thoracic radiographs were performed which revealed cardiomegaly. (b) (6) was treated with hydroxyzine 50mg BID, doxycycline 200mg AM and 100mg PM, and hydrocodone 5mg q8-12h. All medications were stopped on Monday as her cough had worsened and she was presented to the (b) (6) for a cardiac evaluation as her coughing had worsened and she had brought up a small volume of pink-tinged foam after a coughing fit. During this time there has been no evidence of lethargy and she continues to eat and drink normally at home.

PPHx: None
Meds: None
Other: UTD on vaccinations, On HW preventative
Diet: changed from Zignature (Kangaroo) to Royal Canin Early Cardiac

Physical Exam Findings: 3/6 pansystolic murmur, PMI - mitral valve, regular rhythm with S3 gallop; LUNGS - clear all fields, panting, normal effort; Sl. overweight body condition (BCS - 6/9); Pink mm; PP - SS; PLN - WNL; ABD - hepatomegaly; BAR

Echocardiographic Findings

Mild left ventricular eccentric dilation - significant improvement compared to previous exam; mild, improved centrally located mitral regurgitant jet, normal, improved left atrial dimensions on 2D imaging and on M-mode imaging, mild, low velocity eccentric low velocity tricuspid regurgitation, subjectively normal right ventricular and right atrial dimensions, normal left and right ventricular outflow velocities, low normal, improved indices of systolic function (FS% and EF% by modified Simpson's, normal EPSS, normal transmitral inflow velocities and E:A wave ratio on spectral Doppler tracings, normal TDI E':A' ratio of the lateral mitral annulus, no masses, effusions or heartworms observed.

Comments

Dear (b) (6),

Thank you for sending (b) (6) to see us with (b) (6) today. I am quite pleased with (b) (6) exam today. She has had remarkable improvement in her echocardiogram with the cardiac medications, change in diet and supplementation with Taurine and L-carnitine. Her risk for congestive heart failure at this point is very low so we will be weaning (b) (6) off the Lasix/furosemide while (b) (6) monitors (b) (6) respiratory rate. Her current cough is likely due to respiratory disease and if the cough progresses/worsens, we will consider adding in a bronchodilator, such as Theophylline. Right now, with the marked improvement, (b) (6) long-term prognosis has improved considerably. I suspect we will be able to further discontinue cardiac medications if her heart remains stable. We will continue to closely monitor (b) (6) heart disease via serial echocardiography and institute further therapy when progression is noted. While on this course of medication, it is important to monitor the chemistry profiles and blood pressures. Hopefully (b) (6) will continue to do so well - she's a sweety!

We appreciate your continued referrals and the trust you place in CVCA to co-manage your cardiac patients. We look forward to working with you on this case and others. In an effort to continue to improve CVCA's service to both you and your clients, please visit our website at www.cvcavets.com and complete our online referring veterinarian survey.

Sincerely,

(b) (6)

(b) (4)

(b) (6)

(b) (6)

Account: (b) (6)

(b) (6)

Owner: (b) (6)
Patient:
Species: CANINE
Breed: LABRADOR_RETRIE
Age: 11Y
Gender: FS

Requisition #: (b) (6)
Accession #:
Order recv'd: 11/03/2017
Ordered by: (b) (6)
Reported: 11/10/2017

TAURINE (WHOLE BLOOD)

Test	Result			
TAURINE	168	(200 - 350)	L	

Testing performed at University of California, Davis

Vet-LIRN Final Case Report

A. Case Identification:

Case Number: 800.218

Vet-LIRN Director: Renate Reimschuessel, VMD, PhD

Program: Vet-LIRN

Division Code: HFV – 500

Other Investigators:

Jennifer Jones, DVM	Vet-LIRN
Sarah Nemser, MS	Vet-LIRN
Olgica Ceric, DVM, PhD	Vet-LIRN
Jake Guag, MPH	Vet-LIRN
David Rotstein, DVM, MPH	OS&C CERT
Lee Anne Palmer, VMD, MPH	OS&C DVPS
Lauren Carey, DVM	OS&C DVPS

B. Descriptive Title of Case:

Investigation of two dogs with dilated cardiomyopathy after consuming California Natural Venison and Green Lentil food and California Natural Kangaroo and Lentil dog foods.

Address of Vet-LIRN Program Office:

Mod II
Center for Veterinary Medicine
Office of Research
8401 Muirkirk Road
Laurel, MD 20708

C. Initiation and Completion Date: Initiation Date: 7/13/2017
Completion Date: 8/22/2017
Final Report Submission Date: 11/1/2017

Case Summary

Complaint: July 13, 2017, Vet-LIRN received consumer complaint, EON-323515, reporting dilated cardiomyopathy in two dogs after consuming California Natural Venison and Green Lentil food and California Natural Kangaroo and Lentil dog foods.

Signalment:

- (b)(6) 7 yr MC Miniature Schnauzer
- (b)(6) 2 yr MC Miniature Schnauzer-deceased

Signs: syncopal episodes, dyspnea, cough, heart failure

Medical Records: Vet-LIRN collected and reviewed medical records.

