From: Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: 'Guag, Jake * (Jake.Guag@fda.hhs.gov)'
Sent: 8/3/2017 11:17:34 AM
Subject: 2 boxes in need of shipping labels (800.218)

Jake, Please make 2 shipping labels (no return label needed). There is dog food in the boxes, no hazardous materials. Shipping in small B4 express boxes.
The first box will go to B4 : F:\6-CASES\800.04-ChickenJerky\3-Jerky-TESTS\1-B4-Nutr\01-SAMPLES\Samples-2017\07-Taurine-Carnitine-8.3.2017

The second will go to B4 F:\6-CASES\800.218-EONB4 19-B6-CA Naturals-DCM\3-samples\B4
For B4

B6

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

U.S. FOOD & DRUG ADMINISTRATION Vet-LIRN

From: Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: Scalera, Alexander
Sent: 7/21/2017 12:37:40 PM
Subject: 2 Shipping labels-one to a vet office, one back to Vet-LIRN (800.218)

Hi Alex,
Can you make another set of shipping labels for me please? I plan to ship the box to the vet today or Monday, as your schedule allows.

This time, the box will be sent overnight to: Dr. Darcy Adin, 1060 William Moore Dr, Raleigh, North Carolina, 27607, Tel: 919-513-6694
Dimensions: 12.5" x 12.5" x 10.5"
Weight: 1.7 lbs
Contents: packing peanuts, empty (to collect dog food), no hazardous materials

Overnight Shipping-Return Shipping label for the box:
Dimensions: 12.5" x 12.5" x 10.5"
Projected weight: 2.75 lbs.
Contents: Dog food, no hazardous materials
Ship to: Jennifer Jones, Vet-LIRN, 8401 Muirkirk Rd, Laurel, MD 20708

Thank you,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
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8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Nemser, Sarah </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=SARAH.YACHETTI>
To: Jones, Jennifer L
Sent: 7/31/2015 1:00:02 PM
Subject: 800.131 - B6 case

The dog was euthanized? What does ARF stand for?

Presenting complaint: since switching the food-would eat fast-vomit after occasionally, borborygmous, inappetance x 3 episodes, last 2 inappetance episodes occured over 1.5 wk span, episodes of lethargy lasting about a day and a half
Diet: primary diet-Grandma Lucy's Artisan Chicken Grain Free/Freeze Dried Dog Food-fed Oct 2014-April 2015, owner had another dog w/ kidney & liver disease-low P and chose this diet for both of the dogs; 1 cup daily-split into 3 doses; also got carrots & sweet potatoes; treats occasional component of diet: 1.) Fresh Pet Turkey Jerky-started last summer-currently receiving, given 1x per week max from owner's mother in law; 2.) Grandma Lucy's Apple Treats & Honest Kitchen Smooches Treats-both started around 9-10/2014 and last given unknown, total of 2 treats given daily-combo of the 2 brands
Exposures: indoor & outdoor dog; drugs-heartworm (heartgard), only use an herbal spray Earth Animals Flea and Tick; owners with him when go outside; owner has some herbs outside and weeds but no types of poisonous plants in yard; been to a dog park maybe 1-2 times in past month but doesn't go on a regular basis; owners found a tick a few weeks ago, but not attached/only on coat; no psoriasis creams or rat baits w/ Vitamin D; no pesticides or sprays in house or used outside; rural environment; one other dog in house-got the dog food; euthanized of ARF

Sarah Nemser M.S.

U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Vet-LIRN
8401 Muirkirk Road, G202, HFV 500
Laurel, Maryland 20708
tel: 240-402-0892
fax: 301-210-4685
sarah.nemser@fda.hhs.gov

Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'
Sent: 10/16/2017 4:55:14 PM
Subject: 800.218-Final report for review
Attachments: 800.218-FinalReport-B6-draft-10.16.2017.doc

F:\6-CASES\1-Working on report\sent to rr for review\800.218-EON-323515-19-B6-Naturals-DCM\6-REPORT

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fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: B6
CC: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'; Peloquin, Sarah
Sent: B6 5:40:43 PM
Subject: 800.267-cc-295-RE: Necropsy authorization
Attachments: 02-Vet-LIRN-NetworkProceduresVets-12.22.2015.pdf; 03-Vet-LIRN-Network ProceduresOwners-12.22.2015.pdf

Good afternoon B6
Thank you for contacting us about your case. As we discussed on the phone, for me to send you a box to collect the samples, I'll need an official report. You can mention in the report, that I recommended you submit a complaint. Can you please submit a consumer complaint here?
https://www.safetyreporting.hhs.gov/

- Please send me the ICSR number (confirmation code) from the report.

We will send you 2 boxes with the materials to collect the fixed and frozen samples, including jars with formalin. You will reuse the boxes we send and package the samples per the instructions in the box.

- Please send me an estimate for the necropsy. After the necropsy is complete, we will call back with our VISA information to reimburse your hospital.
- After the necropsy is complete, please send me the approximate weight of the following individual groups:
  - Fixed tissues in the jars
  - Frozen tissues

  We will use this information to make prepaid shipping labels for you. You'll affix the prepaid shipping label to the box and call UPS for a pick-up on Monday-Wednesday.

I attached a copy of our network procedures. They explain how Vet-LIRN operates and how veterinarians help with our case investigations. An owner friendly version is also attached.
For more information, please also visit our open access article in JAVMA that explains the FDA Animal Food Concern Reporting process. It's free and located here: https://avmajournals.avma.org/doi/pdf/10.2460/javma.253.5.550

Thank you again,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: B6 <B6 com>
Sent: Tuesday, B6 12:33 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Necropsy authorization

Dear Dr. Jones,
I left a message on your number this morning but figured I would also follow up with an email. B6 gave us your contact information – I reached out to both Renate and Sarah but both appear out of the office today. We have a nutrition mediated DCM case, diagnosed at UC Davis that will be euthanized this afternoon. B6 is in CHF and isn't responding to treatment. She is a 3.5yrold, FS, Golden Retriever. The owner is willing to submit the body/tissues towards research on this condition. Please give me a call at your earliest convenience

to discuss next steps B6

Sincerely,

B6

B6

AAHA ACCREDITED The Standard of Veterinary Excellence

B6 BS, CVPM, PHR

Tel:
Fax: B6
www. B6

Like us on Facebook

Find us on Yelp

From: Peloquin, Sarah </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8607F880DF2B494AA639E6D9A3874132-SARAH.PELOQ>
To: B6, DVM
CC: Jones, Jennifer L
Sent: 8/15/2019 1:08:36 PM
Subject: 800.267-cc-297-FDA Case Investigation for B6 and B6 (cc-297)

Good morning B6!

Please send us the invoices for B6 and B6 necropsies at your earliest convenience (by email or fax to 301-210-4685). We want to make sure we reimburse your hospital for these costs.

Thank you!
Sarah

Sarah Peloquin, DVM
Veterinary Medical Officer
tel: 240-402-1218

From: Jones, Jennifer L
Sent: Friday, B6 9:10 AM
To: B6 DVM <B6 com>
Subject: RE: Re[2]: 800.267-cc-297-FDA Case Investigation for B6 (cc-297)

Absolutely. We will send a copy of the results as soon as they are read.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: B6 DVM <B6 com>
Sent: Friday, B6 8:55 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Re[2]: 800.267-cc-297-FDA Case Investigation for B6 (cc-297)

Thank you Jennifer. I did receive an email from Jake.

Also, I believe that I read I should get a copy of the pathology results. Is this correct? I am interested in the results from B6

Thank you again.
I appreciate the work you all are doing for this.

B6

B6 DVM

B6

B6

B6

------ Original Message ------
From: "Jones, Jennifer L" <Jennifer.Jones@fda.hhs.gov>
To: "B6 DVM" <B6 com>
Cc: "Peloquin, Sarah" <Sarah.Peloquin@fda.hhs.gov>; "Guag, Jake" <Jake.Guag@fda.hhs.gov>
Sent: B6 11:01:47 AM
Subject: RE: 800.267-cc-297-FDA Case Investigation for B6 (cc-297)

Thank you, B6
We'll ship the box, and it should arrive before close of business Monday. Jake will send you a copy of the tracking when it ships.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: B6 DVM <B6 com>
Sent: Tuesday, B6 9:22 AM
To: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Re: 800.267-FDA Case Investigation for B6 cc-297)

Good morning,
Weights for the samples from B6 are as follows:
Frozen tissue is 6ounces
Refrigerated samples (urine and small intestinal fluid) 2ounces
Formalin fixed samples 2 pounds 6 ounces

Thank you

B6

B6 DVM

B6

B6

B6

------ Original Message ------
From: "Peloquin, Sarah" <Sarah.Peloquin@fda.hhs.gov>
To: "B6 DVM" <B6 com>
Cc: "Jones, Jennifer L" <Jennifer.Jones@fda.hhs.gov>
Sent: B6 11:59:32 AM
Subject: 800.267-FDA Case Investigation for B6 (cc-297)

Good morning B6,

I'm filling in on the DCM case investigation for Dr. Jennifer Jones this week. Dr. Lisa Freeman informed me that B6 will be euthanized—I'm sorry to hear this. If you are willing, please collect the same samples from B6 as you did for B6 (i.e. intact heart in formalin; and if possible, fixed/frozen tissues as described in the rapid necropsy document).

Dr. Jones will return at the end of next week, and we will send you boxes then for shipment.

Please send me the approximate weights of the samples, as you did for B6

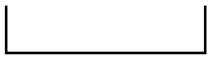
Let me know if you have any additional questions.

Thank you!
Dr. Sarah Peloquin

Sarah K. Peloquin, DVM
Veterinary Medical Officer

U.S. Food & Drug Administration
Center for Veterinary Medicine
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
tel: 240-402-1218
fax: 301-210-4685
e-mail: sarah.peloquin@fda.hhs.gov

FDA U.S. FOOD & DRUG ADMINISTRATION



From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Burkholder, William
CC: Peloquin, Sarah; Ceric, Olgica
Sent: 7/8/2019 1:52:32 PM
Subject: 800.267-DCM Food Testing

We've gotten some suggestions from the public for food toxicant testing. Looks like some (diquat, cyanamide) do cause cardiomyopathies.

- Dessicant herbicides-glyphosate, glufosinate, diquat, paraquot, cyanamide, cinidon-ethyl, pyraflufen-ethyl

B5

Any thoughts from the group?

Jennifer L. A. Jones, DVM
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new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Peloquin, Sarah </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8607F880DF2B494AA639E6D9A3874132-SARAH.PELOQ>
To: B6 DVM
CC: Jones, Jennifer L
Sent: 6/7/2019 3:59:32 PM
Subject: 800.267-FDA Case Investigation for B6 (cc-297)

Good morning B6

I'm filling in on the DCM case investigation for Dr. Jennifer Jones this week. Dr. Lisa Freeman informed me that B6 will be euthanized—I'm sorry to hear this. If you are willing, please collect the same samples from B6 as you did for B6 (i.e. intact heart in formalin; and if possible, fixed/frozen tissues as described in the rapid necropsy document).

Dr. Jones will return at the end of next week, and we will send you boxes then for shipment.

Please send me the approximate weights of the samples, as you did for B6

Let me know if you have any additional questions.

Thank you!
Dr. Sarah Peloquin

Sarah K. Peloquin, DVM
Veterinary Medical Officer

U.S. Food & Drug Administration
Center for Veterinary Medicine
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
tel: 240-402-1218
fax: 301-210-4685
e-mail: sarah.peloquin@fda.hhs.gov

From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: cvca[B6]@cvcavets.com
Sent: 4/15/2019 1:31:21 PM
Subject: 800.267-FDA Case Investigation for [B6] (cc-039)

Good morning,

As part of the Dilated Cardiomyopathy Investigation, we are currently requesting a copy of any recent echocardiogram reports for select cases. Are you willing to email or fax (301-210-4685) us a copy?

Here are our recent updates to the public on our testing and investigation.

https://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm630738.htm

https://www.fda.gov/AnimalVeterinary/NewsEvents/ucm630993.htm

Thank you,

Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
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new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From:	Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To:	'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'; Ceric, Olgica; Rotstein, David; Palmer, Lee Anne; Carey, Lauren
Sent:	5/25/2018 11:32:55 AM
Subject:	Action Item: Please Review-800.267-DCM draft testing plan
Attachments:	800.267-draft-Sample Testing Procedures-v1.doc

Please review by COB 6/1.

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
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e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

B4, B5

II. PARTICIPANT INFORMATION

B5

B5

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From:	Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To:	Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David
Sent:	5/20/2019 6:00:05 PM
Subject:	Adin -cardio cases
Attachments:	Acana Heritage Poultry dry: Darcy Adin - EON-388255; Blue Buffalo Large Breed Adult: Darcy Adin - EON-388253; Honest Kitchen Turkey dehydrated: Darcy Adin - EON-388245; Natural Balance Venison: Darcy Adin - EON-388246; Origins 6 Fish Grain Free dry: Darcy Adin - EON-388256; Pure Balance Salmon and Potato dry: Darcy Adin - EON-388254; RE: Dr. Adin - U Fla?; Taste of the Wild Pacific Salmon Grain Free: Darcy Adin - EON-388244

Jen and Sarah,

Here are all of the cases. Please note that while there are mostly DCM, there are few with endocardiosis.

Report Details - EON-388255

ICSR:	2067176	
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:	2019-05-20 10:58:30 EDT	
Reported Problem:	**Problem Description:**	Dirty presented to the UF Cardiology Service for a 5 month history of progressive exercise intolerance and increased respiratory rate and effort. Patient was diagnosed with Dilated Cardiomyopathy. She has been rechecked once 5/15/19 - clinically stable but no improvement noted on echocardiogram. Her blood taurine results were discordant so she has been on supplementation
	Date Problem Started:	02/14/2019
	Concurrent Medical Problem:	Yes
	Pre Existing Conditions:	Patient was bred by artificial insemination over the summer and became pregnant with one pup. The fetus was eventually absorbed. She was returned to the owner in September, at which time the owner noticed exercise intolerance and occasional abdominal distention.
	Outcome to Date:	Stable
Product Information:	**Product Name:**	Acana Heritage Poultry dry
	Product Type:	Pet Food
	Lot Number:	
	Product Use Information:	

Description:	2 cups dry food fed twice per day Patient also has been receiving deer antlers once per week since Aug 2015 as treats/chews.
First Exposure Date:	08/01/2015
Last Exposure Date:	02/14/2019
Time Interval between Product Use and Adverse Event:	3 Years
Product Use Stopped After the Onset of the Adverse Event:	Yes
Adverse Event Abate After Product Stop:	Unknown
Product Use Started Again:	No
Perceived Relatedness to Adverse Event:	Possibly related
Other Foods or Products Given to the Animal During This Time Period:	Yes

	Manufacturer /Distributor Information:	
	Purchase Location Information:	
Animal Information:	**Name:**	**B6**
	Type Of Species:	Dog

Type Of Breed:	Shepherd Dog - German	
Gender:	Female	
Reproductive Status:	Intact	
Pregnancy Status:	Not Pregnant	
Lactation Status:	Not lactating	
Weight:	36 Kilogram	
Age:	4 Years	
Assessment of Prior Health:	Good	
Number of Animals Given the Product:	1	
Number of Animals Reacted:	1	
Owner Information:	**Owner Information provided:**	No
Healthcare Professional Information:	**Practice Name:**	University of Florida
	Contact:	**Name:** Darcy Adin
		Phone: (614) 582-9798
		Other Phone: 3522948606
		Email: adind@ufl.edu
	Address:	2015 SW 16th Ave 2015 SW 16th Avenue Gainesville Florida 32608 United States

Sender Information:	**Name:**	Darcy Adin
	Address:	2015 SW 16th Ave 2015 SW 16th Avenue Gainesville Florida 32608 United States
	Contact:	**Phone:** 6145829798
		Other Phone: 3522948606
		Email: adind@ufl.edu
	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
	Reported to Other Parties:	None
Additional Documents:		

Report Details - EON-388253

ICSR:	2067174		
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:	2019-05-20 10:54:51 EDT		
Reported Problem:	**Problem Description:**	Patient had been stable on Pimobendan for dilated cardiomyopathy for the past two years prior to presentation at UF Cardiology. A few weeks prior to presentation, he was started on Furosemide for coughing episodes. The day of presentation, an EKG performed at the primary care veterinarian showed a ventricular arrythmia. On presentation to UF Cardiology, patient had collapsed suddenly and was in cardiopulmonary arrest. After CPR and a lidocaine bolus, he converted to sinus tachycardia. Patient was diagnosed with dilated cardiomyopathy. B6 was euthanized two days later due to gastric dilation volvulus (GDV).	
	Date Problem Started:	B6	
	Concurrent Medical Problem:	Yes	
	Pre Existing Conditions:	B6 was diagnosed with dilated cardiomyopathy two years prior to presentation at UF Cardiology and had been previously stable on Pimobendan for the past two years. B6 also underwent TPLO surgery in the past for a torn CCL on the left hind limb. The implant has since been removed due to infection. B6 was also on carprofen of unknown dose and frequency and Spring Hill Fish Oil 1 pill per day.	
	Outcome to Date:	Died Euthanized	
	B6		
Product Information:	**Product Name:**	Spring Hill Fish Oil	
	Product Type:	Other	
	Lot Number:		
	Product Use Information:	**Description:**	1 pill daily as supplement
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
	Product Name:	Paul Newman Dog Biscuits, various	
	Product Type:	Pet Food	
	Lot Number:		
	Product Use Information:	**Description:**	used as treats patient also received fat free greek yogurt once per day since 2015 and raw carrots as treats
		First Exposure Date:	01/01/2010
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
	Product Name:	Blue Buffalo Large Breed Adult	
	Product Type:	Pet Food	
	Lot Number:		
	Product Use Information:	**Description:**	2 cups dry fed twice per day
		First Exposure Date:	12/31/2007
		Last Exposure Date:	B6
		Time Interval	9 Years

		between Product Use and Adverse Event:	
		Product Use Stopped After the Onset of the Adverse Event:	No
		Perceived Relatedness to Adverse Event:	Possibly related
		Other Foods or Products Given to the Animal During This Time Period:	Yes
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
Animal Information:	Name:	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Doberman Pinscher	
	Gender:	Male	
	Reproductive Status:	Neutered	
	Weight:	38 Kilogram	
	Age:	11 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:	Owner Information provided:	No
	Healthcare Professional Information:	Practice Name:	University of Florida
		Contact: Name:	Darcy Adin
		Phone:	(614) 582-9798
		Other Phone:	3522948606
		Email:	adind@ufl.edu
		Address:	2015 SW 16th Ave 2015 SW 16th Avenue Gainesville Florida 32608 United States
Sender Information:	Name:	Darcy Adin	
	Address:	2015 SW 16th Ave 2015 SW 16th Avenue Gainesville Florida 32608 United States	
	Contact:	Phone:	6145829798
		Other Phone:	3522948606
		Email:	adind@ufl.edu

	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
	Reported to Other Parties:	None
Additional Documents:		

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Jones, Jennifer L; Rotstein, David; Carey, Lauren; Peloquin, Sarah
Sent: 5/20/2019 5:52:14 PM
Subject: RE: Dr. Adin - U Fla?

Interesting... she must have settled in and is now sending cases our way! 😊

From: Jones, Jennifer L
Sent: Monday, May 20, 2019 1:51 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Dr. Adin - U Fla?

Yes-she's been at UFL for about 6 mo?

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Monday, May 20, 2019 1:04 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: Re: Dr. Adin - U Fla?

Thanks Lee Anne

From: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>
Date: May 20, 2019 at 1:02:38 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>, Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: Dr. Adin - U Fla?

Hi there – I see a "dump" of DCM cases just rolled in. Is Darcy Adin now at Florida? Looks like she's moved from NC State. I'll let Dave do the forwards as he usually does, just an observation!

Lee Anne

Lee Anne M. Palmer, VMD, MPH
Team Leader HFV-242, Supervisory VMO

Center for Veterinary Medicine
OSC, Division of Veterinary Product Safety
U.S. Food and Drug Administration
Tel: 240-402-5767
Leeanne.palmer@fda.hhs.gov

U.S. FOOD & DRUG ADMINISTRATION

From: ADIN,DARCY BRITTAIN <adind@ufl.edu>
To: Jones, Jennifer L
Sent: 12/7/2018 12:48:35 PM
Subject: article
Attachments: Published diet manuscript.pdf

Hi Jen,

Just thought I'd share out diet DCM paper from NCSU with you. It is available for sharing but won't be in the journal til 2019.

It was great to talk this week and hear all the progress you've made!

Take care
Darcy

Darcy B. Adin, DVM, Diplomate ACVIM (Cardiology)
Clinical Associate Professor, Cardiology
University of Florida
College of Veterinary Medicine
PO Box 100136
2015 SW 16th Ave
Gainesville, FL 32608
(352) 294-8606

From: Steven Rosenthal <Steven.Rosenthal@cvcavets.com>
To: Jones, Jennifer L
Sent: 7/30/2019 2:44:45 PM
Subject: AVMA covention and publication names

Dr Jones
Unfortunately I have a full day of appointments booked on Friday. I can see if another Dr from our team can come to AVMA on Friday in support of your presentation.
Let us know how we can help

Going though the list of cases the most active enrollers of cases were myself and B6
In addition to myself and B6 was active in promoting and contributing to the study.
B6 had 1 case or saw a recheck of the patients.
B6 our technician in B4 was the most active in helping getting the data points squared away

--
Steven L. Rosenthal DVM Dip ACVIM Cardiology
CVCA: Cardiac Care for Pets
1209 Cromwell Bridge Road
Towson, MD 21286
Phone: 410.339.3461
Fax: 410.828.5315
Email: Steven.Rosenthal@cvcavets.com
Visit our website at: www.cvcavets.com
"Like" us on Facebook at: www.facebook.com/CVCAVETS
"Follow" us on Instagram at: www.instagram.com/CVCAVETS

Report Details - EON-358131

ICSR:	2051199		
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:	2018-07-02 16:17:19 EDT		
Reported Problem:	**Problem Description:**	Presented as emergency appointment for evaluation of intermittent, persistent cough, first documented five weeks ago. After cough did not respond to course of doxycycline and "cough tabs," Hycodan was added with no improvement. rDVM thoracic radiographs taken on 6/22/18 showed cardiomegaly. Owner describes cough as dry and harsh, which is worse in the evening and when B6 is in sternal recumbency. B6 is very active, without any exercise intolerance or weakness. She tends to graze throughout the day, though has been slower to finish her meals recently. B6 has lost a noticeable amount of weight in the last four weeks. Diagnosed with DCM and taurine level is pending.	
	Date Problem Started:	05/30/2018	
	Concurrent Medical Problem:	Yes	
	Pre Existing Conditions:	Hx of being Lyme positive.	
	Outcome to Date:	Better/Improved/Recovering	
Product Information:	**Product Name:**	4Health Grain Free	
	Product Type:	Pet Food	
	Lot Number:		
	Package Type:	BAG	
	Possess Unopened Product:	No	
	Possess Opened Product:	Yes	
	Product Use Information:	**Description:**	4Health grain free dry- 4 cups daily since late 2016. Also offered rawhide chews from Walmart for years, Canine Carryout Treats for years, and varous ham, chicken, and beef table scraps for years.
		Time Interval between Product Use and Adverse Event:	2 Years
		Product Use Stopped After the Onset of the Adverse Event:	No
		Perceived Relatedness to Adverse Event:	Probably related
		Other Foods or Products Given to the Animal During This Time Period:	Yes
	Manufacturer /Distributor Information:		
	Purchase Location Information:	**Address:**	B6 United States
Animal Information:	**Name:**	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Mixed (Dog)	

	Gender:	Female	
	Reproductive Status:	Neutered	
	Weight:	29.9 Kilogram	
	Age:	9 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Reacted:	1	
	Owner Information:	**Owner Information provided:**	Yes
		Contact:	**Name:** B6 **Phone:** **Email:**
		Address:	B6 United States
	Healthcare Professional Information:	**Practice Name:**	B6
		Contact:	**Name:** B6 **Phone:** **Other Phone:** **Email:**
		Address:	B6 United States
Sender Information:	**Name:**		
	Address:	B6 United States	
	Contact:	**Phone:** B6 **Other Phone:** **Email:**	
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
	Reported to Other Parties:	None	
Additional Documents:			
	Attachment:	cardio0013.pdf	
	Description:	echo report, diet history	
	Type:	Medical Records	

CC-503-800.04-EON-276400

by Vet-LIRN

B6

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B6

CC-503-800.04-EON-276400-Heart 10X

B6

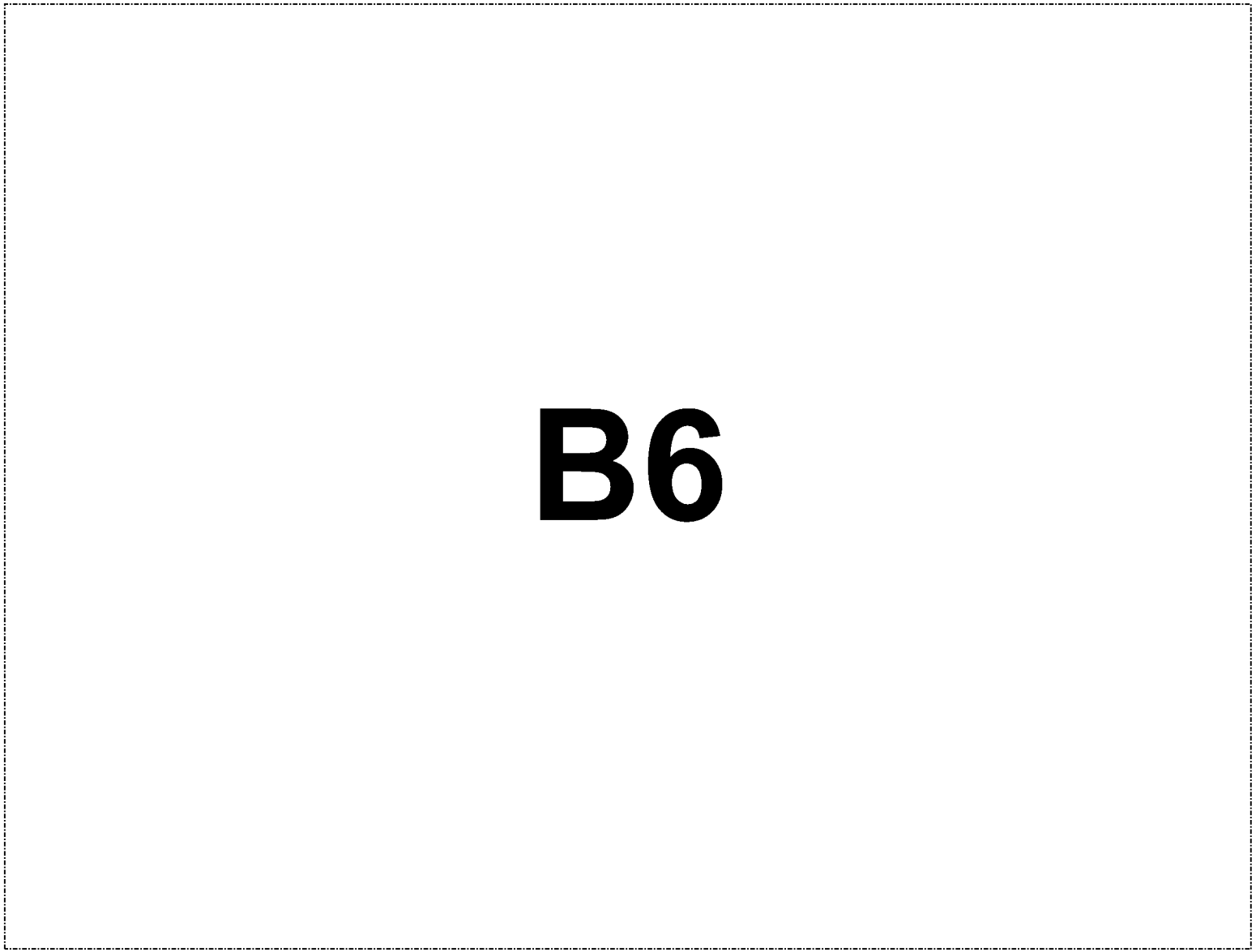
CC-503-800.04-EON-276400-Heart 20X

CC-503-800.04-EON-276400-Heart 20X-2

B6

CC-503-800.04-EON-276400-Intestine 4XX

CC-503-800.04-EON-276400-Intestine 20X



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B6

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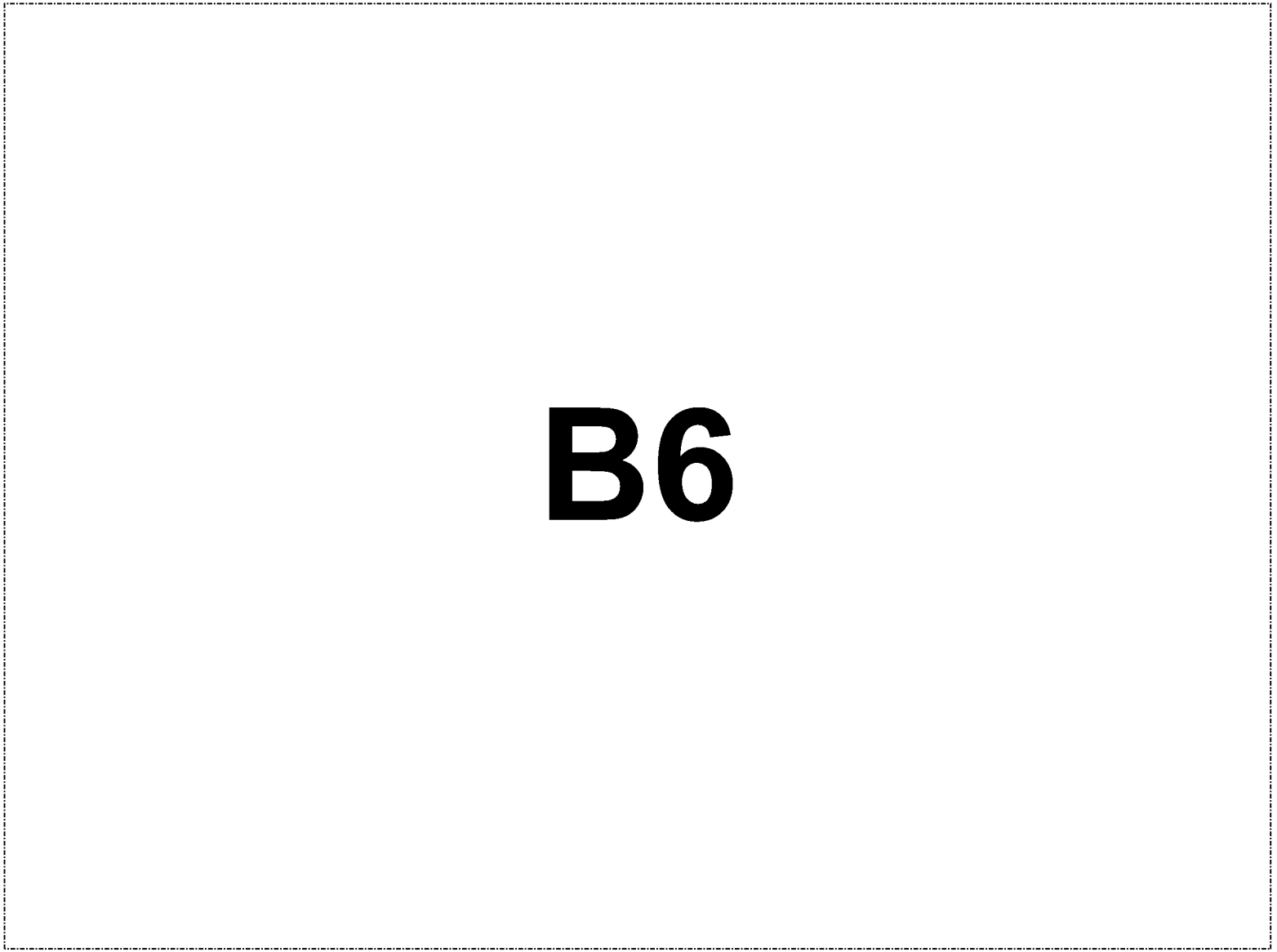