Name	Clinical Signs	Physical Exam	Lab Work	Significant Medical History
(b)(6)	syncopal episodes, hyporexia	P 130 bpm, mild increased breath sounds-all lung fields	suspected DCM, taurine & carnitine normal; negative infectious disease & nutritional disease testing	
(b)(6)	dyspnea, cough, inappetance, regurgitation,	P 160 bpm, R 64 rpm, pale pink mm, Gr I-II/VI left apical systolic murmur; hypokinetic, synchronous femoral pulse, jugular venous distention	P 11.7, BG 225, ALT 147, AST 1006, CK 35,930; Toxic NP, Plt 97; hepatomegaly, biventricular heart failure, cardiogenic edema; Necropsy: Suspect primary non-cardiogenic etiology	coffee brown urine with clumps after strenuous activity & hot outside-resolves with 24-36 hours; Crystalluria

Owner Interview: Vet-LIRN did not conduct an owner interview. However, the veterinarian mentioned:

- The owner alternated feedings between the two products
- The owner did not feed anchovies, sardines, or seafood in February or chronically
- The two dogs were from genetically different lineages
- (b)(6) had clinical signs at the time (b)(6) was treated but didn't present with CHF for several months

Response: Vet-LIRN collected medical records for review and leftover open product (Kangaroo flavor) for taurine, carnitine, and fumonisin testing.

Results: The food tested negative for fumonisin. The food taurine level (0.26% estimated Dry Matter Basis) was above the minimum level in cats (no AAFCO minimum for dogs). The food carnitine level is 0.0077% estimated on a Dry Matter Basis. There is no AAFCO carnitine minimum for dogs or cats. It is unclear whether or not the food carnitine is low, normal, or high.

Conclusion: Dilated cardiomyopathy (DCM) can be caused by a variety of etiologies including, genetic[2] (breed related), toxic[3,4] (fumonisin, acrolein[5], domoic acid, doxorubicin, lily of valley, digitalis, ionophores, sicklepod, gossypol, white snake root, ethyl alcohol, foxglove, buttercups), infectious (Bartonellosis, *Trypanosoma cruzi*), and nutritional deficiency[1] (e.g. taurine, protein restricted diets with stones, carnitine deficiency). The two genetically unrelated dogs were fed the same foods and began to experience clinical signs approximately the same time. The medical records indicate infectious disease and nutritional deficiency are unlikely etiologies. (b)(6) records indicated elevated liver enzymes and CK values, which could support a hepatotoxic and myotoxic (cardio +/- muscle) exposure. Because (b)(6) presented six months after (b)(6), it is unknown if (b)(6) also had elevated liver enzymes when (b)(6) was ill. The history also suggested no exposure to doxorubicin or domoic acid. Vet-LIRN tested the leftover bag of food from (b)(6) illness time (June 2017), but not from January, when both dogs were initially ill. A test for acrolein was not available.

The cause of the two dogs' DCM is unclear, but is likely an environmental toxin exposure. Based on the dogs' blood taurine/carnitine levels and the dry dog food test results, it is unlikely that Fumonisin, taurine, or carnitine levels in the food caused the dogs' illness.

References:

1. Sanderson SL. Taurine and Carnitine in Canine Myopathy. Vet Clin Small Anim 36 (2006) 1325–1343.
2. Borde D, Calvert CA, Darien BJ, Guerrero J, and Wall M. Acquired Heart and Blood Vessel Disorders in Dogs. Merck Veterinary Manual. Found at: http://www.merckvetmanual.com/dog-owners/heart-and-blood-vessel-disorders-of-dogs/acquired-heart-and-blood-vessel-disorders-in-dogs
3. Valberg SJ. Toxic Myopathies in Ruminants and Pigs. Merck Veterinary Manual. Found at: http://www.merckvetmanual.com/musculoskeletal-system/myopathies-in-ruminants-and-pigs/toxic-myopathies-in-ruminants-and-pigs
4. Garland T. Overview of Gossypol Poisoning. Merck Veterinary Manual. Found at: http://www.merckvetmanual.com/toxicology/gossypol-poisoning/overview-of-gossypol-poisoning
5. Ismahil MA, Hamid T, Haberzettl P, Gu Y, Chandrasekar B, Srivastava S, Bhatnagar A, and Prabhu SD. Chronic oral exposure to the aldehyde pollutant acrolein induces dilated cardiomyopathy. Am J Physiol Heart Circ Physiol 301: H2050–H2060, 2011.

Supplemental Information:

01-800.218-EON-323515 (b) (6) -CC: Consumer Complaint
02-800.218-EON-323515- (b) (6) -MedRec: Medical Records
03-800.218-EON-323515- (b) (6) -Results: Testing Results
04-800.218-EON-323515- (b) (6) -Summary: Vet-LIRN Summary

SIGNATURES

Mary E. Allen -S

Digitally signed by Mary E. Allen -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Mary E. Allen -S, 0.9.2342.19200300.100.1.1=1300365061
Date: 2017.11.17 14:21:13 -05'00'

Deputy Director OR **Date**

John Graham -S

Digitally signed by John Graham -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=John Graham -S, 0.9.2342.19200300.100.101=2001387754
Date: 2017.11.17 18:07:25 -05'00'

Director OR **Date**

(b) (6)

Digitally signed by Renate Reimschuessel -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.101=1300140413, cn=Renate Reimschuessel -S
Date: 2017.11.20 14:27:01 -05'00'

Vet-LIRN Director **Date**

	(b) (4)	6979064	6979065	6979066	6979067	6979068	6979069	6979070	6979071	6979072	6979073	6979074
	Client ID	800.218-sub 1	800.218-sub 2	800.218-sub 4	800.218-sub 5	800.218-sub 6	800.238-sub 1	800.238-sub 1	800.238-sub 3	800.238-sub 3	800.219-sub 5	800.219-sub 6
	Sample Description	dog food	dog food	dog food	dog food	dog food	dog treat piece 1	dog treat piece 2	dog treat piece 1	dog treat piece 2	dog treat	dog treat
Component	**Unit**											
Chloride	%						1.39	0.589	0.70	0.33	0.078	1.15
Taurine	mg/g		1.06	1.84	1.08	1.22						
Methionine	mg/g	5.78	5.53	4.76	6.20	7.78						
Cystine	mg/g	2.32	2.31	3.15	3.20	2.50						

(b) (4)

Report Number: 1894242-0
Report Date: 15-Aug-2017
Report Status: Final

Certificate of Analysis

Food and Drug Administration - CVM - Invoice Denise Durham

8401 Muirkirk Rd.
Laurel Maryland 20708 United States

Sample Name:	800.218 (b) (4)	**Sample:**	6406524
Project ID	FDA_CVM-20170804-0007	**Receipt Date**	04-Aug-2017
PO Number	HHSF223201610005I/HHSF22301002T	**Receipt Condition**	Ambient temperature
Sample Serving Size	100 g	**Login Date**	04-Aug-2017
		Online Order	20

Analysis	Result
L-Carnitine *	
L-Carnitine	69900 ppb
Taurine	
Taurine	231 mg/Serving Size

Method References	Testing Location
L-Carnitine (CARNITNE_S)	(b)(4)
STAREY ET AL.: JOURNAL OF AOAC INTERNATIONAL VOL. 91, NO.1, 2008. (Modified).	
Taurine (TAUR_LC_S)	(b) (4)
R. Schuster, "Determination of Amino Acids in Biological, Pharmaceutical, Plant and Food Samples by Automated Precolumn Deravitization and HPLC", Journal of Chromatography., 1988, 431, 271-284, Henderson, J.W., Ricker, R.D. Bidlingmeyer, B.A., Woodward, C., "Rapid, Accurate, Sensitive, and Reproducible HPLC Analysis of Amino Acids, Amino Acid Analysis Using Zorbax Eclipse-AAA columns and the Agilent 1100 HPLC," Agilent Publication, 2000, and Barkholt and Jensen, , "Amino Acid Analysis: Determination of Cysteine plus Half-Cystine in Proteins after Hydrochloric Acid Hydrolysis with a Disulfide Compound as Additive," Analytical Biochemistry, 177, 318-322 (1989).	

Testing Location(s) (b) (4)

(b) (4)

(b) (4)

ilac-MRA A2LA ACCREDITED

These results apply only to the items tested. This certificate of analysis shall not be reproduced, except in its entirety, without the written approval of (b) (4)

* This analysis is not ISO accredited.

UPS/FedEx Package Information Form

Sender (address, tel #, fax #, e-mail):

Jake Guag, M.P.H, C.P.H.
Biologist
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Vet-LIRN
8401 Muirkirk Road.
Laurel, Maryland 20708
Tel: 240-402-0917
email: **Jake.Guag@fda.hhs.gov**

Recipient (name, address, tel. #, fax #, e-mail):

Attn: Dr. Darcy Adin
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032
Email: dbadin@ncsu.edu

Service (Standard, Priority Overnight, etc.):

Priority overnight

Date:
01/10/2018

Special Needs (Dry Ice, Hazardous Chemicals, etc.). Dry ice shipments must list the weight of the dry ice separately Weight of Dry Ice (kg, lbs)	NO
Total Weight of Package (kg, lbs.):	1.7 lbs
Dimensions of Package (L*W*H):	12x12x10 inches
Value:	/
Content Description	Food collection kit

800.218
We are collecting dog food-weight 0.36 kg. In a plastic tupperware container-~5" x 5" x 2" (0.36kg = ~0.8 lb)
No hazardous materials.
Room temperature.

VETERINARY CARDIOLOGY SPECIALISTS

Taurine Deficiency Induced Dilated Cardiomyopathy in Golden Retrievers

Taurine Deficiency Induced Dilated Cardiomyopathy in Golden Retrievers

by Janet Olson, DVM, DACVIM (Cardiology)

Dilated Cardiomyopathy (DCM) is becoming more prevalent in golden retrievers. Dr. Joshua Stern, DVM, PhD, DACVIM (Cardiology) at UC Davis, starting seeing a pattern and recognized that many cases were due to dietary taurine deficiency in golden retrievers fed grain free diets. Here is what we know so far:

Background

Taurine is an amino acid that is found in high concentrations in heart and muscle. Among its many functions, it aids in normal contractile function. Evidence shows that taurine helps mediate calcium channel transports and modulates calcium sensitivity of the myofibrils.

Taurine deficiency as a cause of dilated cardiomyopathy (DCM) is not a new issue. Taurine deficiency in cats was characterized by Pion et al in the late 1980s. Taurine deficiency has since been characterized as a cause of acquired DCM in dogs as well.

Currently identified diets of concern in these golden retrievers

According to Dr. Stern, the majority of cases they are seeing at UC Davis are from grain free diets that are high in legumes, like acana pork and squash singles.

What can we do? Some Guidelines.