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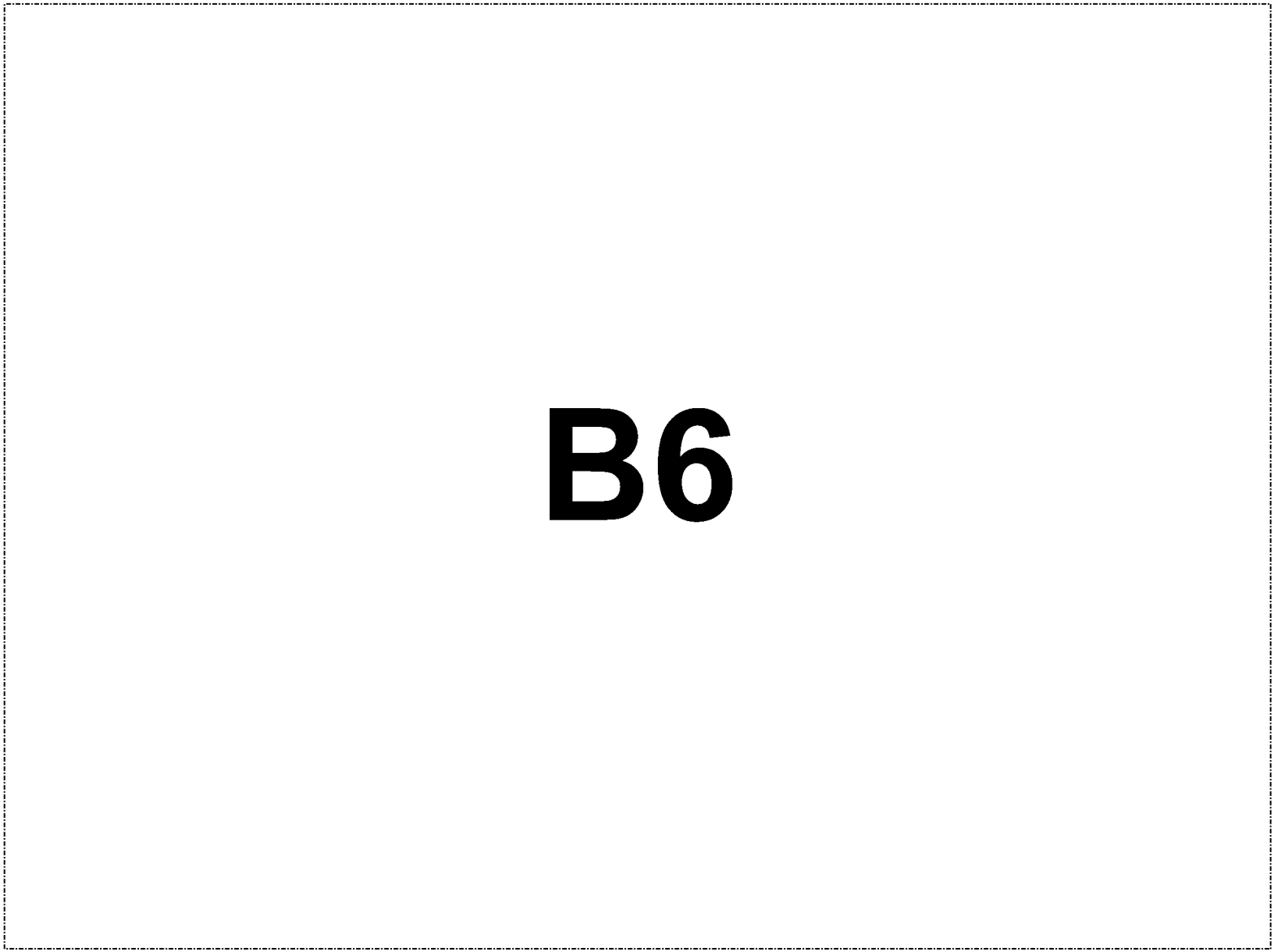


CC-503-800.04-EON-276400-Liver 40X

B6

CC-503-800.04-EON-276400-Pancreas 10X

From: Rotstein, David </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAVID.ROTSTEIN>
To: Jones, Jennifer L
Sent: 12/11/2015 6:51:02 PM
Subject: CC-466-800.04-CC-143384
Attachments: CC-466-800.04-CC-143384.docx; CC-466-800.04-CC-143384-Photomicrographs.pdf

Here you go!

thanks

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison (http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm#Network_Laboratories_)
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
B6

CC-466-800.04-CC-143384

by Vet-LIRN

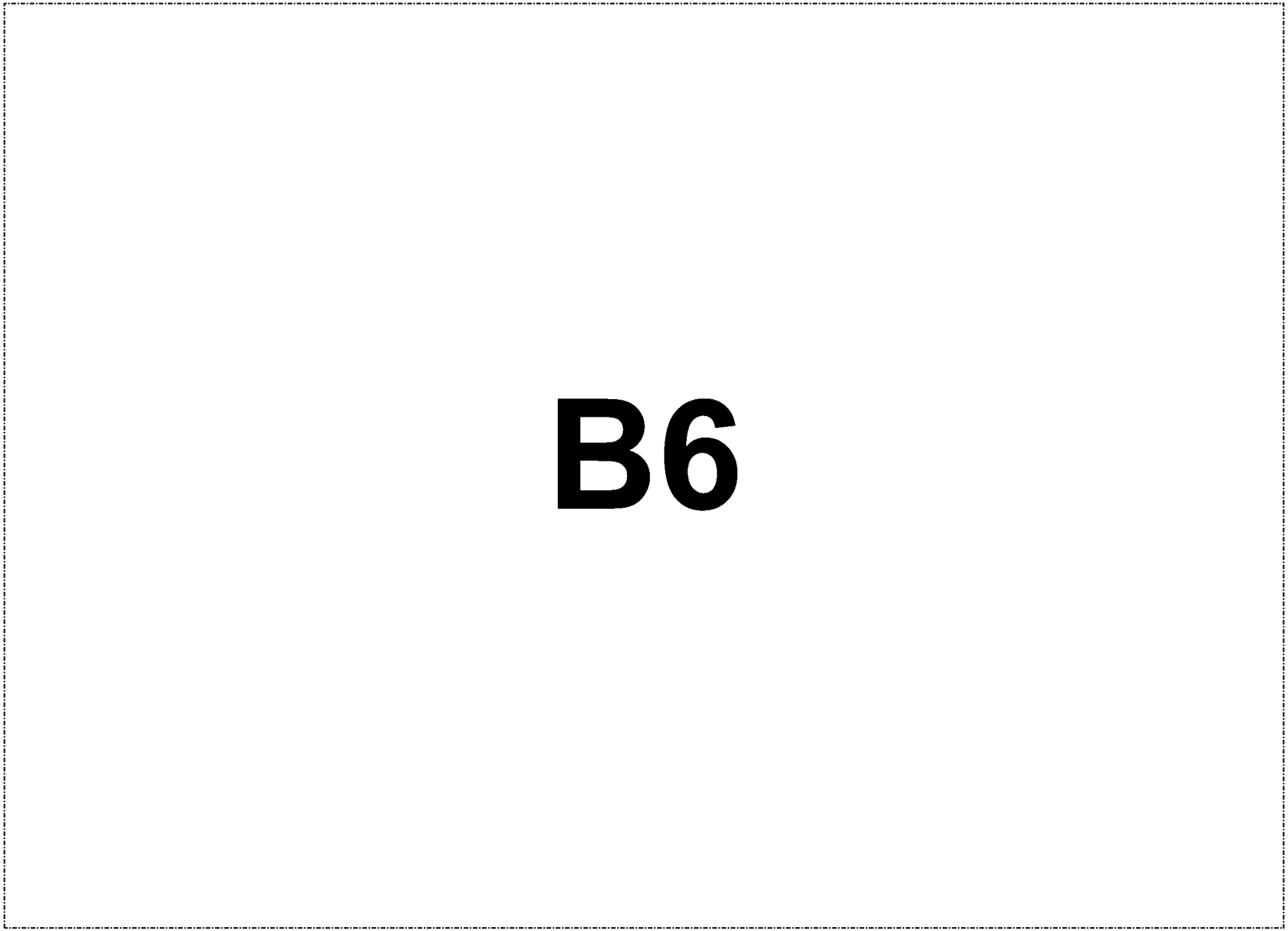
B6

CC-466-800.04-CC-143384-Heart-10X

B6

CC-466-800.04-CC-143384-Heart-20X

CC-466-800.04-CC-143384-Heart-20X-2



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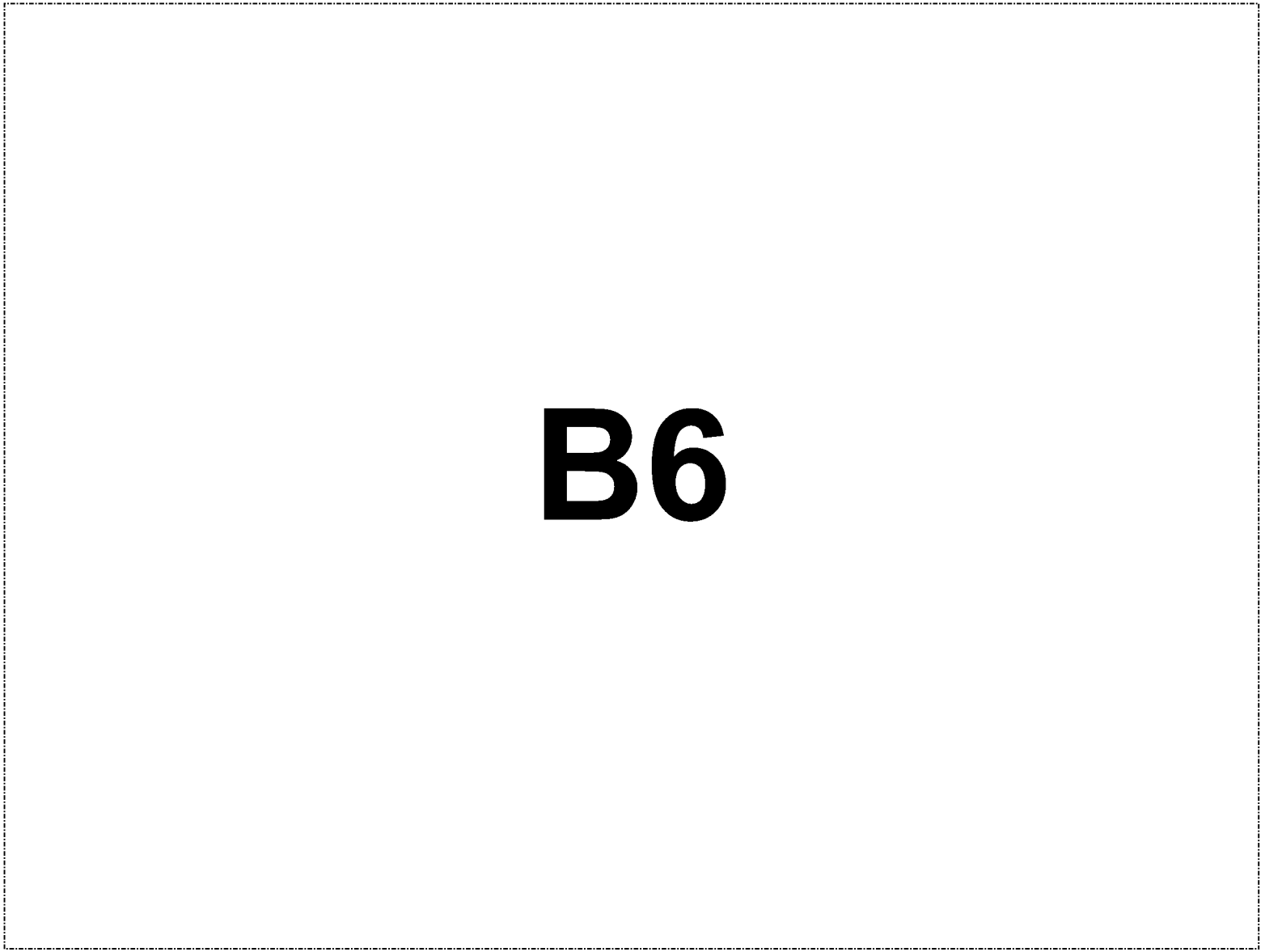
CC-466-800.04-CC-143384-Kidney-Warthin-Starry 20X



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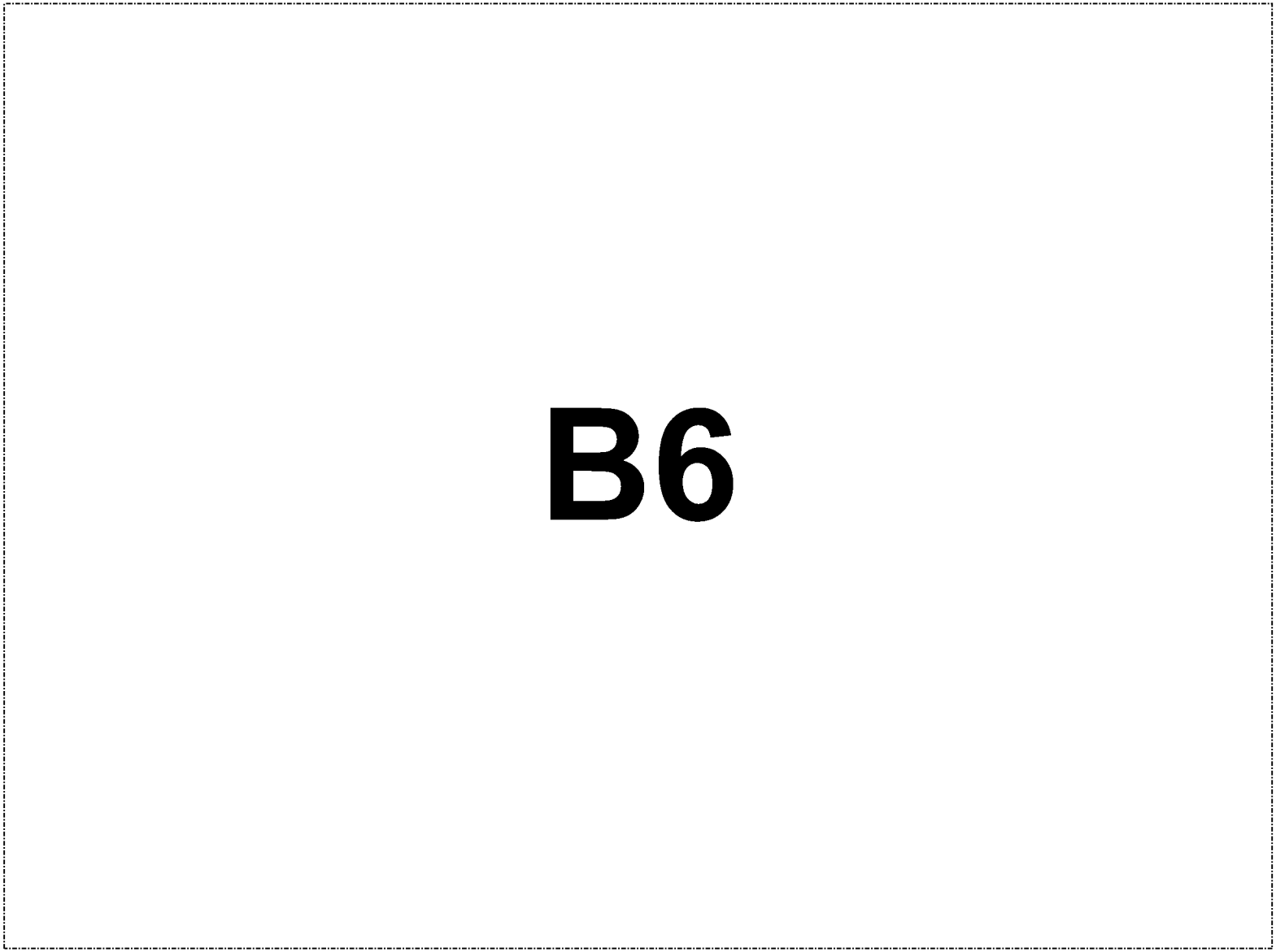

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B6

CC-466-800.04-CC-143384Stomach 10X

B6

CC-466-800.04-CC-143384Stomach 40X

From:	Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To:	Jones, Jennifer L
Sent:	6/6/2018 4:04:44 PM
Subject:	Copy of products/ingredient lists from cases
Attachments:	photos and ingred product info.docx

Hi – I listed all the reported products with ingredients for all the cases from Tufts, NC State, FDA and CVCA.

My spreadsheet is a big mess and probably won't be helpful, but hope this is of some use.

Thanks!

Lee Anne

Lee Anne M. Palmer, VMD, MPH
Team Leader HFV-242, Supervisory VMO

Center for Veterinary Medicine
OSC, Division of Veterinary Product Safety
U.S. Food and Drug Administration
Tel: 240-402-5767
Leeanne.palmer@fda.hhs.gov

From:	Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To:	Rotstein, David; Queen, Jackie L; Palmer, Lee Anne; Carey, Lauren
CC:	'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'; Ceric, Olgica; Nemser, Sarah
Sent:	4/23/2018 2:31:39 PM
Subject:	DCM cases-food-Iodine screening results
Attachments:	800.261-MSU-iodine results.pdf

FYI-Iodine < 10ppm for the foods tested. Exogenous thyrotoxicosis unlikely a cause of the DCM
Multiple EONs Involved:

- 800.218
  - EON-323515
  - EON-345822
- 800.261
  - EON-350158

Jennifer L. A. Jones, DVM
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Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
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new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

FDA Investigating Potential Connection Between Diet and Cases of Canine Heart Disease

July 12, 2018

The U.S. Food and Drug Administration is alerting pet owners and veterinary professionals about reports of canine dilated cardiomyopathy (DCM) in dogs eating certain pet foods containing peas, lentils, other legume seeds, or potatoes as main ingredients. These reports are unusual because DCM is occurring in breeds not typically genetically prone to the disease. The FDA's Center for Veterinary Medicine and the Veterinary Laboratory Investigation and Response Network, a collaboration of government and veterinary diagnostic laboratories, are investigating this potential association.

Canine DCM is a disease of a dog's heart muscle and results in an enlarged heart. As the heart and its chambers become dilated, it becomes harder for the heart to pump, and heart valves may leak, leading to a buildup of fluids in the chest and abdomen. DCM often results in congestive heart failure. Heart function may improve in cases that are not linked to genetics with appropriate veterinary treatment and dietary modification, if caught early.

The underlying cause of DCM is not truly known, but is thought to have a genetic component. Breeds that are typically more frequently affected by DCM include large and giant breed dogs, such as Great Danes, Boxers, Newfoundlands, Irish Wolfhounds, Saint Bernards and Doberman Pinschers. It is less common in small and medium breed dogs, except American and English Cocker Spaniels. However, the cases that have been reported to the FDA have included Golden and Labrador Retrievers, Whippets, a Shih Tzu, a Bulldog and Miniature Schnauzers, as well as mixed breeds.

Diets in cases reported to the FDA frequently list potatoes or multiple legumes such as peas, lentils, other "pulses" (seeds of legumes), and their protein, starch and fiber derivatives early in the ingredient list, indicating that they are main ingredients. Early reports from the veterinary cardiology community indicate that the dogs consistently ate these foods as their primary source of nutrition for time periods ranging from months to years. High levels of legumes or potatoes appear to be more common in diets labeled as "grain-free," but it is not yet known how these ingredients are linked to cases of DCM. Changes in diet, especially for dogs with DCM, should be made in consultation with a licensed veterinarian.

In the reports the FDA has received, some of the dogs showed signs of heart disease, including decreased energy, cough, difficulty breathing and episodes of collapse. Medical records for four atypical DCM cases, three Golden Retrievers and one Labrador Retriever, show that these dogs had low whole blood levels of the amino acid taurine. Taurine deficiency is well-documented as potentially leading to DCM. The Labrador Retriever with low whole blood taurine levels is recovering with veterinary treatment, including taurine supplementation, and a diet change. Four other cases of DCM in atypical dog breeds, a Miniature Schnauzer, Shih Tzu and two Labrador Retrievers, had normal blood taurine levels. The FDA continues to work with board certified veterinary cardiologists and veterinary nutritionists to better understand the clinical presentation of these dogs. The agency has also been in contact with pet food manufacturers to discuss these reports and to help further the investigation.

The FDA encourages pet owners and veterinary professionals to report cases of DCM in dogs suspected of having a link to diet by using the electronic Safety Reporting Portal or calling their state's FDA Consumer Complaint Coordinators. Please see the link below about "How to Report a Complaint about Pet Food" for additional instructions.

Additional Information

- How to Report a Complaint about Pet Food
- Veterinary Laboratory Investigation and Response Network (Vet-LIRN)

Document properties

Author: Norris, Anne
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Paragraph count: 11
Line count: 51
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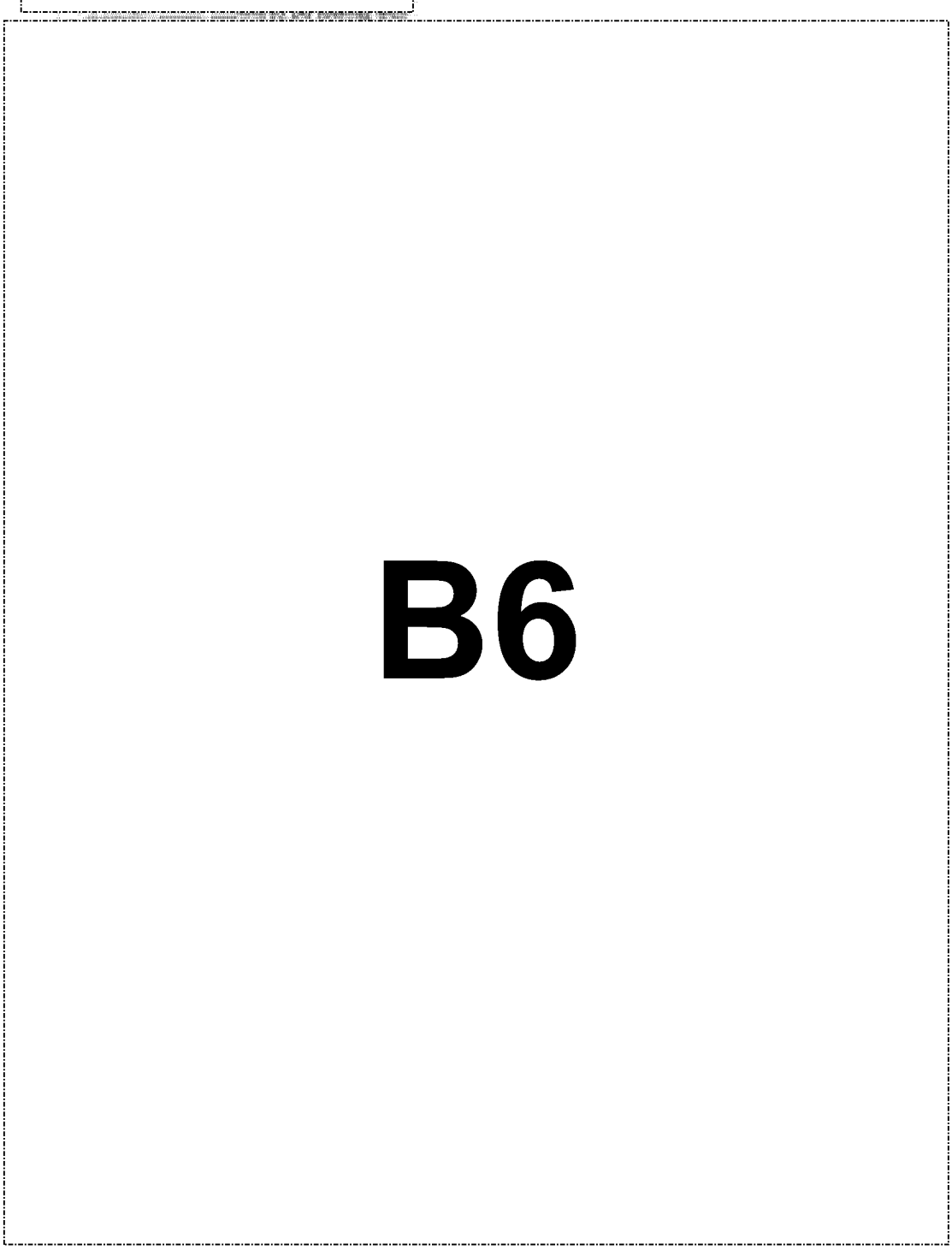