- **ASK:** Make sure to ask your clients (whether they own golden retrievers or not) what diets they are currently or previously have fed their dogs
- **INFORM:** Inform your clients of this issue
- **ACT:** If they are currently on, or have been on grain free diets in the past, submit baseline WHOLE blood taurine levels and AFTER submitting the WHOLE blood taurine levels, switch diets if indicated. Temporary taurine supplementation may be necessary. If levels are low, take baseline chest films, if cardiomegaly noted on the radiographs, an echocardiogram is indicated to complete your baseline evaluation. Additional therapy may be indicated.
- **GET MORE INFORMATION:** Dr. Stern has compiled many of the studies in the following links: https://www.dropbox.com/.../AAB1sDvLZe6gE3httPskz9-0a... Taurine Deficient DCM in Dogs

Medical Record Review:

(b) (6)

Presenting complaint (b) (6)**: dyspnea, cough of 3 week duration-wheezing type more frequent at night → rDVM, treated w/ prednisone and doxycycline for kennel cough →** (b) (6) **inappetance, vomiting →** (b) (6) **dyspneic and recheck, hospitalized and treated for pneumonia, regurgitated →** (b) (6) **treated as outpatient,** (b) (6) **as syring feeding, dog regurgitated and had marked dyspnea → ER → refer to NCSU →** (b) (6) **put on mechanical ventilator →** (b) (6) **euthanized**

PE (b) (6)**: P 160 bpm, R 64 rpm, pale pink mm, Gr I-II/VI left apical systolic murmur, femoral pulse hypokinetic but synchronous, jugular venous distention**

Labwork: (b) (6)

Labs: unremarkable (unclear what was done)

(b) (6)

Big 4: Glu 135, Azo 15-20

- (b) (6) **vBGA: Lact 2.4, rest wnl**
- (b) (6) **Chem: P 6.2, K 4.9, Na 140, TP 4.2**
- (b) (6) **Chem: BG 225, BUN 29, P 11.7, K 3.3, Cl 95, Na 144**
- (b) (6) **Chem: BG 136, P 4.6, CK 13,621, K 4.3, Na 151, Cl 109, AST 577**
- (b) (6) **Chem: BG 165, BUN 37, P 8.1, ALT 147, AST 1006, CK 35,930, Na 135, K 3.8, Cl 90**

(b) (6) **CBC: WBC 9.4, NP 7.9, Band .18, Plt 157**

-2/4: WBC 9.9, NP 8, Band .7

-2/5: WBC 6.8, TP 6.9, NP 4.2, Ban .54, Toxic NP-mild, Plt 97

(b) (6) **BP sys: 90**

(b) (6) **UA post Lasix: 1.011**

Cardiac troponin 0.79

BAP GM-pending

Vector borne panel: pending

Taurine/Carnitine: pending

(b) (6) **Coag: PT 9.1, PTT 14, Dimer 189, Fib 539, INR 1.09**

Urine Creat: 27.9

Urine Na: pending

ECG: suspected atrial tachycardia

Rads (b) (6)**: concern for aspiration pneumonia**

- (b) (6)**: cardiomegaly, severe diffuse mixed interstitial to alveolar pattern most severe caudo-dorsally, hepatomegaly, dec abdominal serosal contrast**
- (b) (6)**: severe generalized cardiomegaly with biventricular heart failure, improved vs rDVM rads**
- (b) (6)**: worsening cardiogenic pulmonary edema, cannot exclude lung induced injury +/- pneumonia**
- (b) (6)**: post ultrafiltration, improved cardiogenic edema, hypovolemia, residual interstitial to patchy alveolar**
- (b) (6)**: improved CHF with possible concern for bronchopneumonia, suspected hiatal hernia**
- (b) (6)**: markedly progressive alveolar pattern with significantly worse cardiogenic edema**

tFAST (b) (6)**: severe cardiomegaly with ventricular hypocontractility**

Echo (b) (6)**: dcm vs. myocarditis vs pacing induce vs. other (severely dilated & hypocontractile left & right ventricles, severely dilated left and right atria)**

Necropsy: Lung-severe diffuse alveolar injury with marked fibrin deposition (hyaline) and marked alveolar histiocytosis and multifocal type II pneumocyte hyperplasia; mod to marked diffuse pulmonary edema; mild cardiomegaly with mild mitral valve endocardiosis and mild left ventricular hypertrophy and left atrial dilation; thorax with mild pleural effusion; Suspect primary non-cardiogenic etiology but if clinical cardiac dysfunction then functional cardiac abnormalities cannot be ruled out

Prior MHx: coffee brown urine including clumping after strenuous activity when it is hot outside and resolves with 24-36 hours; also Crystalluria

(b) (6)

Presented 6/22/2017: episodes of collapse, first occurred mid February, fall 6 seconds without losing consciousness → immediately return to normal →2 weeks later again collapse, then on → 6/3 post 2 hour hike collapsed again; panting more than usual; good appetite for treats but reluctant to eat food since February; → recheck 7/10, doing better, no collapsing episodes except a stumbling moment when excited, respiratory rate normal, diet changed to Hill's

6/22 PE: P 130 bpm, R pant, mild increased breath sounds in all lung fields

-7/10: T 99.7F, P 136 bpm, R 36 rpm, equivocal mild dehydration<5%, Gr II/VI left apical systolic murmur

Labs: 6/22 **Big 4:** BG 64 (recheck 79), BUN 15-26
BP-sys: 130 mmHg
-7/10: 110 mmHg
ECG: left ventricular enlargement suggested
UA: 1.019
Taurine & Carnitine: normal (no values)
Vector borne panel (PCR and IFA): normal
BAP GM
Troponin 1
T4
Toxoplasma/Neospora
Chagas
Complete AA: no significant abnormalities, consulting with UC Davis

-7/10 **Renal Panel:** K 4.0

6/22 Rads: left sided congestive heart failure

-7/10: moderate left sided cardiomegaly without heart failure, moderate hepatomegaly

6**/22 Echo:** mitral valve endocardiosis with left atrial enlargement and heart failure, decreased left ventricular systolic function, suspected DCM

		800.218-sub 1	800.218-sub 2	800.218-sub 6	
		Case Sample	**Storebought**	**Case sample**	**Label**
		California Naturals Kangaroo & Lentil	**California Naturals Kangaroo & Lentil**	**California Naturals Kangaroo & Lentil**	**Product Nutrient Analysis (website label)**
(b) (4)	Ca	1.30%	1%	0.93%	0.83%
	Mg	0.13%	0.14%	0.15%	0.17%
	P	0.74%	0.67%	0.68%	0.71%
	Fe	**30 mg/kg**	**30 mg/kg**	**31 mg/kg**	305 mg/kg
	Co	0.12 mg/kg	0.14 mg/kg	.14 mg/kg	n/a
	Cu	21 mg/kg	19 mg/kg	16 mg/kg	13.61 mg/kg
	Zn	240 mg/kg	280 mg/kg	200 mg/kg	193.37 mg/kg
	Se	0.7 mg/kg	0.65 mg/kg	.68 mg/kg	0.08 mg/kg
	Ca:P	1.76:1	1.49:1	1.37:1	
	Cu:Zn	0.09:1	0.07:1	0.08:1	
(b) (4)	Tau	~0.26%	1.06 mg/g = ~0.11%	1.22 mg/g = ~0.12%	
	Cystine	2.32 mg/g = ~0.23%	2.31 mg/g = ~0.23%	2.5 mg/g = ~0.25%	
	Met	5.78 mg/g = ~0.58%	5.53 mg/g = ~0.55%	7.78 mg/g = ~0.78%	0.61%
	Met-Cys	~0.81%	~0.78%	~1.03%	0.97%

AAFCO	
AAFCO-Adult Maint	**Issues**
0.5 to 2.5%	none
0.06%	none
0.4 to 1.6 %	none
40 mg/kg	**below AAFCO & Label**
25 mg/kg-chicks/rats/sheep max	unlikely
7.3 mg/kg	none
80 mg/kg	none
0.35 to 2 mg/kg	**label should be higher to align w/ AAFCO maintenance claim**
1:1 to 2:1	none
0.09:1-not AAFCO	none
0.1% in Cats	
n/a	
0.33%	none
0.65%	none

http://www.californianaturalpet.com/products/1741

		800.218-sub 4 Case Sample Fromm Heartland Gold Grain Free Large Breed Adult	Product Typical Analysis (website label)	AAFCO Growth & Maint
(b) (4)	Ca	1.20%	1.14%	1.2 to 1.8%
	Mg	0.14%	0.17%	0.06%
	P	1%	1.08%	1 to 1.6%
	Fe	**30 mg/kg**	258.26 mg/kg	88 mg/kg
	Co	0.37 mg/kg	n/a	25 mg/kg-chicks/rats/sheep max
	Cu	25 mg/kg	25.83 mg/kg	12.4 mg/kg
	Zn	170 mg/kg	217.37 mg/kg	100 mg/kg
	Se	0.85 mg/kg	n/a	0.35 to 2 mg/kg
	Ca:P	1.2:1		1:1 to 2:1
	Cu:Zn	0.15:1		0.09:1-not AAFCO
(b) (4	Tau	1.84 mg/g = ~0.18%	n/a	0.1% in Cats
	Cystine	3.15 mg/g = ~0.32%	n/a	n/a
	Met	4.75 mg/g = ~0.48%	n/a	0.35%
	Met-Cys	~0.79%	n/a	0.70%
MSU	Iodione	1.58 ug/g (ppm)		

Issues	https://frommfamily.com/products/dog/gold/dry/heartland-gold-large-breed-adult/typ
label should be higher to align w/ AAFCO growth claim	
none	
none	
below AAFCO & Label	
unlikely	
none	
none	
none	
none	
none	
none	
none	

pical-analysis/

UPS CampusShip: View/Print Label

1. **Ensure there are no other shipping or tracking labels attached to your package.**

2. **Fold the printed label at the solid line below.** Place the label in a UPS Shipping Pouch. If you do not have a pouch, affix the folded label using clear plastic shipping tape over the entire label.