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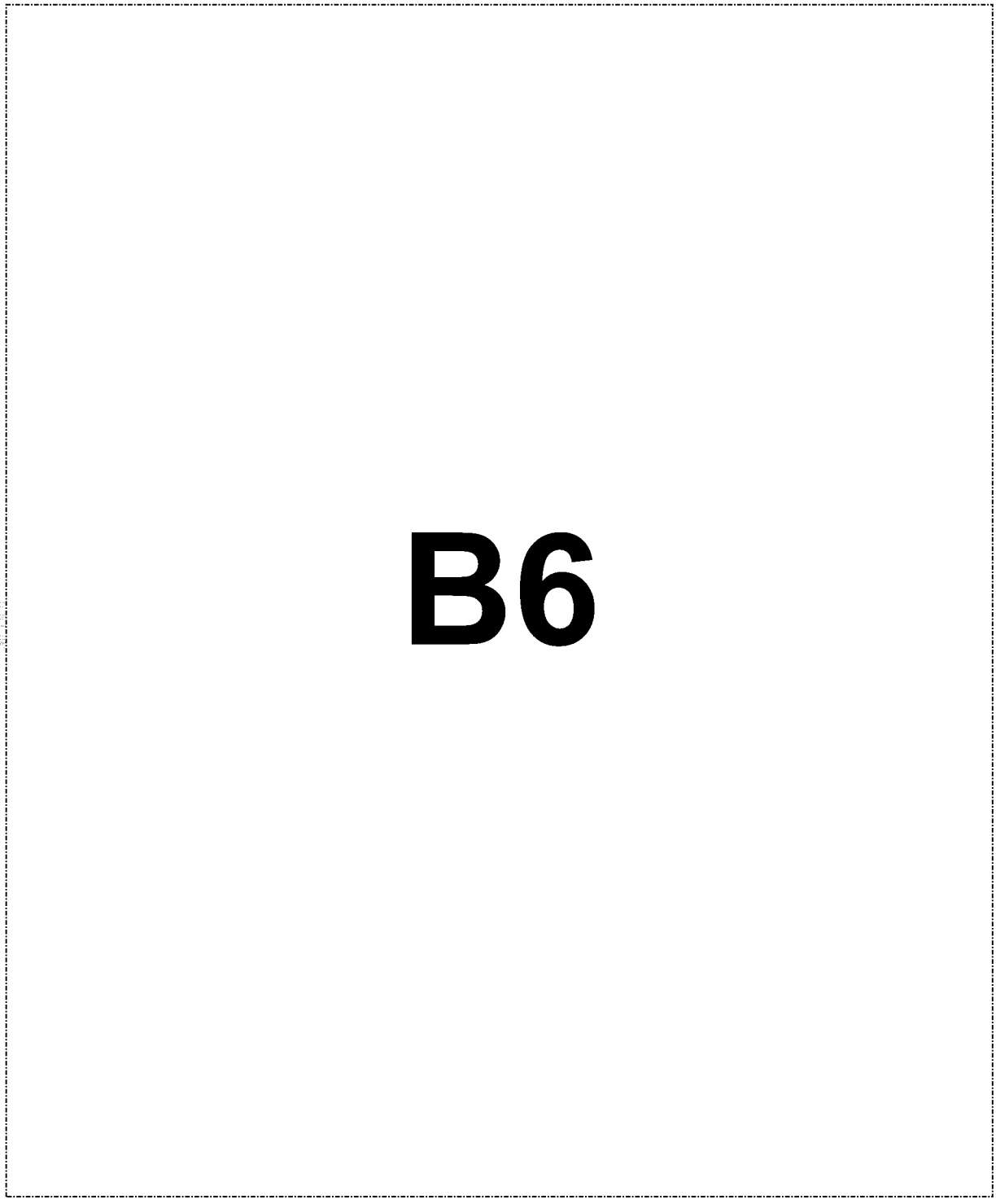

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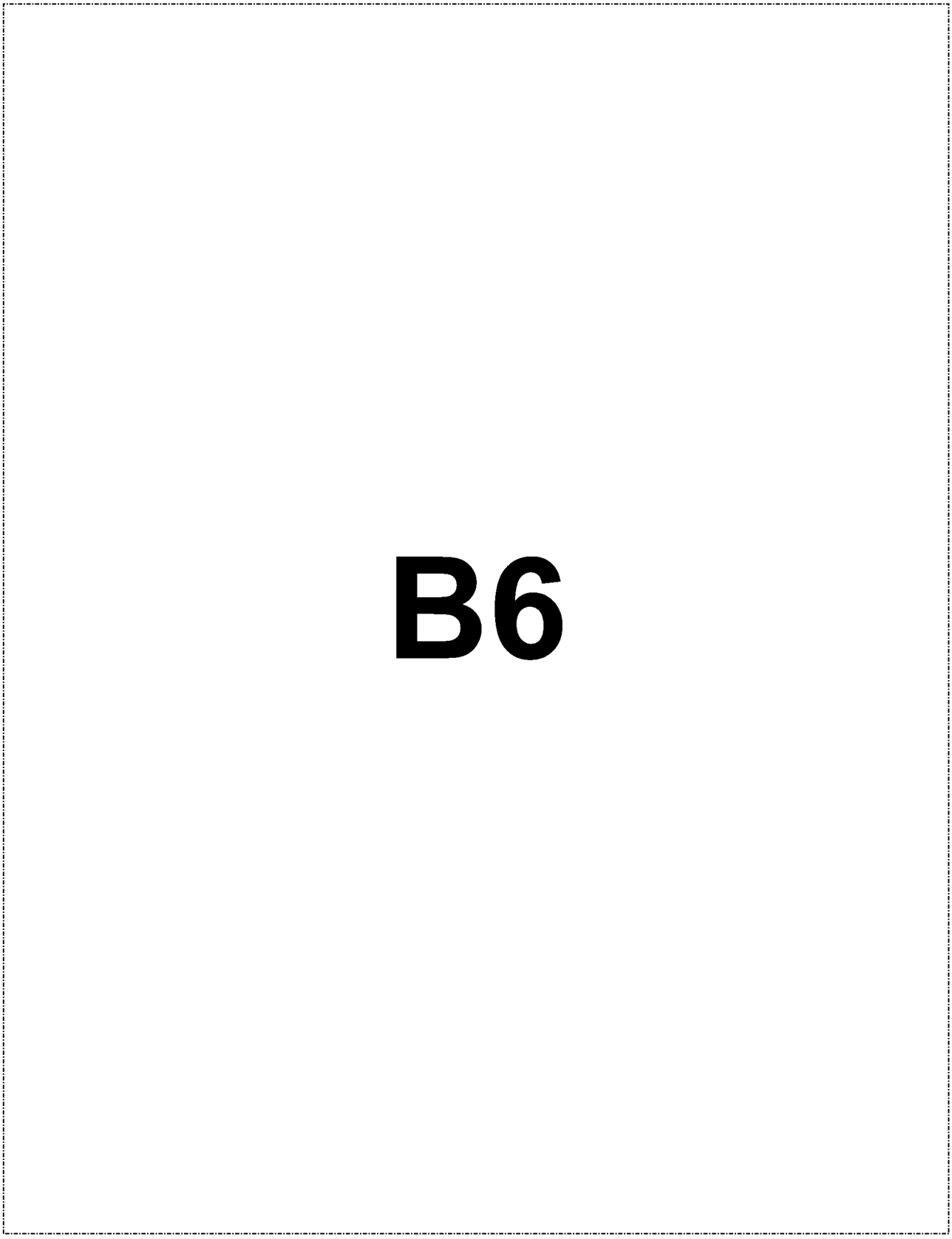

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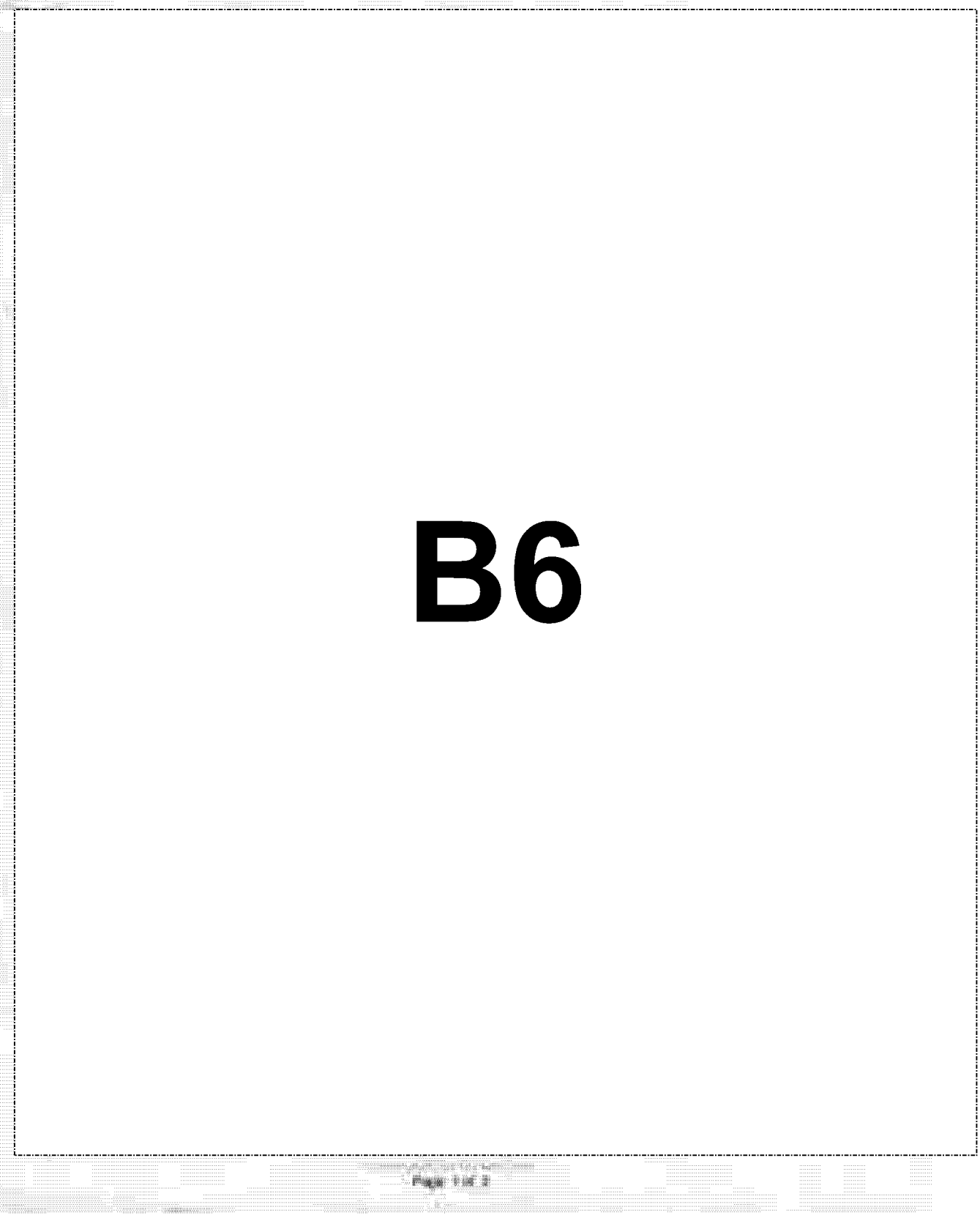

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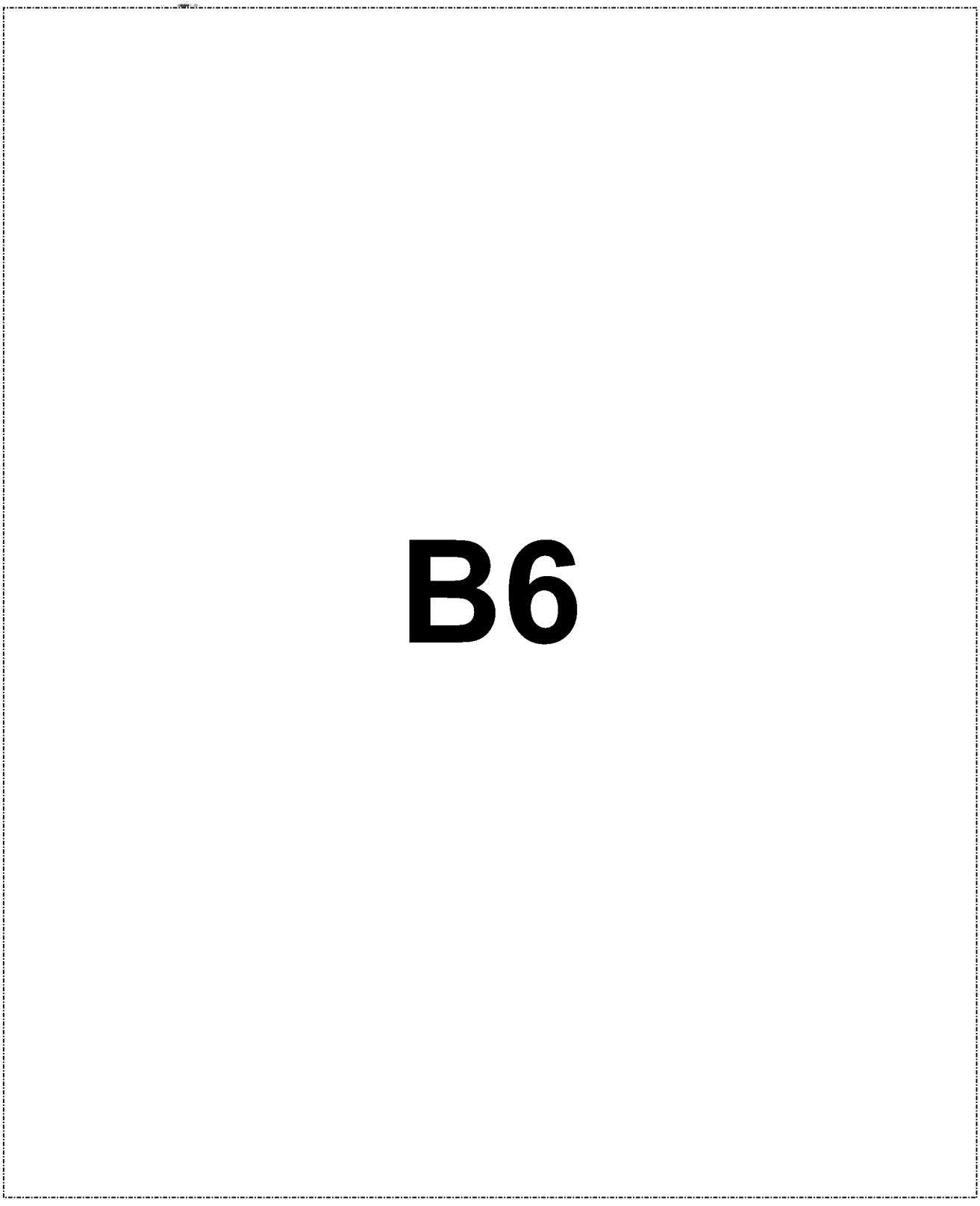
Lab Image Taurine Panel 9/21/18



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Vitals Results

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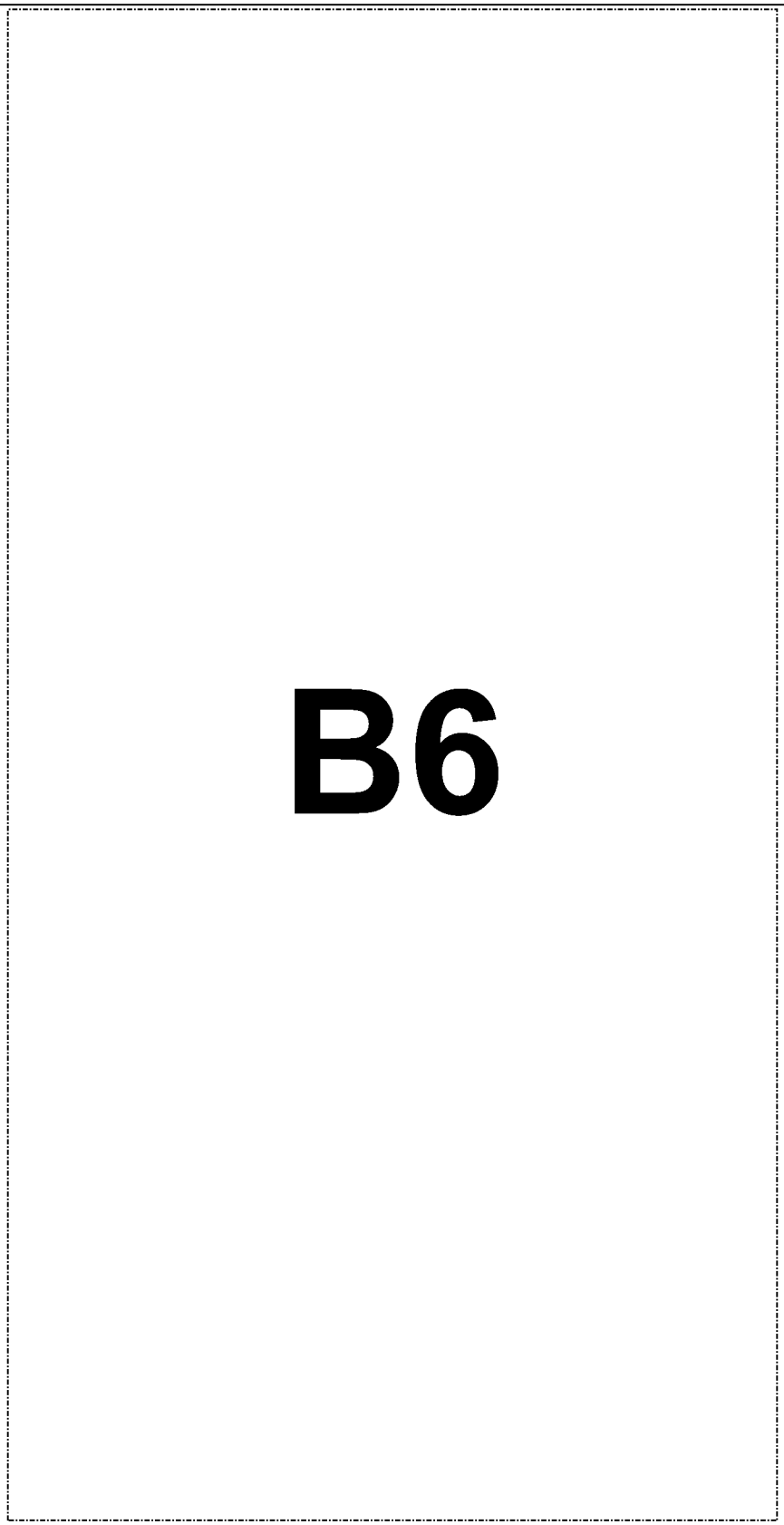

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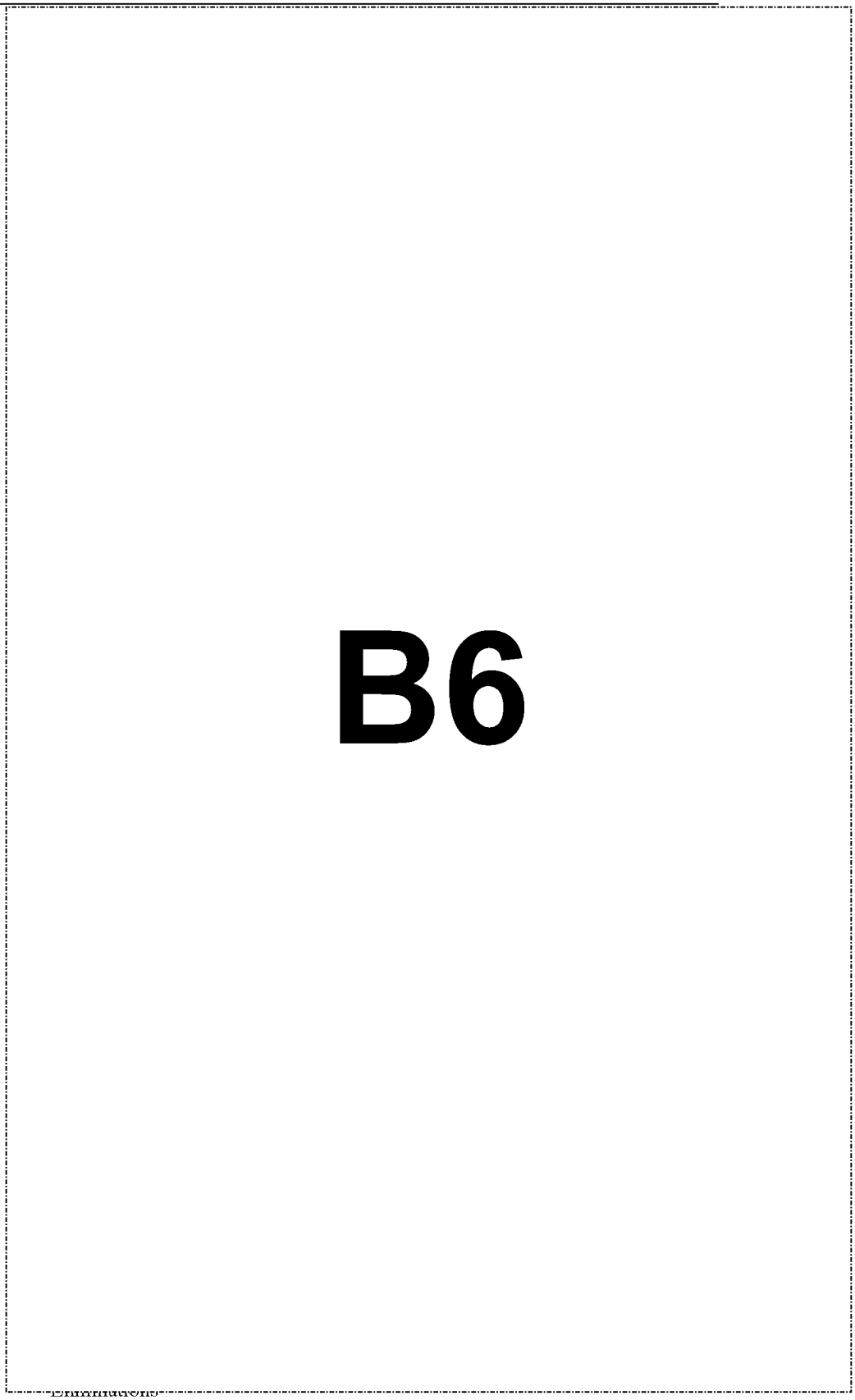

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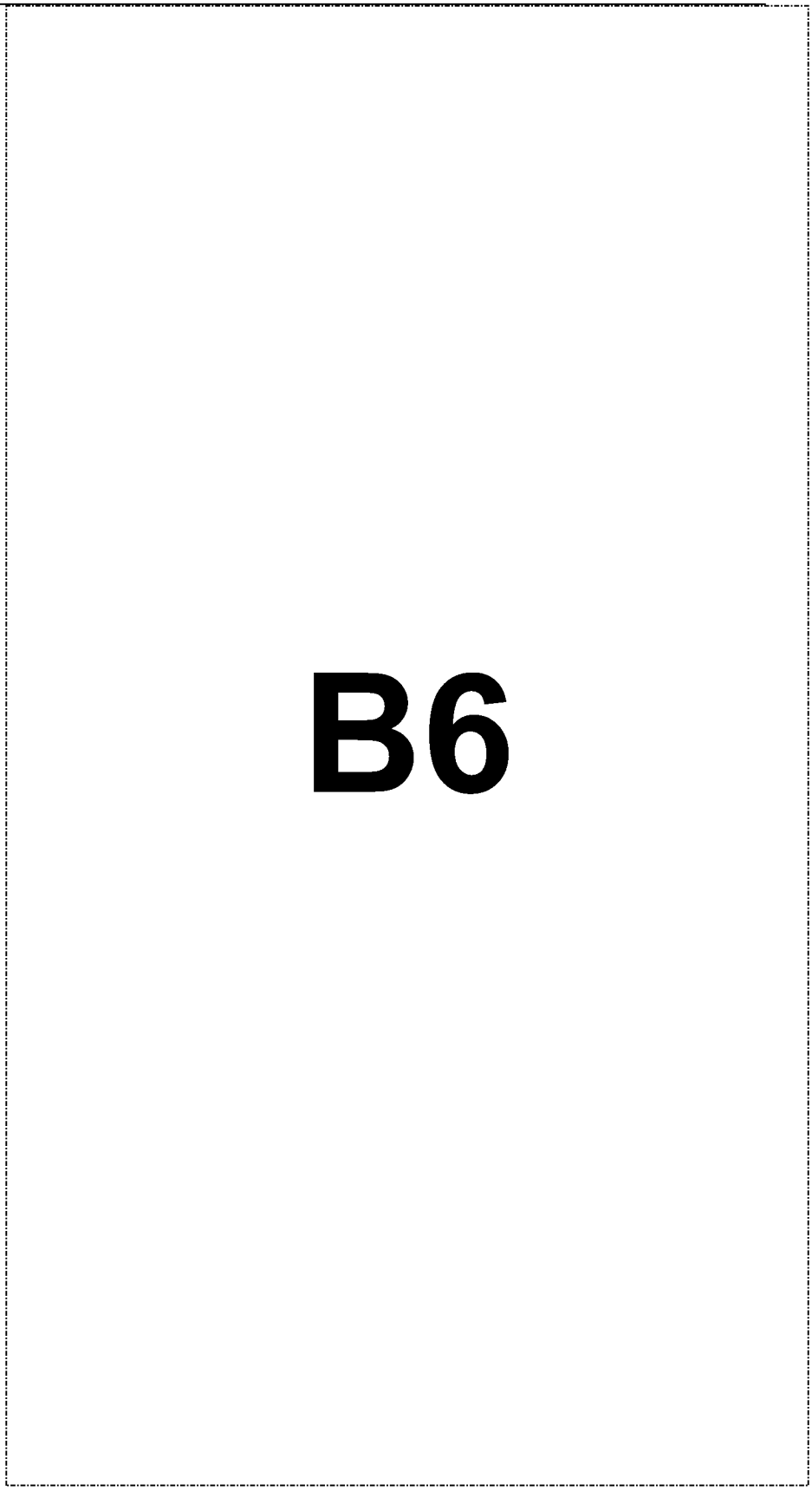

Vitals Results

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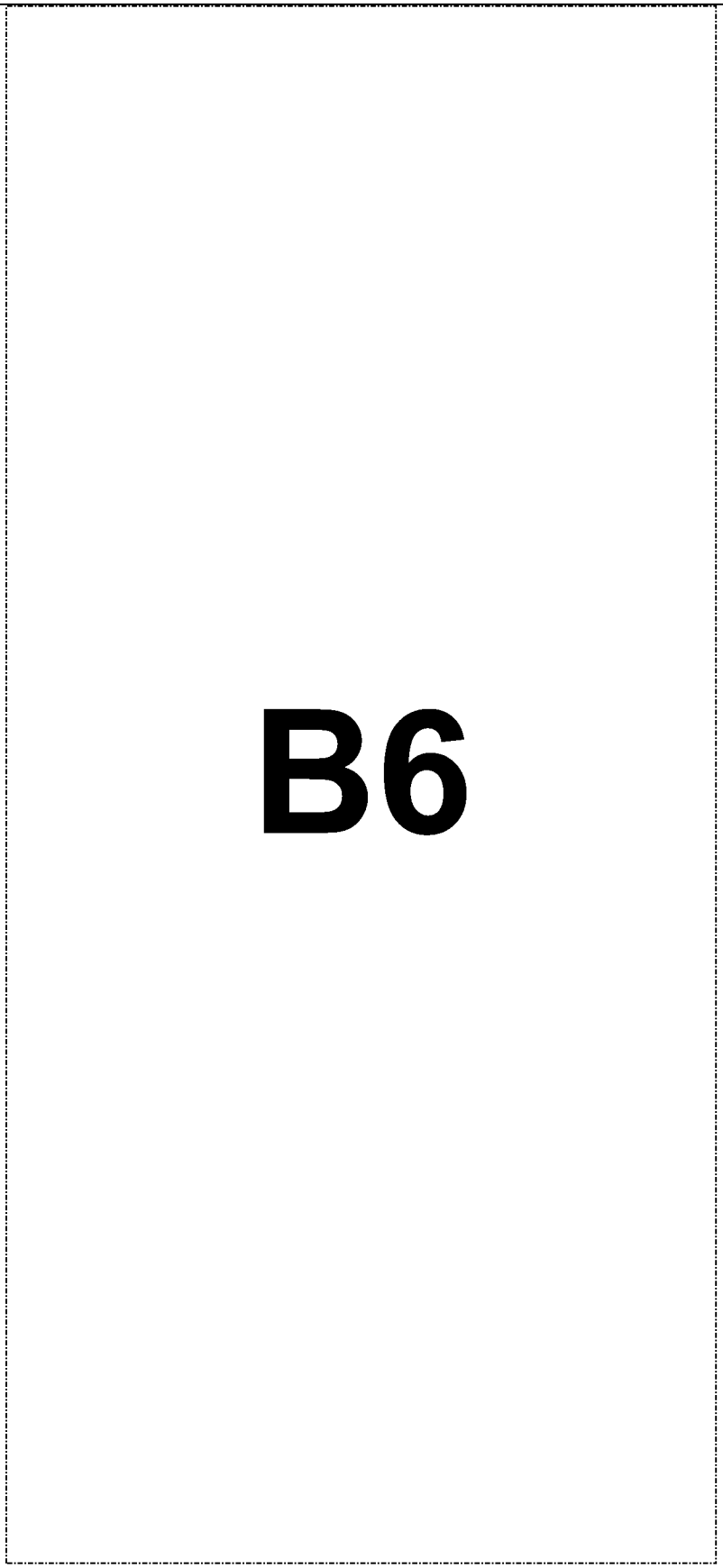