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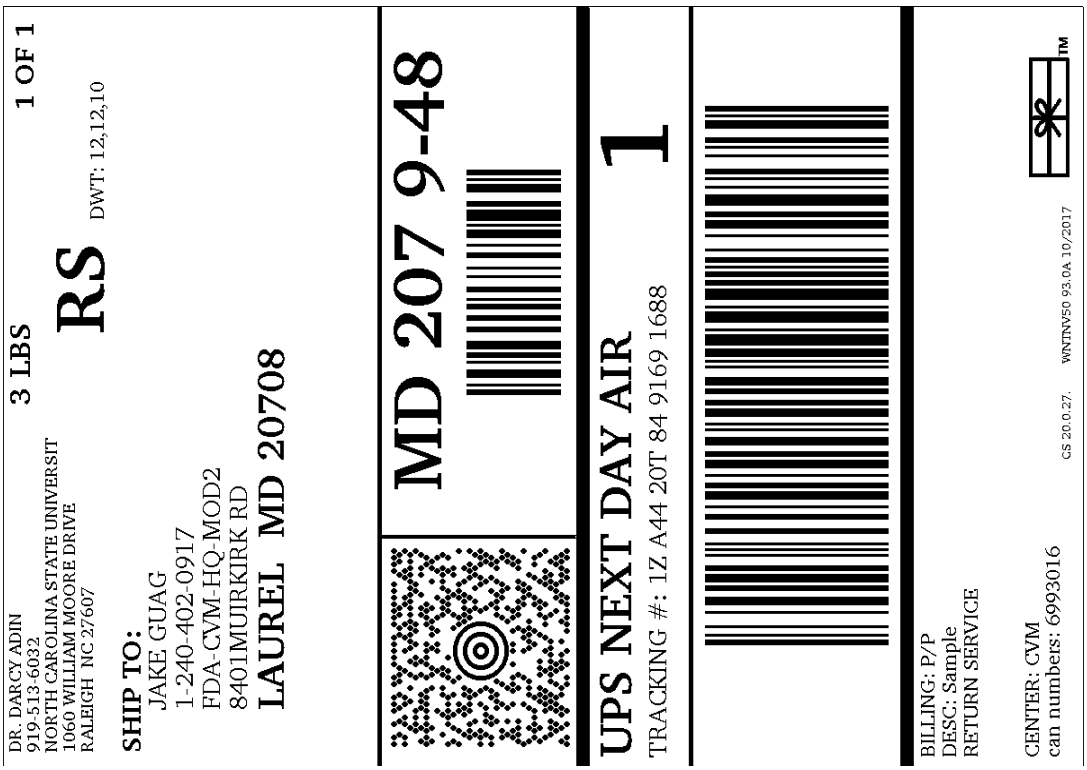

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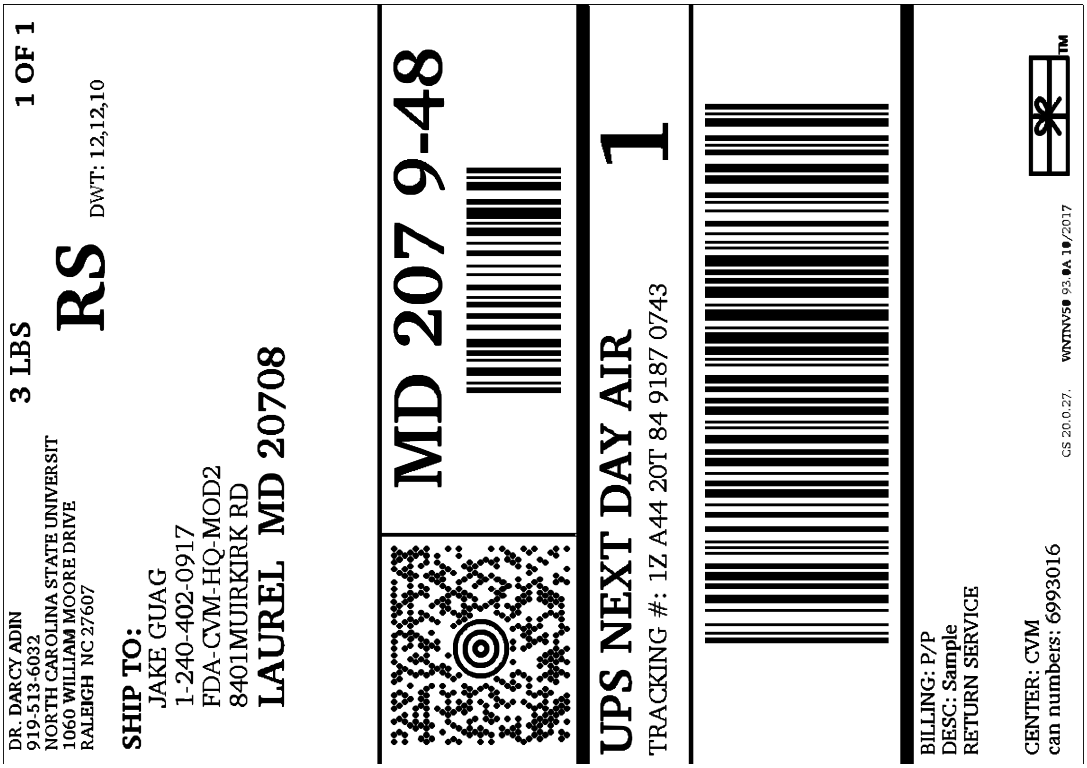

UPS/FedEx Package Information Form

Sender (address, tel #, fax #, e-mail):

Jake Guag, M.P.H, C.P.H.
Biologist
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Vet-LIRN
8401 Muirkirk Road.
Laurel, Maryland 20708
Tel: 240-402-0917
email: **Jake.Guag@fda.hhs.gov**

Recipient (name, address, tel. #, fax #, e-mail):

Attn: Dr. Darcy Adin
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032
Email: dbadin@ncsu.edu

Service (Standard, Priority Overnight, etc.):

Priority overnight

Date:
01/10/2018

Special Needs (Dry Ice, Hazardous Chemicals, etc.). Dry ice shipments must list the weight of the dry ice separately Weight of Dry Ice (kg, lbs)	NO
Total Weight of Package (kg, lbs.):	1.7 lbs
Dimensions of Package (L*W*H):	12x12x10 inches
Value:	/
Content Description	Food collection kit

800.218
We are collecting dog food-weight 0.36 kg. In a plastic tupperware container-~5" x 5" x 2" (0.36kg = ~0.8 lb)
No hazardous materials.
Room temperature.