B6

Vitals Results

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10/1/2018 11:07:38 AM
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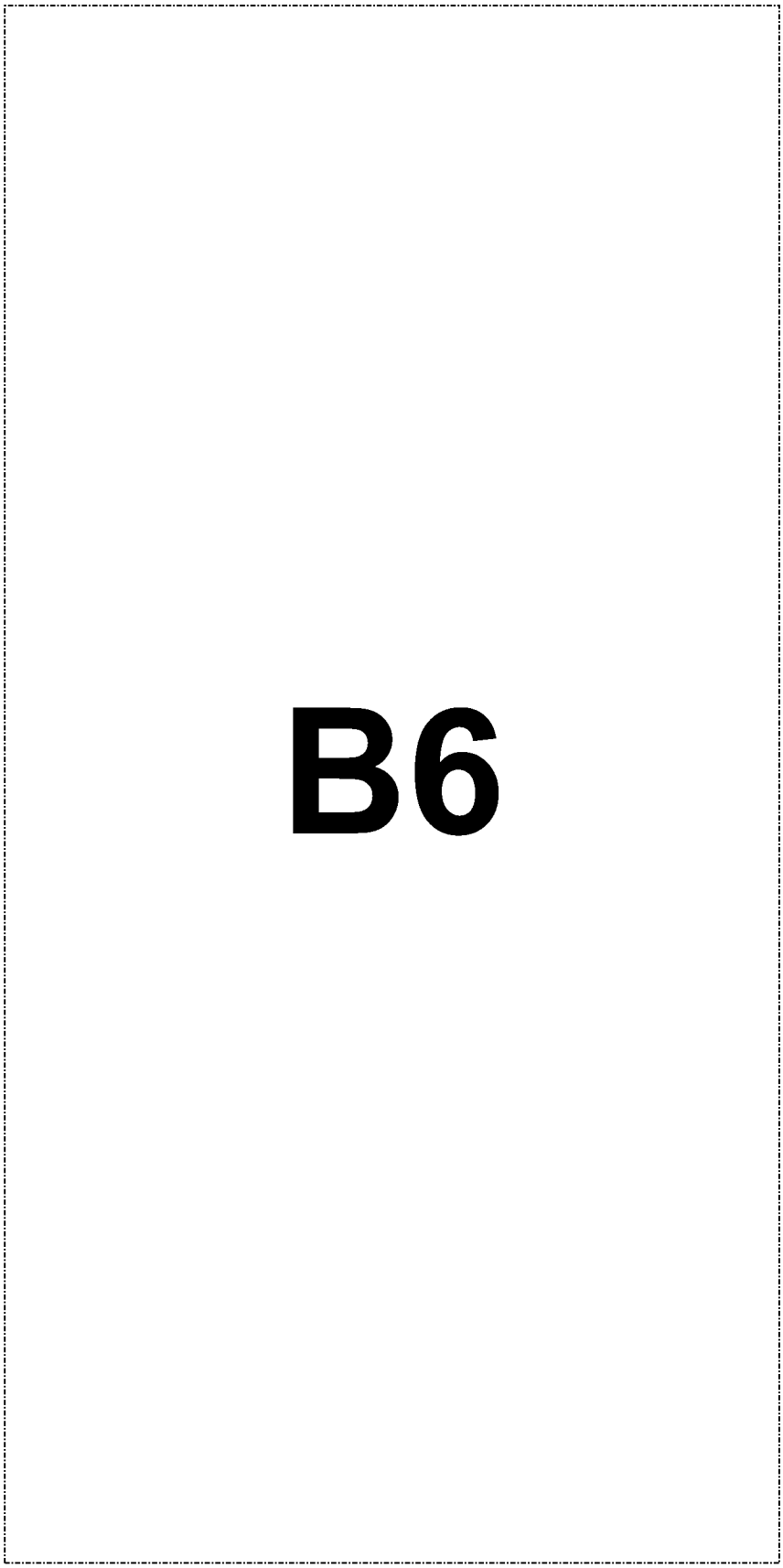

B6

Vitals Results

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B6

Best Available Copy

ECG from cardio

B6

B6

B6

ECG from Cardio

B6

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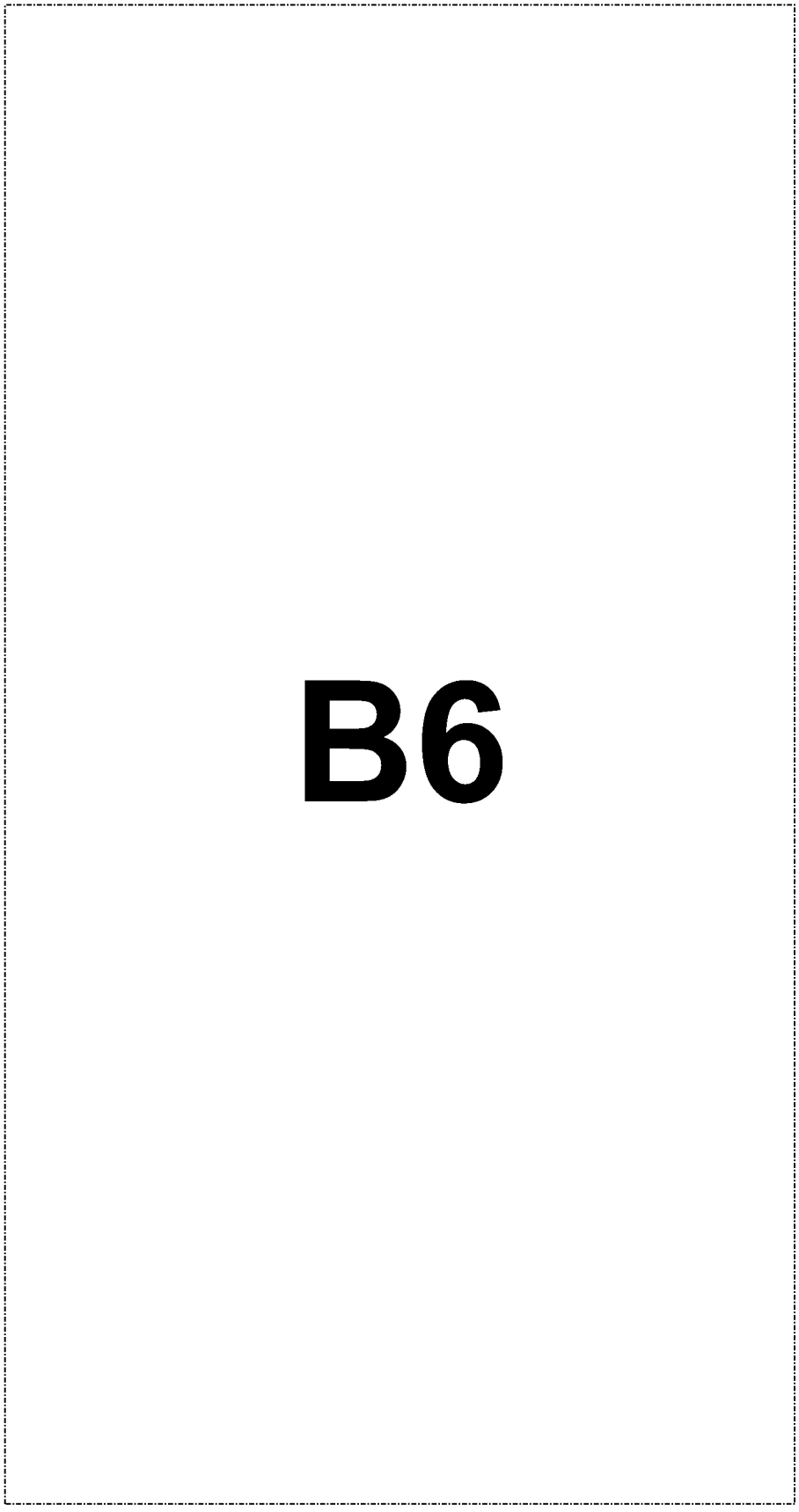

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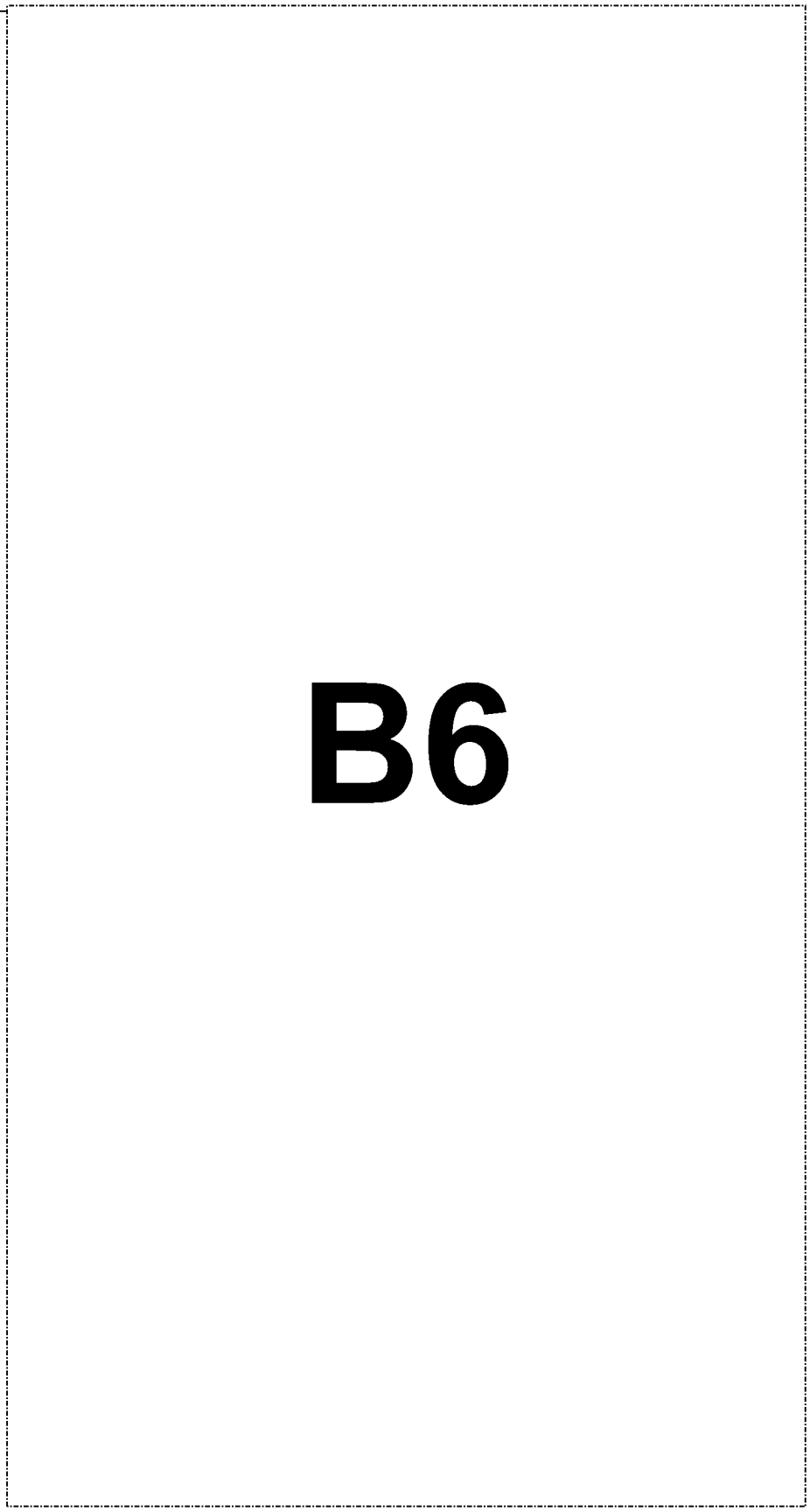

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B6

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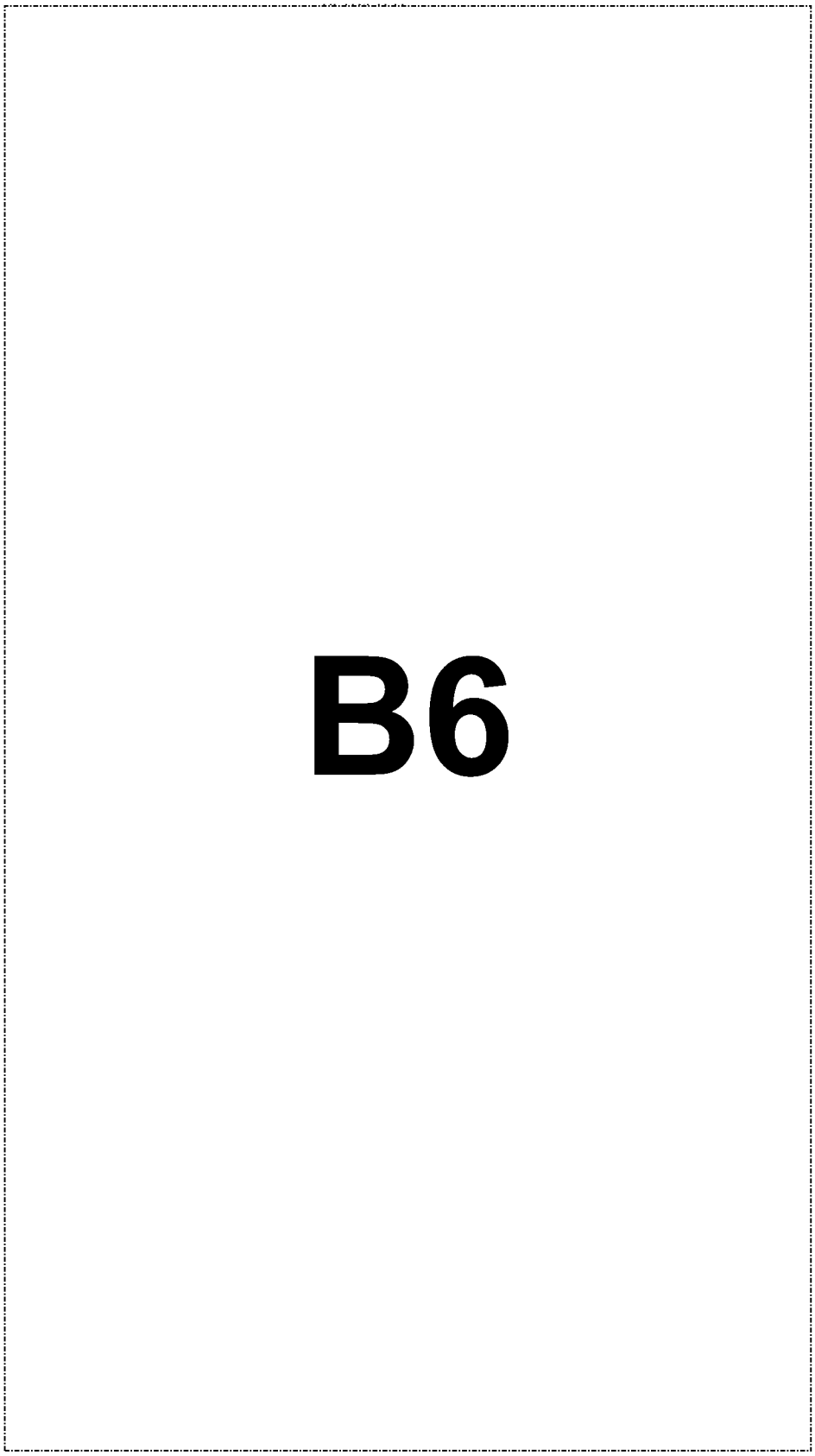

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B6

Patient History

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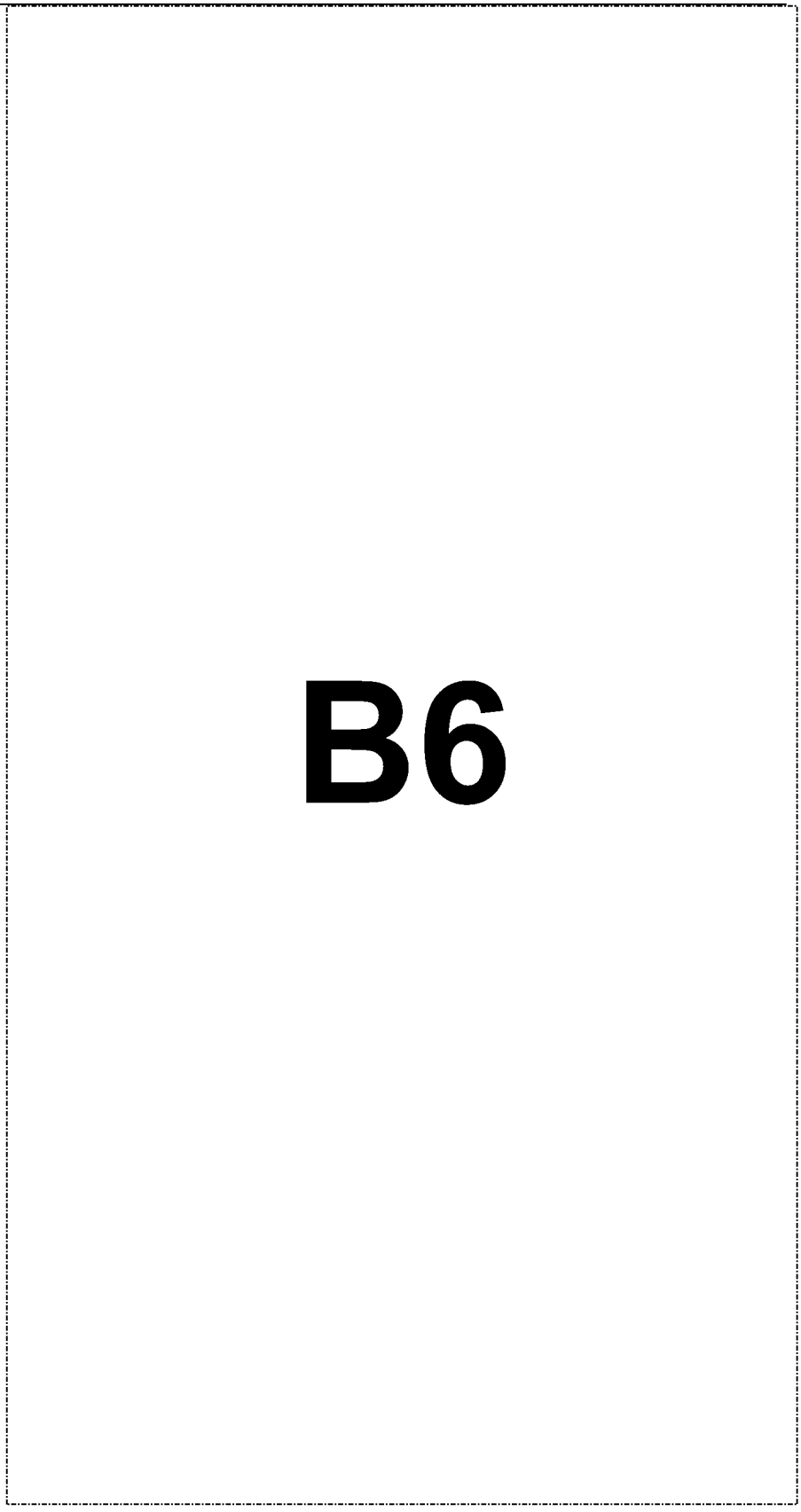

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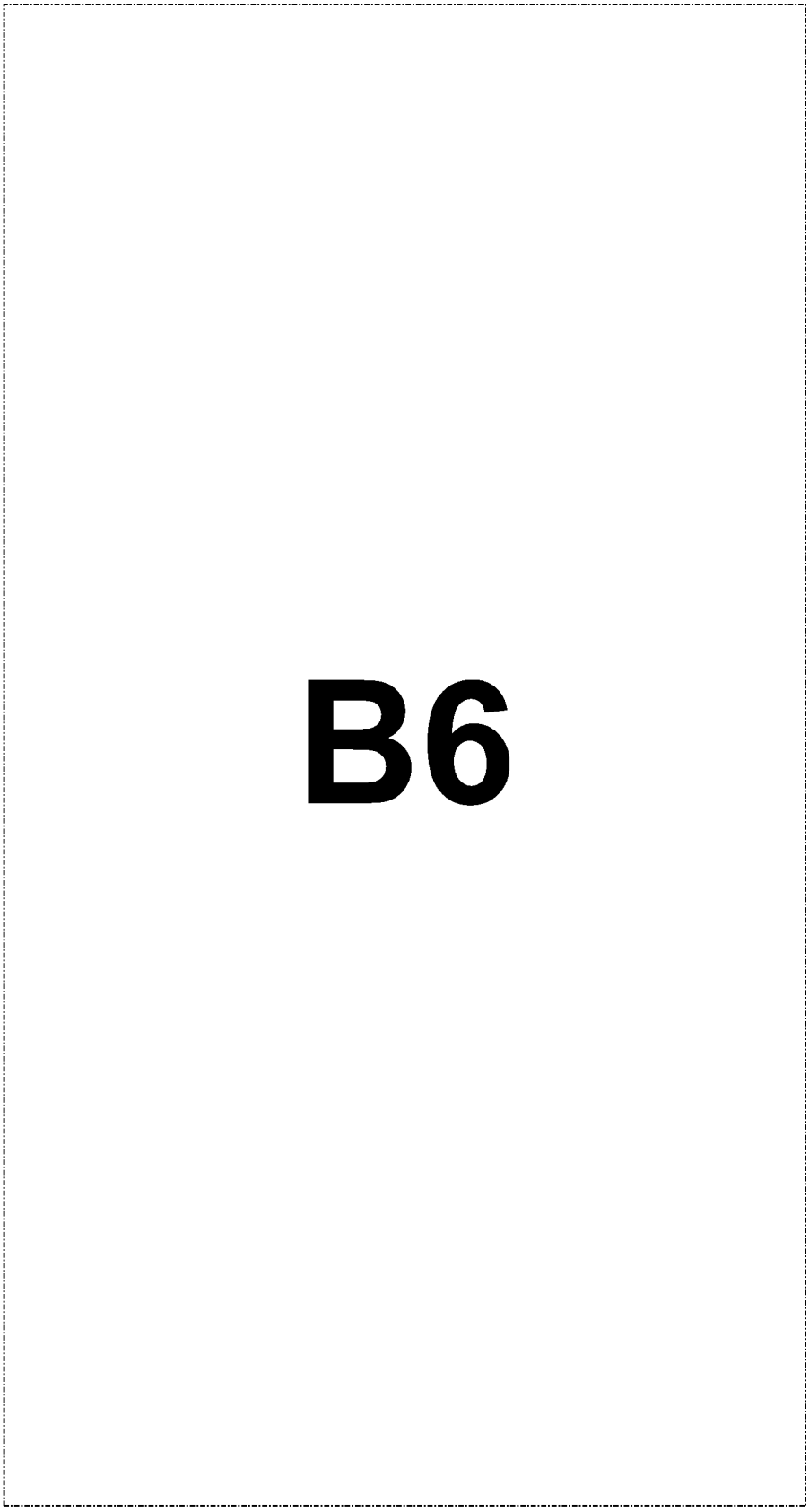

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Patient History

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10/31/2018 04:37 PM
11/01/2018 10:25 AM

11/01/2018 10:26 AM

11/01/2018 10:26 AM

B6

Appears this way on Original

Appears this way on Original

Appears this way on Original

Appears this way on Original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

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Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

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B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Notice of Patient Admit

B6

B6

B6

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Client:
Address: B6

All Medical Records

Patient: B6
Breed: Golden Retriever
DOB: B6

Species: Canine
Sex: Male (Neutered)

Referring Information

B6

Initial Complaint:
Scanned Record

Initial Complaint:
New - B6 - DCM study

SOAP Text B6 **12:08PM -** B6

Disposition/Recommendations

Client:
Patient: B6

B6

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

Client:
Veterinarian:
Patient ID: B6
Visit ID:

Patient:	B6
Species:	Canine
Breed:	Golden Retriever
Sex:	Male (Neutered)
Age:	B6 Years Old

Lab Results Report

B6 1:29:30 PM **Accession ID:** B6

Test	Results	Reference Range	Units
Troponin I Research - FHSA	B6	0 - 0.08	mg/dl

3/22

B6

stringsoft

Printed Friday, November 09, 2018

Best Available Copy

B4, B6 H records

B4, B6

B6

B4, B6

B6

Client: B6
Patient

B4, B6 ecords

B4, B6

B6

B4, B6

B6

Client: B6
Patient:

Best Available Copy

B4, B6

B6

Client: B6
Patient:

B4, B6

B6

Client: B6
Patient:

B4, B6

B6

Client: B6
Patient:

B4, B6

FECAL ANALYSIS (In House)

B6

FECAL ANALYSIS: (In House)

B6

Best Available Copy

B4, B6

B6

FECAL ANALYSIS: (In House)

B6

Client: B6
Patient

B4, B6

B6

Client: B6
Patien

CBC/Chen: B6

Tufts Cummings School Of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

DUPLICATE

B6

Best Available Copy

Client: B6
Patient:

CBC/Chem - B6

Tufts Cummings School Of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

DUPLICATE

B6

B6

Client: B6
Patient:

Vitals Results

B6 11:32:13 AM B6

ECG from cardio

Client:
Patient: B6

ECG from cardio

Client:
Patient: B6

ECG from cardio

Client: B6
Patient:

Patient History

B6

10:46 AM

12:36 PM

10:07 AM
10:48 AM
10:53 AM
11:32 AM
12:08 PM
12:18 PM

01:29 PM
01:30 PM
01:30 PM
01:30 PM

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Client:
Address: B6

All Medical Records

Patient: B6
Breed: Boxer
DOB: B6

Species: Canine
Sex: Male (Neutered)

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Scanned Record

SOAP Text Nov 20 2018 12:22PM B6

Initial Complaint:
DCM Study

SOAP Text Nov 20 2018 1:10PM B6

Disposition/Recommendations

B6

Client:	B6
Veterinarian:	
Patient ID:	433149
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Boxer
Sex:	Male (Neutered)
Age:	B6 Years Old

Lab Results Report

11/20/2018 5:45:23 PM **Accession ID:** B6

Test	Results	Reference Range	Units
Troponin I Research - FHSA	B6	0 - 0.08	mg/dl

B6

stringsoft

Printed Tuesday, December 04, 2018

Client: B6
Patient

B6

B6

B6

Client: Patient: **B6**

Diet hx

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: **B6** Today's date: 20 NOV 2018

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: ***Poor*** _____|_____ ***Excellent***

   Poor _____ **Excellent**

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☑Eats about the same amount as usual ☐Eats less than usual ☐Eats more than usual
   ☐Seems to prefer different foods than usual ☐Other_____

3. Over the last few weeks, has your pet (check one)
   ☐Lost weight ☐Gained weight ☑Stayed about the same weight ☐Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

   Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2018*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
EARTHBORN - MEADOWFEAST	DRY	~1 1/2C +	2X DAY	FEB 2016

**Any additional diet information can be listed on the back of this sheet*

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐Yes ☐No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☐Yes ☐No		
Carnitine	☐Yes ☐No		
Antioxidants	☐Yes ☐No		
Multivitamin	☐Yes ☐No		
Fish oil	☐Yes ☐No		
Coenzyme Q10	☐Yes ☐No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*
SUPPLEMENT		NUPRO - DOG SUPPLEMENT	1 SCOOP (~ 1 TBSP) 1-2X DAY

6. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food
   ☐ I put them in a Pill Pocket or similar product
   ☑ I put them in foods (list foods): BOLOGNA OR CHEESE

Client: B6
Patient:

ECG from Cardio

B6

B6

Client: B6
Patient:

ECG from Cardio

B6

B6

ECG from Cardio

Patient History

B6

B4, B6

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Rotstein, David; Jones, Jennifer L
Sent: 5/1/2018 1:40:27 PM
Subject: RE: DCM cases - proposed diet history

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I'm attaching a proposed diet history form B5

B5

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Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu>, B6
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Hi everyone
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sending out to all clients (dog and cat) to have them fill it out ahead of time and bring it with them to the appointment.

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Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

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Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

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Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 ; B6
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Please email or call me with any questions. Thank you again for your time and expertise,
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Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

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Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 ; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
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B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

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Meeting password: B6

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US Toll Free
Global call-in numbers | Toll-free calling restrictions

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--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Rotstein, David; Jones, Jennifer L
Sent: 5/1/2018 1:56:59 PM
Subject: RE: DCM cases - proposed diet history

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B5

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Join WebEx meeting

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Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
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To:	Rotstein, David; Jones, Jennifer L
Sent:	5/1/2018 3:08:12 PM
Subject:	Last one, I promise: DCM cases - proposed diet history
Attachments:	diet history form 4-27-18 external.doc

If they can add a question to each food: are you still feeding it? I tried to add edits to the form as well. (I did a rough job, though L).