Network Procedures for Shipping Vet-LIRN Samples

Introduction

The purpose of this Network Procedure is to provide general information on shipping for Vet-LIRN samples. There are 5 different kinds of samples that will be covered including:

- Room Temperature samples (non-histological)
- Histological Samples
- Frozen Samples
- Urine Samples
- Exempt Patient Specimen

Including inventory and any paperwork provided by Vet-LIRN in shipment sealed in a plastic bag.

****

Room Temperature

Non-Histological

- Room Temperature
- Secondary packaging
- Provide cushion as needed (eg. Bubblewrap)

Histological

- Room Temperature
- Place in secondary container
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- Must have Exempt Animal Specimen sticker on packaging

****

Frozen

Tissues

- Ice packs frozen for 24 hours
- Secondary packaging
- Provide cushion as needed (eg. Bubblewrap)

Urine

****

Exempt Patient Specimen

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- Serum sent for antibody testing
- Tissues sent in 10% formalin (higher than 10% formalin requires further marking, UN 3334)
- Samples to be tested for therapeutic drug monitoring or toxins
- Environmental samples not expected to contain a pathogen
- Dried blood spots placed on absorbent filter paper

Guag, Jake

From: Guag, Jake
Sent: Wednesday, January 17, 2018 9:13 AM
To: 'dbadin@ncsu.edu'
Cc: Jones, Jennifer L
Subject: FDA (Vet-LIRN) shipped sample collection kit

Dear Dr. Adin,
We shipped a food sample collection kit to your place this morning. Its tracking number is 1ZA4420T0194648732 with UPS. It is expected to arrive on tomorrow (Jan 18, 2018).

Thank you
Jake Guag

Jake Guag, MPH , CPH
Biologist
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Vet-LIRN
8401 Muirkirk Road.
Laurel, Maryland 20708
tel: 1-240-402-0917
email: Jake.Guag@fda.hhs.gov

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11118 BALTIMORE AVE
BELTSVILLE, MD 20705

FOLD HERE

Return Label to Vet-ICRN (FOIA)

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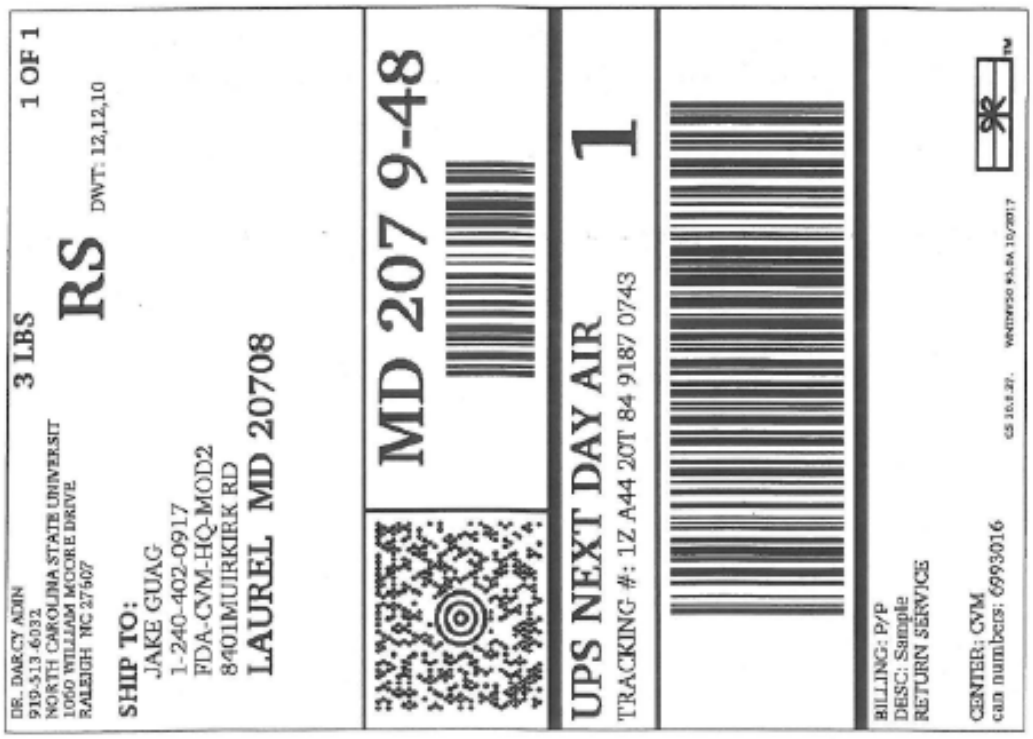

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Attn: Dr. Darcy Adin
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

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Priority overnight

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Return Label to Ver-Lab (FDA)

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11118 BALTIMORE AVE
BELTSVILLE ,MD 20705

FOLD HERE

JAKE GUAG
1-240-402-0917
FDA-CVM-HQ-MOD2
8401MURKIRK RD
LAUREL MD 20708

2 LBS 1 OF 1

DWT: 12,12,10

SHIP TO:
DR. DARCY ADIN
919-513-6032
NORTH CAROLINA STATE UNIVERSITY
NC STATE VETERINARY HOSPITAL
1060 WILLIAM MOORE DRIVE
RALEIGH NC 27607

NC 276 9-07

UPS NEXT DAY AIR 1

TRACKING #: 1Z A44 20T 01 9190 2873

BILLING: P/P

CENTER: CVM
can numbers: 6993016

CS 20.0.27. WNTN950 93.0A 10/2017

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ADULT 1+ YEARS

CALIFORNIA NATURAL™

GRAIN FREE

LIMITED INGREDIENT DIET

Kangaroo & Red Lentils Recipe

ADULT 1+ YEARS

WHY LESS IS MORE

The more ingredients a food has, the higher the likelihood it may include an ingredient your dog may be sensitive to. CALIFORNIA NATURAL™ grain-free dog food recipes use fewer ingredients and zero grains to help dogs avoid the dietary triggers commonly found in many other foods.

HIGH-QUALITY KANGAROO
for dogs in need of a novel protein source

FLAXSEED
for nourishing omega-3 fatty acids and fiber

RED & GREEN LENTILS
for a unique carbohydrate alternative

ONLY 5 KEY INGREDIENTS
+ ADDED VITAMINS, MINERALS, OTHER TRACE NUTRIENTS & NATURAL FLAVORS

SUNFLOWER OIL
for healthy skin and coat

PEAS & PEA FIBER
for nutritious grain replacement and fiber

Kangaroo is the #1 ingredient

No white potatoes, corn, soy, dairy or eggs

INGREDIENTS:
Kangaroo, Red Lentils, Green Lentils, Peas, Sunflower Oil (preserved with mixed Tocopherols), Flaxseed, Pea Fiber, Dicalcium Phosphate, Natural Flavors, Calcium Carbonate, Salt, DL-Methionine, Minerals (Zinc Proteinate, Iron Proteinate, Copper Proteinate, Manganese Proteinate, Calcium Iodate), Vitamins (Betaine Hydrochloride, Vitamin A Supplement, Niacin Supplement, Calcium Pantothenate, Beta Carotene, Vitamin B12 Supplement, Vitamin D3 Supplement, Riboflavin Supplement, Pyridoxine Hydrochloride, Thiamine Mononitrate, Biotin, Folic Acid), Vitamin E Supplement, Rosemary Extract

GUARANTEED ANALYSIS:

Crude Protein (Min)	21%
Crude Fat (Min)	11%
Crude Fiber (Max)	6.5%
Moisture (Max)	10%
Linoleic Acid (an Omega-6 Fatty Acid) (Min)	1.1%
Iron (Min)	100 mg/kg
Zinc (Min)	140 mg/kg
Vitamin E (Min)	300 IU/kg
Omega-3 Fatty Acids* (Min)	1%

*Not recognized as an essential nutrient by the AAFCO Dog Food Nutrient Profiles

CALORIE CONTENT:
Metabolizable Energy - Calculated
3,487 kcal/kg
434 kcal/cup
1 cup = 4.36 oz (124 g)

FEEDING GUIDELINES: Every cup of our food is nutrient dense so your dog gets the right amount of calories in a complete and nutritious meal. Adjust amount fed to obtain or maintain your dog's optimal weight.

To help maintain freshness, seal bag tightly and store in a cool, dry location.

Suggested Amounts to Feed Per Day (Cups)

WEIGHT (lbs.)	FEEDING AMOUNT (cups/day)
10	7/8
20	1 3/8
30	1 7/8
40	2 1/4
50	2 5/8
60	3
70	3 3/8
80	3 5/8
90	3 7/8
100	4 1/4
120	4 3/4
140	5 1/4

Approximate Kibble Size:

CALIFORNIA NATURAL™ Limited Ingredient Diet Grain Free Kangaroo & Red Lentils Recipe Dog Food is formulated to meet the nutritional levels established by the AAFCO Dog Food Nutrient Profiles for adult maintenance.

TRANSITIONING TO OUR FOOD: If feeding CALIFORNIA NATURAL™ Dog Food for the first time or changing recipes, we suggest you blend increasing amounts of the new recipe with your old dog food for six days.

MADE IN OUR NEBRASKA PLANT WITH THE WORLD'S FINEST INGREDIENTS

QUALITY STANDARDS AS HIGH AS YOURS

[illegible] with quality ingredients and [illegible] into every batch of CALIFORNIA NATURAL™ dog food and why we [illegible] every bag of it for ourselves [illegible] quality checks a day based on [illegible]

[illegible] CHECKS PER DAY

[illegible] Satisfaction Guarantee [illegible] for any reason you [illegible] product, return the unused portion [illegible] this bag to the [illegible] retailer for [illegible] replacement [illegible] Consumer Department: [illegible] .com

MARS petcare

1348063

PROOF OF PURCHASE ALONG DASHED LINE

Manufactured by:
Natura Pet Products, Inc.
2779 Rademakers Way
Fremont, NE 68025 USA
©/™ Trademarks
© Mars, Incorporated.

Image on Fr[illegible]
Rasheed, a [illegible] and fearless [illegible] through the [illegible] Joshua Tree Na[illegible] in California.

Kangaroo is the #1 ingredient

INGREDIENTS:

Kangaroo, Red Lentils, Green Lentils, Peas, Sunflower Oil (preserved with mixed Tocopherols), Flaxseed, Pea Fiber, Dicalcium Phosphate, Natural Flavors, Calcium Carbonate, Salt, DL-Methionine, Minerals (Zinc Proteinate, Iron Proteinate, Copper Proteinate, Manganese Proteinate, Calcium Iodate), Vitamins (Betaine Hydrochloride, Vitamin A Supplement, Niacin Supplement, Calcium Pantothenate, Beta Carotene, Vitamin B12 Supplement, Vitamin D3 Supplement, Riboflavin Supplement, Pyridoxine Hydrochloride, Thiamine Mononitrate, Biotin, Folic Acid), Vitamin E Supplement, Rosemary Extract

GUARANTEED ANALYSIS:

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