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Sent: Tuesday, May 1, 2018 9:57 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
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Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 >; B6 >
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C

<rfries@illinois.edu>; B6 ;
Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 Freeman, B6 Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6
Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

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Meeting password: B6

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US Toll Free
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IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--

Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

Client: B6 (74646)
Patient Name: B6
Species: Canine
Breed:

Gender: Male/Castrated
Weight:
Age: 4 Years
Doctor: B6

B6

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx (March 17, 2019 10:46 AM)					
RBC	B6	5.65 - 8.87			
HCT		37.3 - 61.7			
HGB		13.1 - 20.5			
MCV		61.6 - 73.5			
MCH		21.2 - 25.9			
MCHC		32.0 - 37.9			
RDW		13.6 - 21.7			
%RETIC					
RETIC		10.0 - 110.0			
RETIC-HGB		22.3 - 29.6			
WBC		5.05 - 16.76			
%NEU					
%LYM					
%MONO					
%EOS					
%BASO					
NEU		2.95 - 11.64			
LYM		1.05 - 5.10			
MONO		0.16 - 1.12			
EOS		0.06 - 1.23			
BASO		0.00 - 0.10			
PLT		148 - 484			
MPV		8.7 - 13.2			
PDW		9.1 - 18.4			
PCT		0.14 - 0.46			
Catalyst Dx (March 17, 2019 11:20 AM)					
GLU	B6	74 - 143			
CREA		0.5 - 1.8			
BUN		7 - 27			
BUN/CREA					
PHOS		2.5 - 6.8			
CA		7.9 - 12.0			
TP		5.2 - 8.2	LOW		
ALB		2.3 - 4.0			
GLOB		2.5 - 4.5	LOW		
ALB/GLOB					
ALT		10 - 125		HIGH	
ALKP		23 - 212	LOW		
GGT		0 - 11			
TBIL		0.0 - 0.9			
CHOL		110 - 320	LOW		
AMYL		500 - 1500			
LIPA		200 - 1800			
Na		144 - 160			
K		3.5 - 5.8	LOW		
Na/K					
Cl		109 - 122			
Osm Calc					

B6

Printed: B6 11:20 AM

IDEXX LABORATORIES

LVPWs	B6	cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV A Vel		m/s
MV E/A Ratio		
PV Vmax		m/s
PV maxPG		mmHg
PR Vmax		m/s
PR maxPG		mmHg
TR Vmax		m/s
TR maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Radiology Request & Report

B6

Species: Canine
Multi Female (Spayed) Chihuahua
Birthdate: B6

B6

B6

Date of request: 1/2/2019

Attending Clinician: B6 DVM (Cardiology) **Student:**

Date of exam: 1/2/19

Patient Location: Ward/Cage: Cardio **Weight (kg)** 3.40

- ☐ Inpatient
- ☐ Outpatient Time:
- ☑ Waiting
- ☐ Emergency

Sedation

- ☐ BAG
- ☐ OBAG
- ☐ 1/2 dose OBAG
- ☐ DexDomitor/Butorphanol
- ☐ Anesthesia to sedate/anesthetize

Examination Desired: DV and right lateral chest

Presenting Complaint and Clinical Questions you wish to answer:
increased coughing, mild heart disease. But do not suspect CHF.

Pertinent History: PDA occluded 2016

Findings:

Conclusions:

Radiologists
Primary:
Reviewing:

Dates
Reported:
Finalized:

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Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

B6

B6

B6

Species: Canine
Multi Female (Spayed) Chihuahua
Birthdate: B6

B6

Date: 1/2/2019

Diagnoses:
1. History of patent ductus arteriosus (PDA) occluded with Amplatz canine ductal occluder (ACDO) device, July 2016
2. Thrombus (blood clot) formation in the coronary sinus, diagnosed 10/13/2016 – stable/less discrete
3. Mild chronic mitral valvular disease
4. Reduced contractile function (either related to previous PDA or related to early cardiomyopathy potentially related to diet)
5. Mild pulmonary hypertension (increased blood pressure in the lungs, suspected to be related to primary lung disease)

Clinical Findings:
Thank you for bringing B6 to the Tufts Cardiology Service for a recheck appointment for her previously diagnosed coronary sinus thrombus and previously occluded PDA. On physical examination today, B6 was bright, alert, and slightly nervous. Her vital parameters (heart rate and respiratory rate) were all within normal limits. Her heart murmur sounded the same as her last visit. Her physical examination was otherwise unremarkable.

Today, we performed an echocardiogram (ultrasound of the heart) that showed that her Amplatz occluder remains in place and is occluding her PDA as it should be. The coronary sinus clot that was previously noted was about the same as at her last exam, which is great news! There is still mildly decreased contractile function in the left side of the heart, and there is still mild mitral valve regurgitation (small leak in her mitral valve of the left heart). B6 contractile function is somewhat worse than it has been in the past, and we discussed that certain diets have been associated with this problem. B6 was enrolled in a study about dogs with cardiomyopathy, and we submitted some blood work today though the study. We will call you with the blood work results tomorrow or the next day. One of the blood tests is called an NTproBNP test, and if her value comes back markedly elevated we may want to consider starting a medication called pimobendan.

Chest radiographs today showed that B6 trachea did not look compressed, which is good news. She had an area of mild irregularity on one view, but on other views her lungs looked clear. For now we recommend avoiding any airway

irritants such as perfume, smoke, or other aerosols. A mild amount of weight loss can also help with her breathing.

Because B6 has been doing so well on her B6 we would like to continue this medication for now.

Monitoring at Home:
Please continue to monitor B6 for any signs of lethargy, coughing, weakness, or breathlessness. If B6 experiences an increase in breathing rate or effort, she should be evaluated by a veterinarian.

Diet Suggestions:
Please gradually transition to the Royal Canin Early Cardiac food. Once you let Dr Freeman know the size of your food scoop she will proved recommendation of how much to feed. In the mean time you can just replace a few kibbles of her current food with the new food. Please email **cardiovet@tufts.edu** with the cup size information.

Recommended Medications:

B6 **CONTINUE**

Give 0.45mL (8.4mg) by mouth once daily.

Recheck Visits: A recheck visit is scheduled for **Friday April 5th at 4PM**. At this visit we will recheck her echocardiogram and submit some blood work. If you could bring a small stool sample to this visit, that would be great. This visit will be covered under the study. Another recheck for the study will performed 6 months from now.

Thank you for entrusting us with B6 care. She is such a sweet girl! Please contact our Cardiology liaison at (508)-887-4696 or email us at cardiovet@tufts.edu for scheduling and non-emergent questions or concerns.

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:
Please check with your primary veterinarian to purchase the recommended diet(s). If you wish to purchase your food from us, please call 7-10 days in advance (508-887-4629) to ensure the food is in stock. Alternatively, veterinary diets can be ordered from online retailers with a prescription/veterinary approval.

Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

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B6

Radiology Request & Report

B6

B6

B6

Species: Canine
Multi Female (Spayed) Chihuahua
Birthdate: B6

Date of request: 1/2/2019

B6

Student:

Date of exam: 1/2/19

Patient Location: Ward/Cage: cardio

Weight (kg) 3.40

- ☐ Inpatient
- ☐ Outpatient Time:
- ☑ Waiting
- ☐ Emergency

Sedation

- ☐ BAG
- ☐ OBAG
- ☐ 1/2 dose OBAG
- ☐ DexDomitor/Butorphanol
- ☐ Anesthesia to sedate/anesthetize

Examination Desired: Left lateral chest

Presenting Complaint and Clinical Questions you wish to answer:
increased coughing, mild heart disease. But do not suspect CHF.

Pertinent History: PDA occluded 2016

Findings:

B6

B6

Conclusions:
-Mild to moderate generalized cardiomegaly consistent with previous PDA. There is no evidence of left atrial enlargement of cardiac decompensation.
-The changes superimposed with the right 6th intercostal space described on the DV view are most likely the result of superimposed normal structures.
-Dorsal tracheal membrane redundancy is of unknown clinical significance. A dynamic airway disease is possible. Consider airway sampling and tracheoscopy.

B6

Reviewing:

Dates
Reported:1-2-18
Finalized:

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AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

B6 Canine
8.85 Years Old Female (Spayed) Chihuahua
Multi

Cardiology Appointment Report

Date: 1/2/2019

B6

Presenting Complaint: Here for routine recheck. Doing well at home. Gag like cough started a few months ago, becoming more frequent. After drinking water and playing. Eating/ drinking normally. N V/D. Is on HW prev.

General Medical History: PDA occluded 2016

Diet and Supplements: Solid Gold Wee Bites. Started on lower fat grain free version yesterday.

Cardiovascular History:
Prior CHF diagnosis? N
Prior heart murmur? Y
Prior ATE? N
Prior arrhythmia? N
Monitoring respiratory rate and effort at home? Y
Cough? Y gage like, like she is trying to get something out
Shortness of breath or difficulty breathing? N
Syncope or collapse? N
Sudden onset lameness? N
Exercise intolerance? N

Current Medications Pertinent to CV System:
Medication B6
Formulation ng/ml
Administration Frequency: 0.45 ml by mouth once a day
Need refills?

Cardiac Physical Examination:

General PE: BAR
MM Color and CRT: pk
BCS (1-9): 7
BW (kg): 3.4

Heart rate: 120
Respiratory rate: 32
Temp (if possible):

Muscle condition:

- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:

Murmur Grade:

- [ ] None
- [ ] I/VI
- [x] II/VI to
- [x] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Murmur location/description: systolic left apical

Jugular vein:

- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:

- [ ] Weak
- [ ] Fair
- [x] Good
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:

- [x] None
- [ ] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:

- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:

- [x] Eupneic/mild increased RE
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Normal BV sounds
- [x] Mild pulmonary crackles/referred upper airway noises
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:

- [ ] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:

History of PDA: occluded with ACDO July 2016

History of coronary sinus thrombus October 2016
Mild degenerative mitral valve disease
Coughing (r/o pulmonary disease, tracheal collapse, CHF)

Diagnostic plan:

- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [x] Thoracic radiographs +/-
- [x] NT-proBNP +/-
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:

B6

Mitral inflow:

- [ ] Summated
- [x] Normal
- [ ] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:
NSR, HR

Radiographic findings:

B6

Assessment and recommendations:
Echocardiogram shows stable occlusion of the PDA and stable coronary sinus thrombus, but there is progressive reduction in LV contractile function and progressive dilation of the LV cavity. Patient was enrolled in the DCM study so BNP, troponin, taurine, CBC and chemistry were submitted. Recommend gradual transition from current diet to RC Early Cardiac or another well established company. Recommend a mild amount of weight loss, especially given the increased coughing and concern for possible chronic pulmonary disease. Recommend avoiding airway irritants and monitoring for triggers of cough. A course of doxycycline or a cough suppressant could be considered if cough worsens. The LV dilation is enough to warrant starting pimobendan, but in the absence of LA enlargement we would wait to start unless the BNP is markedly elevated. Continue clopidogrel. Recheck echo and blood work via the study in 3 and 6 months.

Final Diagnosis:
Coronary sinus thrombosis of uncertain etiology and significance (r/o LA aneurysm or other LA communication like a tear in the LA wall at MV annulus)

Occluded PDA
Mild MMVD
Mild PHT (slightly worse today compared to previous exam)
Reduced LV contractile function (r/o dietary cardiomyopathy, early primary DCM, residual LV dysfunction related to longstanding PDA)

Heart Failure Classification Score:

ISACHC Classification:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

B6

M-Mode		
IVSd		cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm

M-Mode Normalized		
IVSdN		(0.290 - 0.520)
LVIDdN		(1.350 - 1.730) !
LVPWdN		(0.330 - 0.530)
IVSsN		(0.430 - 0.710)
LVIDsN		(0.790 - 1.140) !
LVPWsN		(0.530 - 0.780)
Ao Diam N		(0.680 - 0.890) !
LA Diam N		(0.640 - 0.900)

2D		
SA LA		cm
Ao Diam		cm

SA IA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LV Major		cm
LV Minor		cm
Sphericity Index		
LVLd LAX		cm
LVAd LAX		cm
LVEDV A-L LAX		ml
LVEDV MOD LAX		ml
LVLs LAX		cm
LVAs LAX		cm
LVESV A-L LAX		ml
LVESV MOD LAX		ml
HR	B6	BPM
EF A-L LAX		%
LVEF MOD LAX		%
SV A-L LAX		ml
SV MOD LAX		ml
CO A-L LAX		l/min
CO MOD LAX		l/min
Doppler		
MR Vmax		m/s
MR maxPG		mmHg
MV E Vel		m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg
PR Vmax		m/s
PR maxPG		mmHg
TR Vmax		m/s
TR maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

B6 Canine
B6 ears Old Female (Spayed) Chihuahua
Multi

Cardiology Appointment Report

Date: 4/5/2019

B6

Presenting Complaint:
Recheck echocardiogram and bloodwork – part of DCM study

General Medical History
Hx of PDA, occluded with Amplatz (July 2016)
Thrombus in coronary sinus (Oct 2016)
Mild chronic valvular disease
Mild pulmonary hypertension

B6

Very good appetite and energy level.

Diet and Supplements:
Exclusively on RC early cardio dry food
Heartgaurd and NexGaurd

Cardiovascular History:
Prior CHF diagnosis? yes
Prior heart murmur? yes
Prior ATE? no
Prior arrhythmia? none

Monitoring respiratory rate and effort at home? o has not monitored RR. Per O P is breathing normally without effort
Cough? occasionally will "cough" like she has a hairball in her throat
Shortness of breath or difficulty breathing? none
Syncope or collapse? none
Sudden onset lameness? none
Exercise intolerance? none

Current Medications Pertinent to CV System:
Medication: B6 mg/mL
Formulation:
Administration Frequency: SID
Need refills? no

Cardiac Physical Examination:
General PE: alopecia on caudal dorsum, incision scar near OS
MM Color and CRT: pink & moist, <2 sec
BCS (1-9): 7
BW (kg): 3.21 kg

Heart rate: 110
Respiratory rate: 30
Temp (if possible): 100.3

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [ ] None
- [ ] I/VI
- [x] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Murmur location/description: Systolic left apical

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [x] Good (right only)
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [ ] None
- [x] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [ ] Pronounced

- [x] No
- [ ] Intermittent
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Normal BV sounds
- [x] Pulmonary crackles - mild
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
Chronic valvular (MV) disease
Hx thrombus in coronary sinus
Mild pulmonary hypertension
Hx of PDA
Reduced systolic function

Diagnostic plan:
- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [x] NT-proBNP
- [x] Troponin I
- [ ] Other tests:

Echocardiogram Findings:

B6

Mitral inflow:
- [ ] Summated
- [x] Normal
- [ ] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:
Sinus arrhythmia, HR 130 bpm

Assessment and recommendations:
Echocardiogram reveals stable occlusion of the PDA and stable coronary sinus thrombus. Contractile function is still low-normal, but improved compared to all recent exams. LV cavity is slightly smaller than

previous exams. Recommend continuing clopidogrel and RC Early Cardiac diet. No changes are recommended. Recheck echo and study blood work in ~3 months, or sooner if clinical concerns occur.

Final Diagnosis:

Coronary sinus thrombosis of uncertain etiology and significance (r/o LA aneurysm or other LA communication like a tear in the LA wall at MV annulus)
Occluded PDA
Mild MMVD
Mild PHT (stable compared to previous exam)
Reduced LV contractile function (r/o dietary cardiomyopathy, early primary DCM, residual LV dysfunction related to longstanding PDA) – improved compared to previous exam

Heart Failure Classification Score:

ISACHC Classification:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

B6

M-Mode		
IVSd		cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm
M-Mode Normalized		
IVSdN		(0.290 - 0.520) !
LVIDdN		(1.350 - 1.730) !

LVPWdN		(0.330 - 0.530)
IVSsN		(0.430 - 0.710)
LVIDsN		(0.790 - 1.140) !
LVPWsN		(0.530 - 0.780)
Ao Diam N		(0.680 - 0.890) !
LA Diam N		(0.640 - 0.900)
2D		
SA LA		cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LVLd A4C		cm
LVEDV MOD A4C		ml
LVLs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml
Doppler		
MR Vmax		m/s
MR maxPG		mmHg
MV E Vel		m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
AV Vmax		m/s
AV maxPG		mmHg
AR Vmax		m/s
AR maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg
PR Vmax		m/s
PR maxPG		mmHg
TR Vmax		m/s

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TR maxPG

B6

mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

B6

B6

B6

Species: Canine
Multi Female (Spayed) Chihuahua
Birthdate B6

B6

Date: 4/5/2019

Diagnoses:
1. History of patent ductus arteriosus (PDA) occluded with Amplatz canine ductal occluder (ACDO) device, July 2016
2. Thrombus (blood clot) formation in the coronary sinus, diagnosed 10/13/2016 - stable/less discrete
3. Mild chronic mitral valvular disease
4. Reduced contractile function (either related to previous PDA or related to early cardiomyopathy potentially related to diet) - improved today
5. Mild pulmonary hypertension (increased blood pressure in the lungs, suspected to be related to primary lung disease)

Clinical Findings:
Thank you for bringing B6 to the Tufts Cardiology Service for a recheck appointment. She was previously diagnosed coronary sinus thrombus and previously occluded PDA. She is very sweet! On physical examination today, B6 vital parameters (heart rate and respiratory rate) were all within normal limits. Her heart murmur sounded the same as it did at her last visit. Her physical examination was otherwise unremarkable.

Today, we performed an echocardiogram (ultrasound of the heart) that showed that her Amplatz occluder remains in place and is occluding her PDA as it should be. The coronary sinus clot that was previously noted looks to be the same as what we noted on her last exam. Her cardiac contractile function has improved since the last time we saw her. It is hard to say for certain whether this is all a result of her diet change, but regardless this is great news! There is still mild mitral valve regurgitation (small leak in her mitral valve of the left heart), and the chambers of her heart about the same size as they previously were. We also took a blood sample (to measure pro-BNP and troponin) for the DOM study she is enrolled in, and we will call you with the blood work results once the lab gets back to us.

Since B6 has been doing well on h B6 we would like to continue this medication.

Monitoring at Home:
Please continue to monitor B6 for any signs of lethargy, coughing, weakness, or breathlessness. If B6 experiences an increase in breathing rate or effort, she should be evaluated by a veterinarian.

Diet Suggestions:
Please continue the Royal Canin Early Cardiac food.

Recommended Medications:

B6

Recheck Visits: A recheck visit is scheduled for **Thursday July 18th at 4pm.** At this visit we will recheck her echocardiogram and submit some blood work. This visit will be covered under the study.

Thank you for entrusting us with B6 care. She is such a wonderful girl! Please contact our Cardiology liaison at (508)-887-4696 or email us at cardiovet@tufts.edu for scheduling and non-emergent questions or concerns.

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

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Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

---

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Crude Protein (Min)	26.0%	Phosphorus (P) (Min)	0.8%
Crude Fat (Min)	16.0%	Zinc (Zn) (Min)	150 mg/kg
Crude Fiber (Max)	3.0%	Selenium (Se) (Min)	0.35 mg/kg
Moisture (Max)	12.0%	Vitamin A (Min)	13,000 IU/kg
Linoleic Acid (Min)	1.4%	Vitamin E (Min)	250 IU/kg
Calcium (Ca) (Min)	1.0%	Glucosamine* (Min)	350 ppm
		Omega-6 Fatty Acids* (Min)	1.6%

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

INGREDIENTS: Chicken (source of *glucosamine*), rice flour, corn gluten meal, whole grain corn, chicken by-product meal (source of glucosamine), whole grain wheat, soybean meal, beef fat naturally preserved with mixed-tocopherols, glycerin, liver flavor, calcium carbonate, mono and dicalcium phosphate, salt, caramel color, dried carrots, dried peas, potassium chloride, **VITAMINS** [Vitamin E supplement, niacin (Vitamin B-3), Vitamin A supplement, calcium pantothenate (Vitamin B-5), thiamine mononitrate (Vitamin B-1), Vitamin B-12 supplement, riboflavin supplement (Vitamin B-2), pyridoxine hydrochloride (Vitamin B-6), folic acid (Vitamin B-9), menadione sodium bisulfite complex (Vitamin K), Vitamin D-3 supplement, biotin (Vitamin B-7)], **MINERALS** [zinc sulfate, ferrous sulfate, manganese sulfate, copper sulfate, calcium iodate, sodium selenite], choline chloride, L-Lysine monohydrochloride, sulfur.

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Animal feeding tests using AAFCO procedures substantiate that Purina ONE SMARTBlend Chicken & Rice Formula provides complete and balanced nutrition for maintenance of adult dogs.

B6

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GUARANTEED ANALYSIS:

Crude Protein (Min)	26.0%	Selenium (Se) (Min)	0.35 mg/kg
Crude Fat (Min)	16.0%	Vitamin A (Min)	15,000 IU/kg
Crude Fiber (Max)	3.0%	Vitamin E (Min)	460 IU/kg
Moisture (Max)	12.0%	Ascorbic Acid (Vitamin C)* (Min)	70 mg/kg
Linoleic Acid (Min)	1.4%	Glucosamine* (Min)	400 ppm
Calcium (Ca) (Min)	1.0%	Microorganisms	
Phosphorus (P) (Min)	0.8%	*Bacillus coagulans** (Min)	600 million CFU/lb

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

INGREDIENTS: Chicken, rice flour, whole grain wheat, poultry by-product meal (source of glucosamine), soybean meal, beef tallow preserved with mixed-tocopherols, corn gluten meal, whole grain corn, fish meal (source of glucosamine), natural liver flavor, glycerin, wheat bran, mono and dicalcium phosphate, calcium carbonate, salt, dried egg product, soybean oil, potassium chloride, fish oil, **MINERALS** [zinc proteinate, manganese proteinate, ferrous sulfate, copper proteinate, calcium iodate, sodium selenite], **VITAMINS** [Vitamin E supplement, niacin (Vitamin B-3), Vitamin A supplement, calcium pantothenate (Vitamin B-5), thiamine mononitrate (Vitamin B-1), Vitamin B-12 supplement, riboflavin supplement (Vitamin B-2), pyridoxine hydrochloride (Vitamin B-6), folic acid (Vitamin B-9), Vitamin D-3 supplement, menadione sodium bisulfite complex (Vitamin K), biotin (Vitamin B-7)], choline chloride, L-ascorbyl-2-polyphosphate (Vitamin C), dried *Bacillus coagulans* fermentation product, L-Lysine monohydrochloride, garlic oil. Y445517

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Animal feeding tests using AAFCO procedures substantiate that Pro Plan SAVOR Shredded Blend Adult Chicken & Rice Formula provides complete and balanced nutrition for all life stages of dogs including growth of large size dogs (70 lb. or more as an adult).

INGRÉDIENTS: Poulet, farine de riz, blé entier, farine de sous-produits de volaille (source de glucosamine), farine de soja, suif de bœuf conservé avec un mélange de tocophérols, farine de gluten de maïs, maïs entier, farine de poisson (source de glucosamine), arôme naturel de foie, glycérine, son de blé, phosphate mono- et bicalcique, carbonate de calcium, sel, produit d'œufs en poudre, huile de soja, chlorure de potassium, huile de poisson, **MINÉRAUX** [protéinate de zinc, protéinate de manganèse, sulfate ferreux, protéinate de cuivre, iodate de calcium, sélénite de sodium], **VITAMINES** [supplément de vitamine E, niacine (vitamine B3), supplément de vitamine A, pantothénate de calcium (vitamine B5), mononitrate de thiamine (vitamine B1), supplément de vitamine B12, supplément de riboflavine (vitamine B2), chlorhydrate de pyridoxine (vitamine B6), acide folique (vitamine B9), supplément de vitamine D3, complexe de bisulfite de sodium et de ménadione (vitamine K), biotine (vitamine B7)], chlorure de choline, L-ascorbyl-2-polyphosphate (vitamine C), produit de fermentation *Bacillus coagulans* déshydraté, monochlorhydrate de L-lysine, sulfure d'allyle. Y445517

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From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>

To: Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David

Sent: 1/28/2019 3:48:02 PM

Subject: DCM-other including a cat Non-Responsive

Attachments: 1. Blue Wilderness salmon/chicken grain-free.--2 Non-Responsive Non-Responsive; 4 Health Untamed: B6 - EON-375466; 4Health beef and potato and-4health untamed lamb and Lentil: B6 - EON-375168; 4health optimal nutrition for optimal health weight management formula for dogs: B6 - EON-374758; Acana Free Run Poultry dry: Lisa Freeman - EON-374786; ACANA Lamb and Apple Singles Formula: B6 - EON-376195; Arcana lamb and apple - grain free: B6 - EON-375208; BLUE BUFFALO GRAIN FREE LAMB AND POTATO: B6 - EON-377465; BLUE Wilderness with Chicken for Adult Dogs: B6 B6 - EON-374327; Canidae Grain Free Pure Wild Dry Dog Food with Wild Boar-Grain Free Limited Ingredient Diet: B6 - EON-375880; CANIDAE Grain-Free PURE Land with Bison Limited Ingredient Diet Adult Dry Dog Food: B6 - EON-375771; CRAVE Dog Food with Protein from Salmon and Ocean White Fish: B6 - EON-376088; Diamond -Naturals-Skin & Coat-All Life Stages Dog-Salmon & Potato Formula: B6 - EON-376046; Fromm Family-From the Heartland-Grain Free-Dog Food: B6 - EON-374687; Fromm Surf & Turf dry dog food: B6 - EON-375559; GO Venison: B6 - EON-375313; Homecooked diet - see diet history in medical record: Lisa Freeman - EON-374789; Honest Kitchen Grain Free Beef Recipe (Love): B6 - EON-377314; Horizon Pulsar Chicken Flavor Dog Kibble: B6 - EON-375244; Instinct by Nature's Variety Original Grain-Free Recipe with Real Chicken Dry Dog Food: B6 - EON-375409; Merrick Good Earth Grain Free Pork Beef and Lamb Kibble: B6 - EON-376709; Merrick Grain-Free Chicken and Sweet Potato: B6 - EON-375900; Merrick Limited Ingredient Diet Grain-Free Real Lamb & Sweet Potatoes Recipe Dry Dog Food: B6 - EON-376853; Natural Balance L.I.D. Limited Ingredient Diets-Sweet Potato & Fish Dry Dog Formula: B6 - EON-375818; Natural Balance Lamb and Brown Rice: B6 - EON-377272; Natural Balance LID Dry Dog Food - Sweet Potato and Fish Formula: B6 - EON-376311; Now Fresh Grain Free Adult Dog Food-Now Fresh Grain Free Puppy Food: B6 - EON-376136; Nutrisource Small and Medium Breed Puppy Grain Free Dog Food: B6 - EON-375242; NutriSource Super Premium Pet Foods: B6 - EON-374952; NWBARBF-Beef Recipe for Dogs-Ground Bone Added-Not for Human Consumption-Made in the USA by Northwest Naturals: B6 - EON-375869; Orijen Original dry: Lisa Freeman - EON-374783; Orijen Regional Red Dry Dog Food-Fromm Beef Frittata A La Veg Dry Dog Food-From Duck & Sweet Potato Dry Dog Food-Purina Fortiflora: B6 - EON-375393; Ped: B6 - EON-376960; Pure Vita Venison & Red Lentils Grain Free Entree: B6 - EON-375203; Rachel Ray's only six - EON-377164; Solid Gold Wee Bit formula-Bison & Brown Rice Recipe with Pearled Barley Small Breed Dry Dog Food: B6 - EON-375339; Stella & Chewy's -Frozen Raw -Stellla's Super Beef -Dinner Patties: B6 - EON-375865; Taste of the Wild - EON-377564; Taste of the Wild (Pacific Stream formula): B6 - EON-377278; Taste of the Wild High Prairie grain-free with roasted bison and roasted venison: B6 - EON-377174; Taste of the Wild Prey: B6 - EON-374547; Taste of the Wild Sierra Mountain: B6 - EON-377360; Taste of the Wild Wetlands Canine Formula with roasted Fowl: B6 - EON-374534; Taste of the Wild.: B6 - EON-376466; Taste of the Wild: B6 - EON-374698; Under the Sun Grain-Free Lamb Recipe Adult Dry Dog Food: B6 - EON-377156; Wellness Core Ocean Grain Free Protein-Rich Nutrition: B6 - EON-377321; Wellness Core Ocean Grain Free Protein-Rich Nutrition: B6 - EON-377324; Wholesomes Grain-free Food for Dogs: Grain-Free/Gluten-Free. Chicken Meal & Chickpeas Formula Net Wt. 35lbs: B6 - EON-377359

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6

Commentary

Diet-associated dilated cardiomyopathy in dogs: what do we know?

Lisa M. Freeman DVM, PhD
Joshua A. Stern DVM, PhD
Ryan Fries DVM
Darcy B. Adin DVM
John E. Rush DVM, MS

From the Department of Clinical Sciences, Cummings School of Veterinary Medicine, Tufts University, North Grafton, MA 01536 (Freeman, Rush); Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California-Davis, Davis, CA 95616 (Stern); Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois, Urbana, IL 61802 (Fries); and Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27607 (Adin).

Address correspondence to Dr. Freeman (lisa.freeman@tufts.edu).

Diet-associated DCM first came to light in cats in the late 1980s[1] and in dogs in the mid-1990s.[2] The association between diet and DCM in dogs has generally not been much in the news since the early 2000s, but over the past few years, an increasing number of DCM cases involving dogs appear to have been related to diet. The extent of this issue is not clear, not all cases have been confirmed to be linked to diet, and a true association has not been proven to exist. However, when one of the authors (RF) recently surveyed veterinary cardiologists about cases of possible diet-associated DCM in dogs examined in the past 2 years, information for > 240 cases was obtained, with responses received from the United States, United Kingdom, Canada, Israel, and Austria (unpublished data). Dogs for which breed was specified consisted of mixed-breed dogs (n = 134), Golden Retrievers (23), Labrador Retrievers (9), German Shepherd Dogs (8), Cocker Spaniels (7), and between 1 and 5 dogs each of 25 other breeds. Further, possible diet-associated DCM represented 16% of all cases of DCM diagnosed by the respondents during this period.

The recent announcement from the US FDA[3] alerting pet owners and veterinarians about reports of DCM in dogs eating pet foods containing peas, lentils, other legume seeds, or potatoes as main ingredients has raised concerns among the pet-owning public. Therefore, we wanted to increase awareness of this issue among veterinarians, review what is currently known about the possible association between certain diets and DCM in dogs, and discuss what veterinarians can do to help identify underlying causes.

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Idiopathic dilated cardiomyopathy in Dalmatians: Nine cases (1990–1995)

Lisa M. Freeman, DVM, PhD; Kathryn E. Michel, DVM, MS; Donald J. Brown, DVM, PhD; Paul M. Kaplan, DVM; Mark E. Stamoulis, DVM; Steven L. Rosenthal, DVM; Bruce W. Keene, DVM, MS; John E. Rush, DVM, MS

Objective—To describe the historical, clinical, and echocardiographic findings in Dalmatians with dilated cardiomyopathy (DCM).

Design—Retrospective case series.

Sample Population—9 Dalmatians with a diagnosis of DCM and congestive heart failure (CHF), 9 Doberman Pinschers with DCM and CHF, and 9 dogs of other breeds with DCM and CHF.

Procedure—Disease history; signalment; physical, radiographic, and echocardiographic examination findings; treatment; and outcome from medical records were analyzed.

Results—All Dalmatians were male, with a mean age of 6.8 years. Eight dogs had been fed a commercially available low-protein diet formulated for the prevention of urate uroliths. All dogs had clinical signs consistent with left-sided CHF and had marked left ventricular systolic dysfunction and severe left ventricular dilatation, although arrhythmias were not an important finding in this series of dogs. Median duration of survival was 10 months.

Clinical Implications—The DCM syndrome in Dalmatians has some qualities that are distinct from DCM in other breeds of dogs. (*J Am Vet Med Assoc* 1996; 209:1592–1596)

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Relationship Between Circulating and Dietary Taurine Concentrations in Dogs with Dilated Cardiomyopathy

Lisa M. Freeman, DVM, PhD[a]
John E. Rush, DVM, MS[a]
Donald J. Brown, DVM, PhD[a]
Philip Roudebush, DVM[b]

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School of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

[b] *Hill's Science and Technology Center*
PO Box 1658
Topeka, KS 66601

ABSTRACT

A retrospective study was conducted to determine dietary taurine concentrations in dogs with dilated cardiomyopathy (DCM) and to compare the clinical outcome of taurine-deficient and non–taurine-deficient dogs. Taurine concentrations were low in blood samples from 20 of 37 dogs with DCM. Median dietary taurine concentration was not significantly different between taurine-deficient and nondeficient dogs. There was no correlation between dietary and circulating taurine concentrations. The outcome of taurine-deficient dogs supplemented with taurine was not different from the outcome of nondeficient dogs. The role of taurine and its relationship to dietary intake in canine DCM remain unclear.

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The Journal of Nutrition
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

Copper Deficiency Does Not Lead to Taurine Deficiency in Rats[1]

Kwang Suk Ko,[2] Cristina L. Tôrres,[2] Andrea J. Fascetti,[2] Martha H. Stipanuk,[3] Lawrence Hirschberger,[3] and Quinton R. Rogers[2]*

[2]Department of Molecular Biosciences, School of Veterinary Medicine, University of California Davis, CA 95616 and [3]Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853

Abstract

Copper deficiency has been reported to cause a decrease in urinary taurine excretion in rats. We determined whether Cu deficiency would decrease taurine status and the hepatic activities of cysteine dioxygenase (CDO) and/or cysteine sulfinic acid decarboxylase (CSAD) in rats. Ten weanling male rats were assigned to either a Cu-adequate (+Cu) or Cu-deficient (−Cu) group. All rats consumed a Cu-deficient purified diet and water ad-libitum for 16 wk. The water for the +Cu group contained 20 mg Cu/L as $CuSO_4$. At wk 16, the groups differed ($P < 0.05$) in the following variables (means ± SEM, −Cu vs. +Cu): body weight (BW), 375 ± 19 vs. 418 ± 2.9 g; food intake, 16.2 ± 0.7 vs. 18.5 ± 0.4 g/d; hematocrit, 0.294 ± 0.027 vs. 0.436 ± 0.027; hemoglobin, 95.2 ± 9 vs 134 ± 10 g/L; liver Cu, 8.7 ± 2.0 vs. 65.9 ± 2.5 nmol/g; plasma Cu, 0.38 ± 0.09 vs. 13.4 ± 0.61 μmol/L; plasma ceruloplasmin activity, 1.75 ± 1.0 vs. 67.9 ± 8.4 IU; relative heart weight, 0.56 ± 0.04 vs. 0.35 ± 0.02% BW; relative liver weight, 4.06 ± 0.23 vs. 3.37 ± 0.06% BW; and liver CSAD activity, 18.8 ± 1.37 vs. 13.5 ± 1.11 nmol · min^{-1} · mg $protein^{-1}$. The groups did not differ at wk 16 in: plasma taurine, 249 ± 14 vs. 298 ± 63 μmol/L; whole blood taurine, 386 ± 32 vs. 390 ± 25 μmol/L; urinary taurine excretion, 82.5 ± 15 vs. 52.0 ± 8.3 μmol/d; liver taurine, 2.6 ± 0.7 vs. 2.8 ± 0.4 μmol/g; liver total glutathione, 6.9 ± 0.48 vs. 6.3 ± 0.40 μmol/g; liver cyst(e)ine, 96 ± 7.1 vs. 99 ± 5.3 nmol/g and liver CDO activity, 2.19 ± 0.33 vs. 2.74 ± 0.21 nmol · min^{-1} · mg $protein^{-1}$. These findings support the conclusion that Cu deficiency does not affect body taurine status. J. Nutr. 136: 2502–2505, 2006.

Introduction

Taurine (2-aminoethanesulfonic acid) is a beta-amino sulfur amino acid, but it is neither an essential amino acid in most animals nor a building block of proteins. Taurine is known to be synthesized from the sulfur amino acids, methionine/cyst(e)ine (1) at a sufficient rate to meet biological needs in most animals. However, since taurine deficiency was found to be a cause of dilated cardiomyopathy (DCM)[4] in cats (2), taurine deficiency has been considered by many nutritionists and veterinarians as a possible causative factor for DCM in dogs.

Moise et al. (3) reported that taurine deficiency was linked to DCM in foxes, a canid, which suggests that taurine deficiency may occur in dogs under certain metabolic conditions, even though it has been shown that with many diets no dietary taurine is required for normal taurine status. Clinical signs of DCM associated with taurine deficiency in dogs have been reported by various cardiologists. Although the metabolic basis for the taurine deficiency has not been elucidated, it is thought to involve abnormal energetics via calcium channel disregulation in mitochondria (4). The majority of clinical signs of DCM in dogs were in large-breed dogs that had been fed commercial dog foods for long periods of time that were composed primarily of lamb meal and rice (5). This suggests a dietary link between certain dog foods and the development of DCM in dogs.

Because Gray and Daniel (6) reported that urinary taurine excretion was reduced in Cu-deficient rats and suggested that it may be the result of a decreased synthesis of taurine, we examined the Cu content of the dog foods reported to be associated with taurine deficiency. The lamb and rice diet, which most of the affected dogs were consuming, was not supplemented with Cu [3.1mg/1000 kcal (4184 kJ) ME], but was supplemented with Zn at several-fold (84mg/1000 kcal ME) the minimum requirement for the dog. This resulted in a relatively high Zn to Cu ratio of a magnitude known to induce metallothionein formation in some species (7) which, in turn, binds Cu and decreases Cu bioavailability (8). We hypothesized that the high Zn to Cu ratio present in the diet may have decreased the availability of Cu and thereby had an effect on taurine status via the activity of cysteine dioxygenase [CDO, Enzyme Commission(EC) 1.13.11.20] and/or cysteine sulfinic acid decarboxylase (CSAD, EC 4.1.1.29), key enzymes for the synthesis of taurine from cysteine.

To test this hypothesis, Cu deficiency was induced in male weanling rats and taurine status and the activities of the 2 enzymes involved in taurine synthesis were examined as a model to determine whether Cu deficiency in dogs may be involved in causing DCM in dogs.

[1] Supported by the Center for Companion Animal Health (CCAH), the School of Veterinary Medicine, University of California, Davis.

[4] Abbreviations used: BW, body weight; CDO, cystein dioxygenase; CSAD, cystein sulfinic acid decarboxylase; +Cu, copper-adequate; −Cu, copper-deficient; DCM, dilated cardiomyopathy.

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Manuscript received 2 June 2006. Initial review completed 17 June 2006. Revision accepted 25 July 2006.

Materials and Method

Rats and diets. The husbandry and treatment of the rats were approved by the Animal Use and Care Administrative Advisory Committee at University of California, Davis and were in compliance with the NRC guidelines for laboratory animals (9). Ten male weanling rats were purchased (Harlan-Sprague-Dawley) and were divided into 2 groups. Both groups, Cu deficient group (−Cu) and Cu adequate group (+Cu), were fed the same Cu-deficient diet (**Table 1**), throughout the entire experimental period. The mineral composition of the Cu deficient diet was based on the AIN-76A diet (10) except that the diet contained no added Cu. The diet provided protein at 180 g/kg with no supplementation of methionine to avoid excess substrates for taurine biosynthesis. In addition to the diet, the +Cu group was given Nanopure water (Barnstead Nanopure II System, Barnstead International) containing 20 mg Cu/L as $CuSO_4$. To ensure the consumption of satisfactory amounts of Cu for +Cu group, the amount of Cu-supplemented water consumed for 3 d was recorded once every 4 wk, and the amount of Cu consumed was calculated to be adequate. The mean Cu consumption by the +Cu group was 0.155 mg/d, which exceeds the Cu requirements of growing rats. The −Cu group was given Nanopure water without any supplementation. All rats had free access to food and water throughout the experiment. The rats were housed in hanging stainless-steel cages with a 12-h light-dark cycle. The room temperature ranged between 14 and 29°C.

Sampling. To determine the Cu status of the rats, ~500 μL of blood was collected every 2 wk from the saphenous vein (11), using heparinized Microvette CB300 (Sarstedt) blood collection tubes. When the −Cu group showed hematological and biochemical signs of Cu deficiency (hematocrit <40, hemoglobin concentration <120g/L, and/or ceruloplasmin activity <10 IU), the rats were placed in metabolic cages to collect urine for taurine analysis (3 d for adaptation and 4 d for collection). At the end of the urine collection period, the rats were anesthetized with ethyl ether, and the blood, liver, and heart collected. Blood was taken from abdominal aorta using heparinized syringes (~20 μL of sodium heparin solution, 1000 USP kU/L, Baxter HealthCare). A portion of blood was centrifuged, at 15,800 × *g* for 15 min, immediately after collection to obtain plasma for determination of taurine concentration and ceruloplasmin activity. Liver samples for assays of CDO and CSAD activities and metabolite concentrations were frozen at −80°C until analyses. Other samples were stored at −20°C.

TABLE 1 Composition of copper-deficient diet

Ingredients	*g/kg*[1]
Casein, high protein[2]	180.00
Sucrose[3]	518.53
Corn starch[4]	159.27
Corn oil[5]	50.00
Fiber (Cellufil)[6]	50.00
Mineral mix (modified AIN-76)[7]	35.00
Vitamin mixture[8]	5.00
50% Choline chloride in water[9]	2.20
Total	1000.00

[1] As-fed basis.
[2] New Zealand Milk Products.
[3] Westco Products.
[4] National Starch and Chemical Co.
[5] ACH Food Companies.
[6] Amersham Life Science.
[7] No supplementation of copper; modified AIN-76 mineral mix (10) (g/kg mineral mix): Calcium phosphate-dibasic, 500.00; sodium chloride, 74.00; potassium citrate-monohydrate, 220.00; potassium sulfate, 52.00; magnesium oxide, 24.00; manganese sulfate, 5.14; ferric citrate, 6.00; zinc sulfate-septahydrate, 3.67; cupric carbonate, 0.00; potassium iodate, 0.01; sodium selenate, 0.007; chromium potassium sulfate, 0.55; sucrose-finely powdered, 114.623.
[8] Vitamin mixture for adult cats (29) which exceeds all of minimum vitamin requirements of growing rats.
[9] International Mineral and Chemical Corp.

Measurements. During the experiment, daily food intakes were recorded and body weights (BW) were measured every 3 d. Hematocrits and hemoglobin concentrations were measured every 2 wk. The weights of hearts and livers were measured immediately after collection. A portion of the collected blood was prepared by centrifugation in a model MB micro-capillary centrifuge (IEC) at 10,285 × *g* for 4 min before hematocrit measurements were taken. Hemoglobin concentration was measured as described by van Kampen and Zijlstra (12). Cu concentrations in the diets, plasma, and liver were measured by atomic absorption spectrometry (AAnalyst 800, Perkin Elmer Instrument) and samples were prepared as described by Clegg et al. (13). Taurine concentrations in whole blood, plasma, and urine were determined using an amino acid analyzer (Beckman 7300 Analyzer C7 Model, Beckman Instruments) (14). Plasma ceruloplasmin activity was measured as its oxidase activity using the modified *o*-dianisidine dihydrochloride method (15). Liver samples were transported on dry ice from the University of California to Cornell University. Then, CDO and CSAD activities in the livers and concentrations of taurine, total glutathione, and cyst(e)ine in the livers were measured. CDO activity was measured as described by Bagley et al. (16). CSAD activity was measured as described by Bella et al. (17). Total glutathione and cyst(e)ine were quantified by the HPLC method of Fariss and Reed (18) as modified by Stipanuk et al. (19). Protein concentration was determined by the method of Smith et al. (20).

All results are expressed as means ± SEM. Differences between groups at wk 16 were compared using 1-way ANOVA (SYSTAT 10.2, SYSTAT Software). For all analyses, differences were considered significant at $P < 0.05$. Probability values in the range of $0.05 \leq P < 0.1$ indicated a noteworthy trend.

Results

The diets were prepared 3 times during the experiment. The Cu concentrations in the 3 batches of the experimental diets were 1.16, 0.11, and 0.13 mg/kg diet (as-fed basis), respectively. All were lower than the minimum Cu requirement for growing rats (5.0 mg/kg diet) as listed by the NRC (21).

The −Cu group consumed 12% less food and had a 10% lower BW than the +Cu group ($P < 0.05$; **Table 2**). However, relative heart ($P < 0.01$) and liver ($P < 0.05$) weights were greater in the −Cu group than in the +Cu group (Table 2).

Several metabolic indicators of Cu deficiency differed between the groups at wk 16 ($P < 0.01$, Table 2). The hematocrit and hemoglobin concentrations of the −Cu group were 67 and 71%, respectively, of those of the +Cu group. Liver and plasma

TABLE 2 Anthropometric variables and indicators of copper and taurine status in rats fed −Cu or +Cu diets for 16 wk[1]

	−Cu	+Cu	*P*-value
Body weight, *g*	375 ± 19	418 ± 2.9	<0.05
Food intakes,[2] *g/d*	16.2 ± 0.7	18.5 ± 0.4	<0.05
Relative heart wt, *% BW*	0.56 ± 0.04	0.35 ± 0.02	<0.01
Liver weights, *% BW*	4.06 ± 0.23	3.37 ± 0.06	<0.05
Hematocrit	0.294 ± 0.027	0.436 ± 0.027	<0.01
Hemoglobin, *g/L*	95.2 ± 9	134 ± 10	<0.01
Plasma copper, *μmol/L*	0.38 ± 0.09	13.4 ± 0.61	<0.01
Liver copper, *nmol/g wet tissue*	8.7 ± 2.0	65.9 ± 2.5	<0.01
Plasma ceruloplasmin, *IU*[3]	1.75 ± 1.0	67.9 ± 8.4	<0.01
Plasma taurine, *μmol/L*	249 ± 14	298 ± 63	0.45
Whole blood taurine, *μmol/L*	386 ± 32	390 ± 25	0.92
Urinary taurine,[2] *μmol/L*	82.5 ± 15	52.0 ± 8.3	0.087

[1] Values are means ± SEM, $n = 5$.
[2] During wk 16.
[3] IU, International unit, $\mu mol \cdot min^{-1} \cdot L^{-1}$.

TABLE 3 Hepatic cysteine dioxygenase and cysteine sulfinic acid decarboxylase activities in rats fed −Cu and +Cu diets for 16 wk[1]

	CDO			CSAD		
	−Cu	+Cu	*P*-value	−Cu	+Cu	*P*-value
$\mu mol \cdot min^{-1} \cdot liver^{-1}$	5.07 ± 0.95	5.53 ± 0.42	0.60	41.1 ± 1.31	27.3 ± 2.62	0.0008
$\mu mol \cdot min^{-1} \cdot g\ liver^{-1}$	0.33 ± 0.04	0.39 ± 0.02	0.19	2.78 ± 0.21	1.90 ± 0.15	0.005
$nmol \cdot 100\ g\ BW^{-1}$	1.29 ± 0.25	1.34 ± 0.11	0.83	11.0 ± 0.66	6.56 ± 0.59	0.0006
$nmol \cdot min^{-1} \cdot mg\ protein^{-1}$	2.19 ± 0.33	2.74 ± 0.21	0.14	18.8 ± 1.37	13.5 ± 1.11	0.001

[1] Values are mean ± SEM, $n = 5$ except CDO, −Cu, $n = 4$ (due to an outlier).

Cu concentrations in −Cu group were only 13 and 3%, respectively, of those of the +Cu group. The plasma ceruloplasmin activity in the +Cu group was about 40 times that of the −Cu group.

Taurine concentrations in plasma and whole blood did not differ between the groups but urinary taurine excretion tended to be greater in the −Cu group than in the +Cu group ($P = 0.09$, Table 2). The groups did not differ (−Cu vs. +Cu) in liver taurine (2.6 ± 0.7 vs. 2.8 ± 0.4 μmol/g), cyst(e)ine (96 ± 7.1 vs. 99 ± 5.3 nmol/g), and total glutathione (GSH + GSSG) (6.9 ± 0.48 vs 6.3 ± 0.40 μmol/g) concentrations.

Hepatic CDO activity did not differ between the groups whether expressed relative to the total liver, g liver, liver protein, or body weight (**Table 3**). The CSAD activity was greater in the +Cu group, regardless of the base used for calculation than in the −Cu group ($P < 0.005$, Table 3).

Discussion

In this study we focused on the relatively high ratio of Zn to Cu in some lamb and rice diets as a possible factor causing taurine deficiency in dogs. After failing to induce Cu deficiency in 12 medium-to-large mixed breed adult dogs fed a commercial type diet with a Cu chelating agent, Syprine (trientine hydrochloride), for 1 y, we decided to examine a cheaper, more expedient model, the albino rat, to examine the effect of Cu deficiency on taurine status.

The lower BW and food intake in the −Cu group than in the +Cu group and the greater relative heart and liver weights in −Cu group than in the +Cu group (Table 2) are typical and consistent with other reports for Cu-deficient rats (6,22,23). All metabolic indicators of Cu deficiency were significantly lower in the −Cu group than in the +Cu group, confirming that the −Cu group was Cu-deficient after a period of 16 wk (6,23).

Taurine homeostasis is maintained predominantly by the regulation of renal taurine reabsorption so that excess dietary taurine is excreted in the urine (24). Therefore, it is generally assumed that the amount of taurine excreted in urine reflects the extent of excess taurine in the taurine pools of animals. The taurine status of the rats was determined by evaluating plasma and whole blood taurine concentrations and urinary taurine excretion (Table 2). The fact that none of these values were significantly different between the −Cu and +Cu group, and the finding that there was a trend for a higher urinary taurine excretion in the −Cu group, which is the opposite of that found by Gray and Daniel (6), negates our hypothesis that Cu deficiency causes taurine deficiency.

A lower food intake by the −Cu group provided less total substrate and might have been expected to result in less taurine synthesis. Food intakes relative to metabolic body weights of the rats during the last 3 d of the experiment, were 34.3 ± 1.02 g/kg $BW^{0.75}$ for the −Cu group and 41.4 ± 0.95 g/kg $BW^{0.75}$ for the +Cu group ($P < 0.01$). Perhaps the results would have been different if a less severe Cu deficiency had been induced or if the rats were fed on the diets for a longer period of time.

Cu deficiency had no effect on the taurine, cyst(e)ine, or total glutathione concentrations at the major site of taurine synthesis, the liver. These results indicate that Cu deficiency in rats does not affect the major products of cysteine metabolism in the liver. However, some reports indicate that Cu deficiency in rats increases hepatic GSH concentration (25,26). The cause for this inconsistency is unclear. Perhaps a more prolonged Cu deficiency in the earlier studies is responsible.

The only significant effect of Cu deficiency on sulfur amino acid metabolism was a higher CSAD activity in liver ($P < 0.01$). The activities of CDO and CSAD are critical to taurine synthesis because they are the key enzymes in the synthesis of taurine from its direct precursor, cysteine. The regulation of these key enzymes in the synthesis of taurine has been reported (27,28). Bagley and Stipanuk (28) demonstrated that, as the dietary protein concentration increases, CDO activity increases and CSAD activity decreases. That is, CDO and CSAD are regulated in a reciprocal manner in response to dietary protein or sulfur amino acid concentration in the diet. In the current study, the reciprocal regulations of activities in the 2 enzymes were not found because CDO did not change. However, the difference in CSAD activity in this study was consistent with previous finding that CSAD activity decreases with higher protein intake (27,28). The food intake/kg $BW^{0.75}$ of the rats during the last 3 d of the the experiment was higher in the +Cu group ($P < 0.01$) and the CSAD activity was lower in this group. Although the CDO activity did not differ between groups, it was 10% higher in the +Cu group ($P = 0.60$), possibly showing a trend for metabolic adaptation of the taurine synthesis system to maintain taurine homeostasis.

In conclusion, Cu deficiency did not affect taurine or other sulfur amino acid metabolites in plasma or in the liver of rats in this study. CSAD activity appeared to be controlled in a normal manner by the amount of dietary protein ingested. We conclude that Cu deficiency does not affect cysteine metabolism or taurine homeostasis in rats and that it is highly unlikely that DCM-induced taurine deficiency in large-breed dogs is the result of a dietary-induced Cu deficiency.

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The Journal of Nutrition
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

Differences in Taurine Synthesis Rate among Dogs Relate to Differences in Their Maintenance Energy Requirement[1–3]

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Abstract

Diet-induced (taurine deficiency) dilated cardiomyopathy is reported more in large than small dogs possibly because taurine biosynthesis rate (TBR) is lower in large than small dogs. The TBR in 6 mongrels (37.9 ± 2.1 kg) and 6 beagles (12.8 ± 0.4 kg) was determined from the fractional dilution rate of urinary [1,2-$^2H_2$]-taurine, (d4-tau). All dogs were given a 15.6% protein, 0.60% sulfur amino acid (SAA) diet in amounts to maintain an ideal body condition score. After 3 mo, 14.6 mg/kg body weight of d4-tau was given orally and TBR determined from d4-tau to taurine ratio in urine collected each d for 6 d. Enrichments of d4-tau were determined by GC-MS. Thereafter, mongrels and beagles were paired by ranking of SAA intake per metabolic body weight per $kg^{0.75}$. Each pair received the same amount of diet/$kg^{0.75}$ for 2 wk, then TBR was again determined. Concentrations of taurine in plasma, blood, and urine and concentrations of plasma thiols were measured during each TBR determination. In Expt. 1, TBR and taurine concentrations in plasma and urine of mongrels were lower ($P < 0.05$) than those of beagles. In Expt. 2, TBR and taurine concentrations in blood and plasma of mongrels were lower ($P < 0.05$) than beagles. Together, the results support the hypothesis that large compared with small dogs have lower TBR when fed diets near-limiting in dietary SAA, but adequate to maintain ideal body condition. J. Nutr. 137: 1171–1175, 2007.

Introduction

Dilated cardiomyopathy (DCM)[7] is a disease of the myocardium with impaired systolic pumping function in the ventricles of the heart. Approximately 0.5% of dogs are diagnosed for DCM among all of the dogs admitted to veterinary teaching hospitals (1). Interestingly, it has been reported that large breed dogs are predisposed to developing DCM (2). The etiology for DCM has not been clearly elucidated; however, genetic predisposition, viral infection, immune-mediated disorders, toxin, arrhythmias, and nutritional deficiencies such as taurine deficiency or L-carnitine deficiency have been suggested as possible causes (3). Of the nutritional factors, taurine deficiency has gained attention because taurine deficiency in cats was shown to directly cause a DCM that was reversible by taurine supplementation (4).

Taurine (2-aminoethanesulfonic acid) is a beta, sulfur-containing, amino acid ubiquitously found in animals and reported in especially high concentrations in heart, brain, central nervous system, retina, olfactory bulb, and white blood cells (5). The physiological function of taurine in heart is not fully understood. Proposed mechanisms include osmoregulation, calcium regulation, and inactivation of free-radicals (6).

Taurine is synthesized from the sulfur amino acids, methionine and cyst(e)ine (7), by the activities of the enzymes, cysteine dioxygenase (EC 1.13.11.20) and cysteine sulfinic acid decarboxylase (EC 4.1.1.29) in animals, excluding most carnivores (8). Because of this, taurine is not considered as an essential nutrient in many species. However, it is known that generally, carnivores have a dietary requirement for taurine, and there is evidence that under certain dietary conditions dogs require dietary taurine. Sanderson et al. (9) found a significant decrease in plasma taurine concentration in healthy beagles fed a high-fat, protein-restricted (10% dry matter basis) diet that exceeded the NRC minimum protein requirement of maintenance in adult dogs (10). After feeding the diet for 48 mo, these investigators found 1 dog developed DCM. This indicated that prolonged provision of a protein-restricted diet, although above the minimum protein requirement, could result in taurine deficiency in dogs. More recently, Fascetti et al. (11) reported 12 cases of low blood taurine concentration and DCM in large-breed dogs given apparently nutritionally complete and balanced commercial diets. They suggested that body size may be a factor contributing to development of taurine deficiency in dogs.

[1] Supported by Center for Companion Animal Health (CCAH), School of Veterinary Medicine, University of California, Davis and by Royal Canin, Aimargues, France.

[2] Author disclosures: K. S. Ko, no conflicts of interest; R. C. Backus, no conflicts of interest; J. R. Berg, no conflicts of interest; M. W. Lame, no conflicts of interest; and Q. R. Rogers, no conflicts of interest.

[3] Supplemental Tables 1 and 2 and Supplemental Figures 1 and 2 are available with the online posting of this paper at jn.nutrition.org.

[7] Abbreviations used: BCS, body condition score; BFM, body fat mass; BW, body weight; d4-tau, [1,2-$^2H_2$]-taurine; DCM, dilated cardiomyopathy; LBM, lean body mass; MBW, metabolic body weight; MLBM, metabolic lean body mass; RLW, relative liver weight; SAA, sulfur amino acid; TBR, taurine biosynthesis rate; TTR, tracer to tracee ratio.

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Manuscript received 21 November 2006. Initial review completed 12 December 2006. Revision accepted 27 February 2007.

Our research group recently found that plasma taurine concentration and taurine biosynthesis rate (TBR) in Newfoundland dogs, a giant dog breed, are substantially lower than those in beagles when both breeds are fed the same diet (12). We hypothesize that the greater incidence of taurine-deficiency DCM reported in large relative to small dogs is the result of lower TBR in large dogs. In the present study, we compare the abilities of large and small dogs to synthesize taurine when intake of diet is controlled to maintain ideal body condition and when intake is controlled to provide similar dietary sulfur amino acid (SAA) intake on a metabolic body weight (MBW, $kg^{0.75}$) basis.

Materials and Methods

Animals and diet. Husbandry and treatment of the dogs were in compliance with the NRC Guide for Laboratory Animals (13), and were approved by the Animal Use and Care Administrative Advisory Committee at University of California, Davis. Six sexually intact male beagles (12.8 ± 0.4 kg, 5–7 y) and 6 male mongrels (37.9 ± 2.1 kg, 5 intact and 1 neutered, 6–8 y), owned by the University, were designated small dogs and large dogs, respectively. The dogs were individually housed simultaneously in semi-open runs in the same building, and they received an allotment of diet each day that was completely consumed by the following day. Body weights (BW) and body condition scores (BCS) were determined each week.

All dogs were given the same, nutritionally complete and balanced, extruded dry-type diet produced for the study (Royal Canin). Dietary protein was limited to 15.6% to provide adequate but not excessive SAA to maintain nitrogen balance and provide for taurine biosynthesis (**Table 1**). The dietary protein content exceeded recommended allowance for maintenance of adult dogs (10% for 16.7 kJ/g metabolizable energy in the diet, dry matter basis) (10,14). Sulfur amino acid bioavailability of the diet was estimated by cecectomized rooster assay (15).

Expt. 1. For 3 mo, the amount of diet given to each dog was adjusted each wk, as needed, to achieve and maintain ideal BCS (5 on a 9 point scale) (16). After 2 mo, baseline venous blood and urine samples were collected, body composition determined, and 14.6 mg/kg BW of 99 atom % deuterated taurine ([1,2-$^2H_2$]-taurine, d4-tau, CDN Isotopes) was given per os in a gelatin capsule wrapped in a marshmallow. Urine collection was repeated each morning before feeding for 5 d after administration of d4-tau. Concentrations of taurine in blood, plasma, and urine, and concentrations of total glutathione (reduced + oxidized), total cyst(e)ine (free plus bound to protein via a sulfhydryl bond), cysteinyl-glycine and homocysteine in plasma, and complete amino acid profiles (including cysteine and cystine not bound to protein) in plasma were determined as previously described (12). Urinary tracer (d4-tau) to tracee (taurine) ratio (TTR) for calculation of TBR of the dogs was determined by GC-MS.

TABLE 1 Composition and properties of the experimental diet[1]

Crude protein, %	15.6
Acid hydrolyzed fat, %	23.2
Crude fiber, %	1.9
Ash, %	8.3
Metabolizable energy,[2] *kJ/g*	18.0
Metabolizable energy from protein, %	12.7
Sulfur amino acid, %	0.60
Methionine	0.34
Cyst(e)ine	0.24
Taurine, *mg/kg*	280.0
Sulfur amino acid digestibility, %	77.9

[1] Ingredient list as provided by the diet manufacturer, Royal Canin: brewer's rice, rice bran, lamb-meal, poultry fat, lamb digest, and proprietary vitamin and mineral mixtures.
[2] Calculated using modified Atwater coefficients in the equation; metabolizable $energy_{kJ/g}$ = [(crude $protein_g$ × 3.5) + (ether $extract_g$ × 8.5) − (nitrogen free $extract_g$ × 3.5) + (crude $fiber_g$ × 0)] × 4.19 (15).

Expt. 2. Control of diet presentation to maintain ideal BCS was continued after Expt. 1 so that SAA intake per MBW could be calculated for each dog. The dogs were then ranked from least to highest SAA intake per MBW, and large and small dogs were paired by rank of SAA intake per MBW to make 6 experimental pairs. The mean SAA intake per MBW for each pair was determined, and the quantity of diet it represented was given to the pairs each d for 2 wk. After 1 wk, blood, plasma, and urine were sampled, body composition determined, d4-tau administration and urine collection repeated, and biochemical analyses conducted, as described in Expt. 1.

Sample collection, processing, and analysis. Blood (~5 mL) was collected from the cephalic vein by venipuncture into heparinized syringes (~20 μL of sodium heparin solution, 1000 USP kU/L, Baxter Health Care). Urine (≅5 mL) was collected by free-catch before feeding.

Taurine concentrations in blood, plasma, and urine were determined by the method of Kim et al. (17) using an amino acid analyzer (12). To normalize urinary taurine concentration, urinary creatinine concentrations were determined with a commercial kit (Cold Stable, Pointe Scientific).

The GC-MS analysis and calculation of TBR from enrichment of TTR in urine were conducted using a modification (12) of the method of Fay et al. (18). MS of the deuterated taurine derivative revealed a unique fragment of 241 m/z, which was assumed to be an M+3 rather than the expected M+4 fragment. Deuterium on carbon adjacent to the sulfonate group of the taurine label was assumed to exchange with available protium during the derivatization step. Use of the M+3 fragment was justified because its fractional abundance increased linearly with increasing enrichment of the M+4 tracer in standards.

TBR was calculated using equations,

$$TBR = \frac{D}{TTR(t_0)} \times (-K)$$

$$TTR = \left(\frac{P_{M+3}}{P_M}\right)sample - \left(\frac{P_{M+3}}{P_M}\right)nature \times \left(\frac{1}{1+A}\right),$$

where D is the dose in mg given, $TTR(t_0)$ is the TTR at time 0 as interpolated from TTR in d 1–5 urine samples, K is the rate constant, P_{M+3} and P_M are areas of peaks corresponding to ions of tracer and tracee, respectively, and A is natural abundance of the isotope used ($^2H = 0.00015$).

Body composition. Lean body mass (LBM) and body fat mass (BFM) was estimated by isotopic water dilution (19,20). For this, sterile filtered (0.2 μm/25 mm Anotop, Whatman), salinated (90 g/L NaCl), deuterated-water (99.9%, Sigma-Aldrich) was subcutaneously injected (0.4 g/kg), and after 4.5 h, cephalic venous blood (2 mL) was collected by venipuncture. Deuterium enrichment in serum water was measured as previously described (20).

Statistical analysis. Effect of body-size (large and small) and means of food intake control (that supporting ideal body condition [Expt. 1] and that supporting similar SAA intakes between large and small dog pairs [Expt. 2]) on food and SAA intakes, TBR, BW, LBM, BFM, and circulating amino acid and thiol concentrations were evaluated using mixed-model ANOVA (PROC MIXED, version 9.1, SAS Institute). Body-size and means of food intake control were assigned as fixed and random effects, respectively, and Tukey multiple comparisons adjustment were used in post-hoc analyses. Significance of correlations between food intake and taurine entry on taurine concentrations in blood, plasma, and urine were determined by regression analysis. Percentage data were transformed [2 × arcsin × $(observation)^{-1/2}$] prior to analyses. Differences were considered significant at $P \leq 0.05$ or a noteworthy trend at $P > 0.05$ and <0.10. Results are expressed as means ± SEM unless otherwise stated.

Results

Clearly, BW and food intake in large dogs were greater ($P < 0.01$) than those in small dogs in Expt. 1 and Expt. 2 (**Table 2**). However, mean SAA intake per MBW of large dogs was 23.2%

TABLE 2 Body composition and food intake of dogs given enough diet to maintain ideal body condition (Expt. 1) or similar amounts per kg MBW between small and large dog pairs (Expt. 2)[1]

	Expt. 1		Expt. 2	
	Small dogs	Large dogs	Small dogs	Large dogs
Body weight, *kg*	12.7 ± 0.3[a]	36.3 ± 1.9[b]	13.1 ± 0.4[a]	38.3 ± 2.7[b]
Lean body mass, *kg*	9.8 ± 0.5[a]	28.5 ± 1.3[b]	8.9 ± 0.4[a]	27.9 ± 2.1[b]
Body fat mass, *kg*	2.9 ± 0.3[a]	8.1 ± 0.7[b]	4.2 ± 0.3[a]	10.5 ± 0.5[c]
Body fat mass, %	23.2 ± 2.9[a]	21.9 ± 1.6[a]	32.0 ± 2.5[b]	27.5 ± 1.2[ab]
Food intake, *g/d*	208 ± 12[a]	347 ± 24[b]	257 ± 16[a]	570 ± 21[c]
SAA intake, $g \cdot kg^{-0.75} \cdot d^{-1}$	0.19 ± 0.01[ab]	0.14 ± 0.01[a]	0.22 ± 0.01[b]	0.22 ± 0.01[b]

[1] Observations are before d4-tau administration and represent mean ± SEM, $n = 6$. Values in rows with superscripts without a common letter differ, $P \leq 0.05$).

less ($P < 0.05$) than that of small dogs in Expt. 1 and exactly the same for large and small dogs in Expt. 2 because SAA intake was intentionally controlled for each pair of dogs in Expt. 2 to provide the same amount of the precursor for taurine synthesis (Table 2).

In Expt. 1, plasma ($P < 0.06$) and urine ($P < 0.07$) taurine concentrations tended to be lower in large than in small dogs (**Table 3**). Blood taurine and plasma glutathione, cyst(e)ine, cysteinyl-glycine and homocysteine in Expt. 1 did not differ between large and small dogs ($P > 0.05$). Plasma and blood taurine concentrations in Expt. 2 were 110 and 54% greater in small dogs, respectively, than in large dogs ($P < 0.05$). In contrast, concentrations of urine taurine and plasma glutathione and cyst(e)ine did not differ ($P > 0.05$) between small and large dogs in Expt. 2.

Due to limited sample volume, only 5 plasma samples could be submitted for complete amino acid profile analysis in large dogs for Expt. 1. In Expt. 1 but not Expt. 2, plasma concentrations of glycine ($P < 0.01$) and serine ($P < 0.02$) were greater in large than in small dogs (**Supplemental Table 1**). In Expt. 2 but not Expt. 1, plasma concentrations of tryptophan were less ($P < 0.05$) in large than small dogs. Hydroxyproline was less ($P < 0.04$) in small than in large dogs in Expt. 2. All other plasma amino acid concentrations were not significantly ($P > 0.05$) different between small and large dogs in either experiment.

TABLE 3 Taurine and thiol concentrations in dogs given enough diet to maintain ideal body condition (Expt. 1) or similar amounts per kg MBW between small and large dog pairs (Expt. 2)[1]

	Expt. 1		Expt. 2	
	Small dogs	Large dogs	Small dogs	Large dogs
Taurine concentration				
Plasma, *μmol/L*	69 ± 10[ab]	40 ± 6[a]	86 ± 11[b]	41 ± 15[b]
Blood, *μmol/L*	198 ± 18	157 ± 20	232 ± 30	151 ± 21
Urine, $\mu mol \cdot L^{-1} \cdot mg\ creatinine^{-1}$	13 ± 4.5	1.8 ± 0.9	10.0 ± 3.4	3.6 ± 3.3
Thiol concentration in plasma, *μmol/L*				
Glutathione	13 ± 1.3[a]	15 ± 1.2[ab]	16 ± 1.[b]	17 ± 1.0[b]
Cyst[e]ine	182 ± 23	200 ± 10	164 ± 10	170 ± 12
Cysteinyl-glycine	14 ± 1.0	20 ± 3.0	nd[2]	nd
Homocysteine	10 ± 0.9	10 ± 1.9	nd	nd

[1] Observations are before d4-tau administration and represent mean ± SEM, n = 6. Values in rows with superscripts without a common letter differ, $P \leq 0.05$.
[2] nd, not determined.

The TBR were normalized to BW, MBW, relative liver weight (RLW, $kg^{0.87}$), LBM, and metabolic LBM (MLBM, LMB $kg^{0.75}$) (**Table 4**). TBR was normalized to RLW for comparison between large and small dogs because the liver is the major organ of taurine biosynthesis in dogs (21). For Expt. 1, all normalized TBR were lower ($P < 0.05$) in large compared with small dogs, where the per MBW, LBM, MLBM, and RLW TBR were lower by 49, 37, 48, and 43%, respectively. In Expt. 2, TBR/LBM was lower ($P < 0.03$) and TBR/BW tended to be lower ($P = 0.06$) in large than in small dogs.

Taurine entry rate in dogss (taurine synthesized + ingested food each day) was determined for Expt. 1 and 2. The entry rates were then normalized by BW, MBW, RLW, LBM, and MLBM and regressed against the indicators of taurine status. Each of the normalized entry rates and taurine concentrations in blood and plasma were positively correlated ($P < 0.05$) in both experiments (**Supplemental Table 2 and Supplemental Fig. 1**). Relative to the blood and plasma correlations, correlations between urine taurine concentration and taurine entry rates were higher in Expt. 2 and lower or not significant ($0.05 < P < 0.1$) in Expt. 1.

With decreasing percentage of food intake relative to that expected based on BW (10,22), concentrations of taurine in Expt. 1 decreased ($P < 0.05$) in plasma, blood, and urine (Supplemental Table 2 and **Supplemental Fig. 2**). The same relations between food intake and indicators of taurine status were not significant ($P > 0.33$) in Expt. 2, where the range in food intake was substantially less (32–44 g/MBW) than that in Expt. 1 (17–35 g/MBW).

Discussion

The major difference between the 2 experiments of this study was the way in which food intake (i.e., SAA intake) was controlled. In Expt. 1, all dogs were given enough diet to maintain an ideal BCS for 3 mo including the period when TBR was determined. This feeding condition resulted in similar body fat percentages among the small and large dogs (Table 2) and body fat percentages consistent with previously reported ideals in dogs (16). Thus, in Expt. 1, TBR associated with maintenance energy intake of small and large dogs was determined. The most salient finding of Expt. 1 was that, although large dogs consumed 67% more diet than small dogs (Table 2), their TBR were similar to those of small dogs (Table 4), whereas there was a trend for lower plasma taurine concentrations ($P = 0.06$) than those of small dogs (Table 3). It is noteworthy in this context that mean plasma and blood taurine concentrations in the large, but not the small dogs, were indicative of marginal taurine status

TABLE 4 Taurine biosynthesis rate in dogs given enough diet to maintain ideal body condition (Expt. 1) or similar amounts per kg MBW between small and large dog pairs (Expt. 2)[1]

Taurine biosynthesis rate	Expt. 1		Expt. 2	
	Small dogs	Large dogs	Small dogs	Large dogs
Total, *mg/d*	749 ± 53	816 ± 218	752 ± 97	1228 ± 315
BW, $mg \cdot kg^{-1} \cdot d^{-1}$	59.1 ± 4.4[a]	22.3 ± 6.0[b]	58.4 ± 6.5[ac]	3'.6 ± 7.5[bc]
MBW, $mg \cdot kg^{-0.75} \cdot d^{-1}$	112 ± 8[a]	54.7 ± '5[b]	111 ± 13[a]	78.8 ± 19[ab]
RLW, $mg \cdot kg^{-0.87} \cdot d^{-1}$	82.2 ± 6.1[a]	35.5 ± 9.6[b]	80.0 ± 8.9[a]	50.4 ± 12[a]
LBM, $mg \cdot kg^{-1} \cdot d^{-1}$	77.0 ± 5.0[a]	28.3 ± 7.3[b]	83.7 ± 8.0[a]	42.9 ± 9.9[b]
MLBM, $mg \cdot kg^{-0.75} \cdot d^{-1}$	136 ± 8[a]	65.6 ± '7.1[b]	145 ± 15[a]	99.0 ± 23.4[a]

[1] Total and normalized taurine biosynthesis rates are expressed as mean ± SEM, $n = 6$. Values in rows with superscripts without a common letter differ, $P \leq 0.05$.

(11). The plasma taurine concentration observed in 1 large dog (15 μmol/L) was similar to concentrations reported in dogs with DCM that was corrected by taurine supplementation (11,12). These results support the hypothesis that large compared with small dogs are at greater risk for development of taurine deficiency when dietary SAA concentrations are marginal.

Urine taurine concentration was determined because it reflects acute changes in taurine status as a result of renal homeostatic modulation of taurine excretion (23). Variances in urine taurine concentrations within dog groups were great compared with variances observed in blood and plasma taurine concentrations. Nonetheless, there was a trend ($P = 0.07$) for urine taurine concentrations to be lower in large compared with small dogs in Expt. 1(Table 3). This finding is consistent with a trend of a lower taurine status in large compared with small dogs consuming the same diet.

The lower than expected TBR in large dogs appears to be at least partially a result of lower than expected SAA intake by large dogs. Although the large and small dogs were housed in the same environment during the experiments, large dogs consumed less diet (and therefore less SAA) on a MBW basis than small dogs to maintain ideal body condition (Table 2, Expt. 1). Energy intakes of small dogs [555 ± 29 kJ $\cdot$ kg$^{-0.75}$ $\cdot$ d^{-1}] were very close to intakes that would be predicted from body weight using a well established allometric relation [552 kJ $\cdot$ kg$^{-0.75}$ $\cdot$ d^{-1}, (10)]. In contrast, energy intakes of large dogs were substantively less than those that would be predicted [427 ± 37 kJ $\cdot$ kg$^{-0.75}$ $\cdot$ d^{-1}]. Variations in breed attributes other than body weight, such as conformation, hair coat, and physical activity, may account for deviations in scaling of maintenance energy intake (22,24). The observed positive correlations between taurine status indicators (blood, plasma, and urine taurine concentrations) and food intake (Supplemental Fig. 1 and Supplemental Table 2) indicates that food intake differences probably accounted for the observed size-effects on TBR and taurine status.

To the authors' knowledge, the scaling of taurine metabolism with body mass has not been reported. In Expt. 2, exactly the same amount of SAA per MBW was given to each pair of small and large dogs so that effect of metabolic body size on TBR could be evaluated when the same quantity of substrates of taurine metabolism is provided. It was presumed that taurine metabolism scales with MBW as is reported with metabolism of other nutrients (25,26). However, although food intake was controlled according to MBW in Expt. 2, correlations between taurine entry and indicators of taurine status were greatest with taurine entry rate normalization by BW and LBM (Supplemental Table 2). This may indicate taurine entry scales linearly rather than exponentially with body weight.

In Expt. 2, SAA intake relative to that in Expt. 1 was increased in both large and small dogs, but more so in large dogs (69 ± 15 vs. 24 ± 4%). The TBR in large dogs tended to be lower than those in small dogs after normalization to MLBM ($P = 0.32$) and RLW ($P = 0.20$) (Table 4). These normalizations were used because most taurine synthesis occurs in the lean mass, especially liver (23), and the percentage body fat in small compared with large dogs tended to be greater, in Expt. 2 ($P = 0.31$) relative to Expt. 1 ($P = 0.99$) (Table 2). Together, findings of the experiments indicate that the observed body-size effect on TBR was primarily a result of size-related difference in SAA intake relative to expected energy needs.

Plasma thiol concentrations did not differ between large and small dogs but plasma cysteinyl-glycine tended ($P = 0.10$) to be higher in large dogs. However, a trend ($P < 0.10$) of higher cysteinyl-glycine concentration was found in large compared with small dogs in Expt. 1. Lower intake of dietary SAA in large dogs relative to small dogs may result in lower γ-glutamyl transpeptidase (EC 2.3.2.2) and dipeptidase (EC 3.4.3.5) activities to hydrolyze plasma glutathione and cysteinyl-glycine (23). This should spare plasma glutathione and cysteinyl-glycine, maintaining homeostatic concentrations of these thiols.

Most of plasma amino acid concentrations (Supplemental Table 1) were similar to or greater than those in other reports with healthy dogs (27,28). The exceptions were proline, hydroxyproline and a few other dispensable amino acids. This indicates that the experimental diet and amount consumed were adequate for maintenance of protein and amino acid balance, with the exception of taurine (29). The low-normal plasma concentrations of free cyst(e)ine in dogs in this study are consistent with the experimental diet providing SAA sufficient for protein synthesis, but not sufficient for optimal taurine status in large dogs.

In summary when a low, but adequate, protein diet was given to dogs of varying body size to maintain ideal body condition, a trend of lower taurine concentrations in blood, plasma, and urine was found in large dogs, but not in small dogs. Some large dogs had taurine deficiency (plasma taurine ≤40 μmol/L) such that, if continued for the long-term, would be at risk for development of taurine-deficiency DCM. Our results support the hypothesis that the rate of taurine synthesis in large dogs is lower than that in small dogs when taurine precursor SAA are not in excess. In general, large relative to small dogs appear to be at greater risk for taurine deficiency because they ingest less diet for their MBW than small dogs. We conclude that the SAA allowance should be increased enough for large-breed dogs and dogs with low maintenance energy requirement to enable them to maintain an optimal taurine status.

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FDA In Brief

METADATA
Title: FDA investigates cases of canine heart disease potentially linked to diet

Description: FDA investigates dilated cardiomyopathy in dogs that ate certain pet foods labeled as "grain-free."

Short Title: FDA investigates canine heart disease cases potentially linked to diet

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For Immediate Release: July 12, 2018
Media Inquiries: Juli Putnam, 240-402-0537, juli.putnam@fda.hhs.gov

FDA In Brief: FDA investigates cases of canine heart disease potentially linked to diet

"We are concerned about reports of canine heart disease, known as dilated cardiomyopathy (DCM), in dogs that ate certain pet foods containing peas, lentils, other legumes or potatoes as their main ingredients. These reports are highly unusual as they are occurring in breeds not typically genetically prone to the disease," said Martine Hartogensis, D.V.M., deputy director of the FDA's Center for Veterinary Medicine's Office of Surveillance and Compliance. "The FDA is investigating the potential link between DCM and these foods. We encourage pet owners and veterinarians to report DCM cases in dogs who are not predisposed to the disease."

The U.S. Food and Drug Administration's Center for Veterinary Medicine and the Veterinary Laboratory Investigation and Response Network, a collaboration of government and veterinary diagnostic laboratories, are investigating the potential association between reports of canine dilated cardiomyopathy (DCM) in dogs and certain pet foods containing peas, lentils, other legume seeds or potatoes as main ingredients. Canine DCM is a disease of a dog's heart muscle and often results in congestive heart failure. In cases that are not linked to genetics, heart function may improve with appropriate veterinary treatment and dietary modification if caught early.

A genetic predisposition for DCM is typically seen in large and giant breed dogs, such as Great Danes, Newfoundlands, Irish Wolfhounds, Saint Bernards and Doberman Pinschers. The disease is less common in small and medium breed dogs, except American and English Cocker Spaniels. However, recently reported atypical cases have included Golden and Labrador Retrievers, a Whippet, a Shih Tzu, a Bulldog, and Miniature Schnauzers as well as mixed breeds. Early reports from the veterinary cardiology community indicate that the impacted dogs consistently ate foods containing peas, lentils, other legume seeds or potatoes as main ingredients as their primary source of nutrition for time periods ranging from months to years. That's why the FDA is conducting an investigation into this potential link. In the meantime, the FDA continues to recommend that changes in diet, especially for dogs with DCM, should be made in consultation with a licensed veterinary professional.

Cases of DCM in dogs suspected of having a link to diet can be reported to the FDA's electronic Safety Reporting Portal. For additional instructions, see "How to Report a Complaint about Pet Food."

As part of its investigation, the FDA has been in contact with the pet food manufacturers and the veterinary community to discuss these reports and will provide updates as more information becomes available.

###

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

From: Hartogensis, Martine </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02DF91D554D34B948FC58433D0E42073-MHARTOGE>
To: Putnam, Juli; Carey, Lauren; Palmer, Lee Anne; DeLancey, Siobhan; Norris, Anne; Forfa, Tracey; Rotstein, David; Jones, Jennifer L
Sent: 7/13/2018 1:47:16 PM
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Looks good! B5

Martine

From: Putnam, Juli
Sent: Friday, July 13, 2018 9:45 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thanks, I've incorporated Martine's portion below. Just to confirm, B5

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?

Proposed response:

B5

From: Carey, Lauren
Sent: Friday, July 13, 2018 9:37 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

I think Martine's example is good. B5

B5

From: Hartogensis, Martine
Sent: Friday, July 13, 2018 9:33 AM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David

<David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi Juli,

You could also say something like:

B5

Looping in Jen as well…

Martine

From: Putnam, Juli
Sent: Friday, July 13, 2018 9:29 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thank you, Lauren! How's this? I'm adding Dave to take a look as well.

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?

Proposed response:

B5

From: Carey, Lauren
Sent: Friday, July 13, 2018 9:18 AM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi,

B5

B5

Thanks,
Lauren

From: Putnam, Juli
Sent: Friday, July 13, 2018 9:04 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thanks, everyone. B5

B5 See the draft proposed response below for your review.

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?

Proposed response:

B5

From: Hartogensis, Martine
Sent: Thursday, July 12, 2018 6:21 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thanks Lee Anne! B6

From: Palmer, Lee Anne
Sent: Thursday, July 12, 2018 6:20 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

B5

From: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>
Date: July 12, 2018 at 6:16:01 PM EDT
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>, Norris, Anne

<Anne.Norris@fda.hhs.gov>, Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi abou B5 to date . Can't see whole steam - will send them read all

---

From: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Date: July 12, 2018 at 5:28:58 PM EDT
To: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Yes, me too.

As of right now, I believe we have about B5 .

Lee Anne or Lauren, can you confirm?

From: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Date: July 12, 2018 at 4:54:18 PM EDT
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>, Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

That works for me!

Siobhan DeLancey, RVT, MPH
O: 240-402-9973
M: B6

From: Putnam, Juli
Sent: Thursday, July 12, 2018 4:52 PM
To: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

All good points. So can I consider this version CVM-cleared?

B5

B5

From: DeLancey, Siobhan
Sent: Thursday, July 12, 2018 4:47 PM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

B5

Siobhan DeLancey, RVT, MPH
O: 240-402-9973
M: B6

From: Putnam, Juli
Sent: Thursday, July 12, 2018 4:44 PM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP
Importance: High

Hi again - just following on this. Bloomberg is pinging me again. They want the list of brands/products. Can we provide this? OCC has cleared it.

B5

From: Putnam, Juli
Sent: Thursday, July 12, 2018 3:49 PM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan (Siobhan.Delancey@fda.hhs.gov) <Siobhan.Delancey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP
Importance: High

Hi all - I know Dr. Solomon is out this week so including you all in the interest of time. Please let me know if you have edits to the responses and if we can answer the last one. Thanks!
Best,
Juli

Reporter: Aziza Kasumov
Outlet: Bloomberg
Deadline: asap
Background: I'm Aziza, a reporter for Bloomberg News working on a story about your statement from today about the potential link between certain dog foods and canine heart disease. I have a few more questions about the report, can you answer these for me? We're on tight deadline, so the sooner, the better.

Questions and proposed responses:
- Were the foods from several brands or from one brand of dog food? Can you name the companies that produced the foods linked to the reports, and which foods exactly the dogs ate? Was there one particular food brand that was heavily linked to the unusual reports?

B5

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?
CVM, please advise.

From:	Putnam, Juli </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=45A45E85E6E94413A4BD2C9FDBB3DE1B-JULIANN.PUT>
To:	Carey, Lauren; Hartogensis, Martine; Palmer, Lee Anne; DeLancey, Siobhan; Norris, Anne; Forfa, Tracey; Rotstein, David; Jones, Jennifer L
Sent:	7/18/2018 7:48:15 PM
Subject:	RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thank you Lauren!

From: Carey, Lauren
Sent: Wednesday, July 18, 2018 3:41 PM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi Juli,

Sorry, so many emails that things are getting buried. B5

B5

Thanks,
Lauren

From: Putnam, Juli
Sent: Wednesday, July 18, 2018 2:54 PM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

IHi all, can you please confirm B5

B5 Thanks!

Best,
Juli

From: Carey, Lauren
Sent: Friday, July 13, 2018 9:37 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

I think Martine's example is good. B5

B5

From: Hartogensis, Martine
Sent: Friday, July 13, 2018 9:33 AM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee

Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi Juli,

You could also say something like:

B5

Looping in Jen as well…

Martine

From: Putnam, Juli
Sent: Friday, July 13, 2018 9:29 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thank you, Lauren! How's this? I'm adding Dave to take a look as well.

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?

Proposed response:

B5

From: Carey, Lauren
Sent: Friday, July 13, 2018 9:18 AM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Hi,

B5

B5

Thanks,
Lauren

From: Putnam, Juli
Sent: Friday, July 13, 2018 9:04 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: RE: Bloomberg News inquiry re: Dog Food causing canine heart disease - Deadline: ASAP

Thanks, everyone. B5

B5 See the draft proposed response below for your review.

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?

Proposed response:

B5

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Sent: Thursday, July 12, 2018 6:21 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Cc: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
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Thanks Lee Anne! B6

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B5

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Outlet: Bloomberg
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B5

- How many of those unusual reports have you received so far? Can you give us a number of the dogs affected, to FDA knowledge?
CVM, please advise.

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: 'Darcy Adin'
Sent: 7/20/2018 11:35:05 AM
Subject: RE: diet DCM

Thank you for the update, Darcy. I hope you are well!
Take care,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Wednesday, July 18, 2018 5:39 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: diet DCM

Hi Jennifer,

I was glad to see the FDA's statement earlier this week about a possible link between diet and canine DCM - it certainly is causing a buzz!

I just wanted to let you know that NBC news has asked to interview me this friday. I'm assuming they have interviewed someone from the FDA as well?

B5

B5

Just wanted you to know and open to any thoughts you might have!
Take care
Darcy

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Andrea Fascetti <ajfascetti@ucdavis.edu>
To: Jones, Jennifer L
Sent: 5/20/2018 9:14:12 PM
Subject: Re: Question about aminoacid analysis-Matrices
Attachments: 002 Ko 2006 Cu Deficiency and Taurine Deficiency.pdf; **Not Responsive**; Backus 1995.pdf; Backus ACVN 2009 talk.pdf; Backus et al. 2006 J Nutr.pdf; Backus et al. JAVMA 2003.pdf; Backus JAVMA letter to edtior.pdf; Delaney JAPAN.pdf; Fascetti javma.2003.223.1137.pdf; freeman_2001 vet therapeutics.pdf; J. Nutr.-2007-Ko-1171-5.pdf; JAAHA article 2005 Gold Ret DCM and taurine.pdf; Ko et al. J Nutr 2007.pdf; Nofs_et_al-2018-Journal_of_Animal_Physiology_and_Animal_Nutrition.pdf; Pacioretty article.pdf; Rogers taurine article.pdf; Sanderson 2001 AJVR.pdf; Sanderson_taurine_carnitine_K9_cardiomyopathy.pdf; Torres et al. JAPAN.pdf; Vollmar et al. J Vet Cardio 2013.pdf

Hi Jen - Here are a number of articles on dog taurine. I am sure you have many of them, but I am sending what I have just in case. The paper with the bile acid analysis was Ko 2016. Hope these help.

Andrea

On May 18, 2018, at 11:29 AM, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov> wrote:

Hi Andrea,
I had a few questions unrelated to our contract.
Are you able to analyze amino acids in feces?
Is whole blood or plasma best for measuring amino acids in dogs?
-particularly taurine, cystine, and methionine.
Thank you in advance, and I hope you have a great weekend,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

The Journal of Nutrition
Nutrition and Disease

Low Plasma Taurine Concentration in Newfoundland Dogs is Associated with Low Plasma Methionine and Cyst(e)ine Concentrations and Low Taurine Synthesis[1]

Robert C. Backus,[2]* Kwang Suk Ko,[3] Andrea J. Fascetti,[3] Mark D. Kittleson,[4] Kristin A. MacDonald,[4] David J. Maggs,[5] John R. Berg,[6] and Quinton R. Rogers[3]

[2]Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri-Columbia, Columbia MO 65211; and [3]Department of Molecular Biosciences, [4]Department of Medicine and Epidemiology, [5]Department of Surgical and Radiological Sciences, and [6]Department of Chemistry, University of California, Davis, CA 95616

Abstract

Although taurine is not dietarily essential for dogs, taurine deficiency and dilated cardiomyopathy (DCM) are sporadically reported in large-breed dogs. Taurine status and husbandry were examined in 216 privately owned Newfoundlands, a giant dog breed with high incidence of idiopathic DCM (1.3–2.5%). Plasma taurine concentration was positively correlated ($P < 0.01$) with plasma cyst(e)ine ($r = 0.37$) and methionine ($r = 0.35$) concentrations and was similar across age, sex, neutering status, body weight, and body-condition scores. Plasma taurine concentration was low (≤40 μmol/L) in 8% of dogs. Dogs with low plasma taurine were older, less active, had more medical problems and treatments, and had lower plasma albumin, cyst(e)ine, tryptophan, and α-amino-n-butyric acid concentrations than the other dogs ($P < 0.05$). Of 9 taurine-deficient, clinically evaluated dogs, 3 had DCM that was reversed by taurine supplementation and 1 had retinal degeneration. When given a diet apparently adequate in sulfur amino acids (5.4 g/kg) for 3 wk, 6 Newfoundlands (52.5 ± 2.3 kg, 3.5–7 y), compared with 6 Beagles (13.2 ± 2.3 kg, 5.5 y), had lower ($P < 0.01$) concentrations of plasma taurine (49 ± 16 vs. 97 ± 25 μmol/L) and cyst(e)ine and blood glutathione, lower ($P < 0.01$) de novo taurine synthesis (59 ± 15 vs. 124 ± 27 $mg \cdot kg^{-0.75} \cdot d^{-1}$), and greater ($P < 0.05$) fecal bile acid excretion (1.7 ± 0.2 vs. 1.4 ± 0.2 μmol/g). Newfoundlands would appear to have a higher dietary sulfur amino acid requirement than Beagles, a model breed used in nutrient requirement determinations. J. Nutr. 136: 2525–2533, 2006.

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Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997–2001)

Andrea J. Fascetti, VMD, PhD, DACVN, DACVIM; John R. Reed, DVM, MS, DACVIM;
Quinton R. Rogers, PhD, DACVN; Robert C. Backus, DVM, PhD

Objective—To determine signalment, history, clinical signs, blood and plasma taurine concentrations, electrocardiographic and echocardiographic findings, treatment, and outcome of dogs with low blood or plasma taurine concentrations and dilated cardiomyopathy (DCM).

Design—Retrospective study.

Animals—12 client-owned dogs with low blood or plasma taurine concentrations and DCM.

Procedure—Medical records were reviewed, and clinical data were obtained.

Results—All 12 dogs were being fed a commercial dry diet containing lamb meal, rice, or both as primary ingredients. Cardiac function and plasma taurine concentration improved with treatment and taurine supplementation. Seven of the 12 dogs that were still alive at the time of the study were receiving no cardiac medications except taurine.

Conclusions and Clinical Relevance—Results suggest that consumption of certain commercial diets may be associated with low blood or plasma taurine concentrations and DCM in dogs. Taurine supplementation may result in prolonged survival times in these dogs, which is not typical for dogs with DCM. Samples should be submitted for measurement of blood and plasma taurine concentrations in dogs with DCM, and taurine supplementation is recommended while results of these analyses are pending. (*J Am Vet Med Assoc* 2003;223:1137–1141)

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Relationship Between Circulating and Dietary Taurine Concentrations in Dogs with Dilated Cardiomyopathy

Lisa M. Freeman, DVM, PhD[a]
John E. Rush, DVM, MS[a]
Donald J. Brown, DVM, PhD[a]
Philip Roudebush, DVM[b]

[a] *Tufts University*
School of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

[b] *Hill's Science and Technology Center*
PO Box 1658
Topeka, KS 66601

ABSTRACT

A retrospective study was conducted to determine dietary taurine concentrations in dogs with dilated cardiomyopathy (DCM) and to compare the clinical outcome of taurine-deficient and non–taurine-deficient dogs. Taurine concentrations were low in blood samples from 20 of 37 dogs with DCM. Median dietary taurine concentration was not significantly different between taurine-deficient and nondeficient dogs. There was no correlation between dietary and circulating taurine concentrations. The outcome of taurine-deficient dogs supplemented with taurine was not different from the outcome of nondeficient dogs. The role of taurine and its relationship to dietary intake in canine DCM remain unclear.

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Taurine-Deficient Dilated Cardiomyopathy in a Family of Golden Retrievers

A reversible taurine-deficient dilated cardiomyopathy occurred in five related golden retrievers. An apical systolic heart murmur was the most common physical abnormality. According to fractional shortening and end-systolic diameter on echocardiography, significant improvements ($P<0.005$) were recorded within 3 to 6 months of starting taurine supplementation. The dogs regained substantial systolic function, and four were weaned off all cardiac medications except taurine. This response to therapy was unusual, because canine dilated cardiomyopathy is generally progressive and fatal. **J Am Anim Hosp Assoc 2005;41:284-291.**

Marie C. Bélanger, DVM, MS, Diplomate ACVIM

Mathieu Ouellet, DVM

Guillaume Queney, PhD

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This study was supported by a grant from Le Fonds du Centenaire de l'Université de Montréal and from Merial Canada, Inc.

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The Journal of Nutrition
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

Differences in Taurine Synthesis Rate among Dogs Relate to Differences in Their Maintenance Energy Requirement[1–3]

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Abstract

Diet-induced (taurine deficiency) dilated cardiomyopathy is reported more in large than small dogs possibly because taurine biosynthesis rate (TBR) is lower in large than small dogs. The TBR in 6 mongrels (37.9 ± 2.1 kg) and 6 beagles (12.8 ± 0.4 kg) was determined from the fractional dilution rate of urinary [1,2-$^2H_2$]-taurine, (d4-tau). All dogs were given a 15.6% protein, 0.60% sulfur amino acid (SAA) diet in amounts to maintain an ideal body condition score. After 3 mo, 14.6 mg/kg body weight of d4-tau was given orally and TBR determined from d4-tau to taurine ratio in urine collected each d for 6 d. Enrichments of d4-tau were determined by GC-MS. Thereafter, mongrels and beagles were paired by ranking of SAA intake per metabolic body weight per $kg^{0.75}$. Each pair received the same amount of diet/$kg^{0.75}$ for 2 wk, then TBR was again determined. Concentrations of taurine in plasma, blood, and urine and concentrations of plasma thiols were measured during each TBR determination. In Expt. 1, TBR and taurine concentrations in plasma and urine of mongrels were lower ($P < 0.05$) than those of beagles. In Expt. 2, TBR and taurine concentrations in blood and plasma of mongrels were lower ($P < 0.05$) than beagles. Together, the results support the hypothesis that large compared with small dogs have lower TBR when fed diets near-limiting in dietary SAA, but adequate to maintain ideal body condition. J. Nutr. 137: 1171–1175, 2007.

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J. Anim. Physiol. a. Anim. Nutr. 87 (2003), 359–372
© 2003 Blackwell Verlag, Berlin
ISSN 0931–2439

Receipt of Ms.: 15. 04. 2003
Accepted: 14. 05. 2003

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Taurine status in normal dogs fed a commercial diet associated with taurine deficiency and dilated cardiomyopathy

By C. L. Tôrres, R. C. Backus, A. J. Fascetti and Q. R. Rogers

Summary

Taurine (Tau) deficiencies have been associated with the feeding of commercial lamb-meal and rice diets to dogs. We hypothesized that the poor digestibility of some lamb-meals may limit sulphur amino acids availability for Tau synthesis and/or increase of Tau degradation in the gut. Growing dogs were fed either a lamb-meal-based (Diet A) or poultry by-product-based (Diet B) commercial diet. Plasma, whole blood and urinary Tau were measured for 22 weeks. Plasma and whole blood Tau concentrations were similar between the groups throughout the study. Urinary excretion of Tau in dogs fed diet A was 3.2 times greater than that from dogs fed Diet B, suggesting greater renal reabsorption and the need for conservation of Tau in the Diet A group. Food restriction affected Tau status as indicted by a positive correlation of food intake and urinary Tau. Dogs fed Diet A were given antibiotics to inhibit bacterial activity in the gut. Increases in breath hydrogen, indicative of increased bacterial activity, correlated negatively with urinary Tau. Urinary Tau increased by 54% when methionine (Met) was supplemented to Diet A, supporting the suggestion of a low bioavailability of sulphur amino acids and/or an increased fecal loss of Tau in dogs consuming Diet A.

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Starch and Fiber Fractions in Selected Food and Feed Ingredients Affect Their Small Intestinal Digestibility and Fermentability and Their Large Bowel Fermentability In Vitro in a Canine Model[1,2]

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ABSTRACT The digestion of legumes, cereal grains, cereal and potato flours and grain-based foods in dogs was studied using two in vitro model systems. The first simulated the stomach and small intestine through the additions of acid and enzymes and large bowel fermentation through use of fecal inocula from dogs, and the second simulated small intestinal fermentation using canine ileal chyme as the bacterial source. All substrates were analyzed for total dietary fiber (TDF) including insoluble and soluble components, and starch fractions: rapidly digestible starch, slowly digestible starch, resistant starch (RS) and total starch. Legumes had high TDF and RS concentrations (mean 36.5 and 24.7%, respectively), resulting in lower ileal digestible starch and total digestible starch concentrations (mean 21 and 31%, respectively). Seventy-four percent of the TS in the cereal grains group was rapidly digestible starch plus slowly digestible starch compared with the flour group, where the corresponding value was 95%. This related to the processing of cereals to flours, in which TDF and RS concentrations were reduced markedly. This increased ileal digestible starch concentrations in the flour group (65%) versus the cereal grains group (60%). Ileal digestion of starch in grain-based food products like macaroni and spaghetti was high (96 and 92%, expressed as a percentage of TS, respectively). Fermentation of substrates with ileal microflora was influenced by substrate chemical composition, with the flour group exhibiting the highest organic matter disappearance values. The legume group had a high total short-chain fatty acid concentration (7.8 mmol/g organic matter fermented), perhaps as a result of fermentation of TDF as well as starch components. A database such as this one provides information about utilization of foods and feeds in the dog and potentially in humans. J. Nutr. 131: 276–286, 2001.

KEY WORDS: • *starch* • *total dietary fiber* • *digestion* • *fermentation* • *in vitro* • *dog*

Starch is the primary digestible carbohydrate found in plants. It is an important source of energy in the diets of humans and animals. Starch is a cost-effective means of supplying dietary energy. It is digested primarily in the small intestine by enzymatic degradation, but some can escape digestion and be fermented in the large bowel.

Although most fermentation occurs in the large bowel, a few studies (Ruseler-van Embden et al. 1992, Zentek 1995) suggest that fermentative activity can occur in the small intestine. Åman et al. (1995) indicated that substantial degradation of mixed-linked β-glucans may occur in ileostomy subjects, presumable due to bacterial fermentation in the small intestine. The ileum of humans has been reported to contain bacteria in concentrations of 10^5–10^6 colonies/g of contents (Drasar and Hill 1974). Small intestinal bacteria ostensibly could affect digestive processes occurring at this site. Relatively little data are available on the effects of starch and fiber fractions in selected food and feed ingredients on small intestinal and large bowel digestibility characteristics.

The objectives of this research were to first compile a starch and fiber fraction database for common food and feed ingredients. The general categories studied were legumes, cereal grains, cereal and potato flours, grain-based food products and reference substrates. Second, in vitro ileal digestible starch (IDS)[4] and total tract digestible starch (TDS) values were determined using a monogastric starch digestion model. Finally, the ileal disappearance and fermentative characteristics of selected food and feed ingredients were determined using ileal microbes from dogs in an in vitro model. Information gained in this experiment will aid in the understanding of effects of microbes in the distal small intestine on the starch and fiber fraction of food and feed ingredients. The dog was

[1] This article must therefore be hereby marked "advertisement" in accordance with 18 USC section 1737 solely to indicate this fact.

[2] The authors acknowledge the Council on Food and Agricultural Research (C-FAR) for their support of this research.

[3] To whom correspondence should be addressed at Department of Animal Sciences, University of Illinois, 132 Animal Sciences Laboratory, 1207 W. Gregory Drive, Urbana, IL 61801. E-mail: g-fahey@uiuc.edu

[4] Abbreviations used: CP, crude protein; DM, dry matter; FG, free glucose; I, insoluble fiber; IDS, ileal digestible starch; OM, organic matter; OMD, organic matter disappearance; RDS, rapidly digestible starch; RS, resistant starch; SCFA, short-chain fatty acids; SDS, slowly digestible starch; S, soluble fiber; TDF, total dietary fiber; TDS, total digestible starch; TS, total starch.

Manuscript received 24 July 2000. Initial review completed 3 September 2000. Revision accepted 10 November 2000.

used in the in vitro experiments as an animal model for humans. Both dogs and humans are omnivorous monogastrics. The lower gastrointestinal tract of the dog, like that of humans, contains numerous endogenous species of bacteria (Balish et al. 1977; Davis et al. 1977) that contribute significantly to colonic fermentation (Banta et al. 1979). The contribution of the large bowel to total digestive tract volume is also similar in the dog (14%) and the human (17%), in contrast to that in the pig (48%) and the rat (61%) (van Soest 1995).

MATERIALS AND METHODS

All experiments were conducted under protocols approved by the Laboratory Animal Care Advisory Committee, University of Illinois, Urbana-Champaign.

Chemical analyses. All substrates (legumes, cereal grains, cereal and potato flours, grain-based food products and reference substrates) were analyzed for dry matter (DM), organic matter (OM), Kjeldahl nitrogen (N) (Association of Official Analytical Chemists 1985) and total dietary fiber (TDF) (Prosky et al. 1984). Insoluble fiber (I) was determined according to the method of Prosky et al. (1992). Soluble fiber (S) was calculated by subtracting the I from the TDF. Total fat content was determined by acid hydrolysis followed by ether extraction according to the American Association of Cereal Chemists (1983) and Budde (1952).

Starch fractions [free glucose (FG), rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS)] of samples were determined according to the methods of Muir and O'Dea (1992 and 1993). Total starch (TS) values were determined according to the method of Thivend et al. (1972). Both starch fractionation and TS assays used dimethyl sulfoxide to disassociate the retrograded amylose (Englyst and Cummings 1984).

Experiment 1: Quantification of starch and fiber fractions and in vitro IDS and TDS values for common food and feed ingredients

Substrates. Substrates used in the in vitro experiment consisted of seven legumes (black beans, red kidney beans, lentils, navy beans, black-eyed peas, split peas and northern beans) and nine cereal grains (barley, corn, white rice, brewer's rice, brown rice, wheat, millet, oats and sorghum), all purchased from local vendors. The substrates were ground through a 2-mm screen in a Wiley mill. Seven flours (corn, wheat, rice, potato, soy, barley and sorghum) were obtained from a pet food manufacturer. Flours had been prepared according to the normal methods of grinding, fine milling, sieving and steam processing. Other substrates included six prepared grain-based food products (macaroni, spaghetti, corn meal, rice bran, rolled oats and hominy grits) purchased from local vendors. The final set of samples included three reference substrates: corn starch (73% amylopectin, 27% amylose; Sigma Chemical Co., St. Louis, MO), potato starch (approximately 80% amylopectin, 20% amylose; Sigma Chemical Co.) and amylomaize (Crystalean; almost 100% amylose; Opta Food Ingredients, Bedford, MA). These standards were included as part of each fractionation method to validate the efficacy of the experimental conditions imposed (i.e., a database containing information on key response criteria measured in this experiment was available for these standards, and any deviations in results obtained with these standards resulted in invalidation of the entire set of substrates being studied).

Donors. Two mixed-breed purpose-bred mature female ileally cannulated dogs (Walker et al. 1994) with hound bloodlines had ad libitum access twice daily to a commercial diet (Diamond Petfoods, Meta, MO) containing ~21% crude protein (CP) and 12% fat for 14 d before the collection of feces. Major ingredients in the diet included ground corn, poultry by-product meal, chicken fat and beet pulp. Dogs were housed in a temperature-controlled room in 1.2 × 3.1-m solid-floor pens. Free access to water was provided at all times.

Monogastric in vitro digestion model. This model represents a combination of three assays used to determine the amount of digestible starch at the ileum and in the total gastrointestinal tract. The method of Muir and O'Dea (1993) was used to determine the amount of starch digestion in the stomach and small intestine by measuring glucose in the supernatant resulting from acid-enzyme digestion of the substrate. Each substrate in triplicate was exposed to pepsin/hydrochloric acid, amyloglucosidase and α-amylase. Tubes containing reagents but no substrate were run as blanks. Glucose concentrations then were determined on the supernatant. Glucose was measured according to a glucose oxidase method (Glucose Test Kit 510-A; Sigma Chemical Co.). Glucose concentration was determined by reading the absorbance of individual samples at 450 nm on a DU 640 spectrophotometer (Beckman Instruments, Schaumburg, IL) and comparing those values against a glucose standard curve. IDS was determined by subtracting (FG ×0.9) from (total glucose/original sample weight) present in the supernatant after 15 h of digestion. The 0.9 used in the calculation of IDS is a correction factor for the difference in weight between an FG unit and a glucose residue in starch. Because the measurement of glucose is used to determine starch content, the correction factor is needed. The substrate remaining after simulated stomach and small intestinal digestion then was used in a model that simulated large bowel fermentation (Bourquin et al. 1993). Freshly voided feces from two dogs was diluted (1:10) in anaerobic diluting solution. This inoculum was used to inoculate all substrates individually for each dog. Substrates were incubated in an in vitro medium (**Table 1**) at 39°C for 12 h. TS was determined in the pellet that remained after simulated large bowel fermentation according to the method of Thivend et al. (1972) with dimethyl sulfoxide solubilization of amylose. TDS was determined by subtracting [(total glucose/original sample weight) × 0.9] in the remaining sample from the percentage TS.

TABLE 1

Composition of medium used for in vitro fermentation of food and feed ingredients

Component	Concentration in medium
	mL/L
Solution A[1]	330.0
Solution B[2]	330.0
Trace mineral solution[3]	10.0
Water-soluble vitamin mix[4]	20.0
Folate/biotin solution[5]	5.0
Riboflavin solution[6]	5.0
Hemin solution[7]	2.5
Short-chain fatty acid mix[8]	0.4
Resazurin[9]	1.0
Distilled H_2O	296.0
	g/L
Yeast extract	0.5
Trypticase	0.5
Na_2CO_3	4.0
Cysteine HCl · H_2O	0.5

[1] Composition (g/L): NaCl, 5.4; KH_2PO_4, 2.7; $CaCl_2 \cdot H_2O$, 0.16; $MgCl_2 \cdot 6H_2O$, 0.12; $MnCl_2 \cdot 4H_2O$, 0.06; $CoCl_2 \cdot 6H_2O$, 0.06; and $(NH_4)_2SO_4$, 5.4.

[2] Composition: K_2HPO_4, 2.7 g/L.

[3] Composition (mg/L): EDTA (disodium salt), 500; $FeSO_4 \cdot 7H_2O$, 200; $ZnSO_4 \cdot 7H_2O$, 10; $MnCl_2 \cdot 4H_2O$, 3; H_3PO_4, 30; $CoCl_2 \cdot 6H_2O$, 20; $CuCl_2 \cdot 2H_2O$, 1; $NiCl_2 \cdot 6H_2O$, 2; $Na_2MoO_4 \cdot 2H_2O$, 3.

[4] Composition (mg/L): thiamin · HCl, 100; *d*-pantothenic acid, 100; niacin, 100; pyridoxine, 100; *p*-aminobenzoic acid, 5; vitamin B-12, 0.25.

[5] Composition (mg/L): folic acid, 10; *d*-biotin, 2; NH_4HCO_3, 100.

[6] Composition: riboflavin, 10 mg/L in 5 mmol/L of HEPES.

[7] Hemin, 500 mg/L in 10 mmol/L NaOH.

[8] 250 mL/L each of *n*-valerate, isovalerate, isobutyrate and DL-α-methylbutyrate.

[9] Resazurin, 1 g/L in distilled H_2O.

Experiment 2: Determination of the ileal disappearance and fermentative characteristics of selected food and feed ingredients

Substrates. All substrates were the same as those described for expt. 1.

Donors and collection methods. Six mixed breed purpose-bred female ileally cannulated dogs (Walker et al. 1994) had ad libitum access twice daily to the diet used in expt. 1 for a 14-d period before the collection of ileal effluent. Dogs were housed in a temperature-controlled room in 1.2 × 3.1-m clean-floor pens. Free access to water was provided at all times. Fresh ileal fluid was collected from each dog for 15-min intervals in a Whirlpak bag (Pioneer Container Corp., Cedarburg, WI) until sufficient amounts needed to inoculate all tubes were obtained. At the end of each 15-min period, the bags were removed and replaced with new ones. Bags containing samples were sealed immediately after expressing excess air, placed inside a pre-warmed thermos (37°C) and transported to a laboratory within the same building for processing.

Medium composition and substrate fermentation. The composition of the medium used to culture the ileal microflora is presented in **Table 1**. All medium components except the vitamin mixes were added before autoclaving. The vitamin mixes were aseptically added after they were filter-sterilized.

On arrival in the laboratory, fresh ileal samples were immediately pooled under anaerobic conditions and diluted 1:10 (v/v) in a 39°C anaerobic dilution solution (Bryant and Burkey 1953) by blending for 10 s in a Waring blender. Blended, diluted ileal effluent was filtered through four layers of cheesecloth, and the filtrate was sealed in 125-mL serum bottles under CO_2. Appropriate sample and blank tubes containing 26 mL of medium and 300 mg of substrate were aseptically inoculated with 4 mL of diluted ileal effluent. Tubes were flushed with CO_2 and capped with stoppers equipped with one-way gas release valves. Blank tubes contained 4 mL of inoculum and 26 mL of medium but did not contain any substrate.

Triplicate tubes were placed in a forced air incubator at 39°C with periodic mixing for each fermentation time period (2.5, 5 and 7.5 h). At the appropriate time, tubes were removed from the incubator and processed immediately. A 2-mL aliquot was removed from each tube for short-chain fatty acid (SCFA) and lactate analyses. The remaining 28 mL was combined with 112 mL of 95% ethanol and allowed to set for 1 h to precipitate the soluble polysaccharide fractions. To recover unfermented residues, samples were filtered through tared Whatman 541 filter paper and washed sequentially with 78% ethanol, 95% ethanol and acetone. Samples then were dried at 105°C, weighed, ashed in aluminum weigh boats (500°C) and weighed again to determine OM disappearance (OMD). In vitro OMD (percentage) was calculated as {1 − [(OM residue–OM blank)/original OM]} × 100, where OM residue is the OM recovered after 2.5, 5 or 7.5 h of fermentation; OM blank is the OM recovered in the corresponding blank after the same fermentation times; and original OM is the OM of the substrate placed in the tube. Corrected OMD was calculated as the 2.5-, 5- and 7.5-h OMD minus the 0-h OMD.

The 2-mL aliquot of fluid removed from the sample tubes for SCFA and lactate analyses was immediately added to 0.5 mL of metaphosphoric acid (250 g/L), precipitated for 30 min and centrifuged at 20,000 × *g* for 20 min. The supernatant was decanted and frozen at −20°C in microfuge tubes. After freezing, the supernatant was thawed and centrifuged in microfuge tubes at 10,000 × *g* for 10 min. Concentrations of acetate, propionate and butyrate were determined in the supernatant using a Hewlett-Packard 5890A Series II gas-liquid chromatograph and a glass column (180 cm × 4 mm i.d.) packed with 10% SP-1200/1% H_3PO_4 on 80:100 mesh Chromosorb WAW (Supelco, Bellefonte, PA). SCFA concentrations were corrected for by the blank tube production of SCFA. The supernatants also were analyzed for lactate concentration according to the spectrophotometric method described by Barker and Summerson (1941).

Statistical analysis. The General Linear Models procedures of SAS (1994) were used to analyze data from these experiments. In expt. 1, the experimental design was a randomized complete block design with the two fecal donors serving as blocks. Donor × substrate was used in the statistical model. In expt. 2, the experimental design was a factorial arrangement of substrates within groups (legumes, cereal grains, cereal and potato flours, grain-based food products and reference substrates) and fermentation times (0, 2.5, 5 and 7.5 h). Arithmetic means are reported along with the SEM for each group of substrates. When significant ($P < 0.05$) differences were detected, individual means were compared using the least significant difference (LSD) method of SAS (1994).

RESULTS AND DISCUSSION

Chemical composition. The chemical composition of substrates is presented in **Table 2**. Chemical composition of legumes varied widely, corroborating data of Kamath et al. (1980). In our experiment, DM concentrations were similar among legumes, except for navy beans, which were lower in DM. OM concentrations were similar among substrates. CP content ranged from a low for navy beans to a high for lentils and northern beans. The CP concentration of lentils agreed with the reported range of 20.4–30.5% (Salunkhe et al. 1985). The fat concentration of legumes ranged from a low for navy beans to a high for northern beans. Concentrations of TDF were high for the entire legume group, with black beans having the highest TDF content and black-eyed peas having the lowest. The legume group contained mainly I (92.2–100% of TDF), whereas S values ranged from 0 to 7.8% of the TDF.

DM concentrations of the cereal group ranged from a low for corn to a high for sorghum. OM concentrations differed by ~3 percentage units for the cereal group. CP content varied from a low for white rice to a high for wheat. Watson (1953) and Juliano et al. (1964) reported CP values of 11.8 and 11.0% for barley and brown rice, respectively. These values agree with our values of 12.7% for barley and 10.2% for brown rice. Cereal grain fat concentrations ranged from a low for white rice to a high for oats. Total dietary fiber concentrations varied widely, with oats containing ~25 times more TDF than white rice. Cereal grains contain the husk, pericarp and/or bran in varying concentrations, thus providing components that contain fiber, albeit in generally lower concentrations compared with legumes. The majority of TDF found in the cereal group was I, although cereals contained a much greater proportion of S than did legumes.

DM concentrations were similar among the grain and potato flour group. OM concentrations ranged from 92.9% (soy) to 99.6% (sorghum). CP content was highest for soy and lowest for brown rice. Soy flour contained the highest concentration of fat in the flour group. Total dietary fiber concentrations varied from a high for barley flour to a low for sorghum flour. High concentrations of fiber in barley flour may be a result of high concentrations of β-glucans present in the grain (Liljeberg et al. 1992). I concentrations again were higher than S concentrations in the flour group, although large differences in S concentrations occurred among substrates. Overall, grain flours contained less TDF compared with their cereal grain counterparts.

DM concentrations of grain-based food products differed by only 3 percentage units. OM concentrations were similar among substrates except for rice bran, which contained more ash (>10%). CP content ranged from 7.7% (corn meal) to 16.9% (rice bran). Fat concentrations ranged from a high for rolled oats to a low for corn meal. Total dietary fiber varied widely among the prepared grain products, with rice bran being the highest, rolled oats and hominy grits being intermediate, and macaroni, spaghetti and corn meal being the lowest. I concentrations were highest for rice bran and lowest for macaroni. As a percentage of TDF, S concentrations were highest (mean 34.5%) for macaroni, spaghetti, rolled oats and hominy grits.

TABLE 2

Proximate and fiber constituents of selected food and feed ingredients

Substrate	DM[1]	OM	CP	Fat	TDF	I[2]	S[2]
				g/100 g dry matter			
Legumes							
Black beans	89.0	95.5	23.6	3.3	42.6	39.4 (92.5)	3.2 (7.5)
Red kidney beans	89.1	95.6	25.4	3.0	36.8	36.3 (98.6)	0.5 (1.4)
Lentils	90.7	96.6	27.5	2.4	33.1	33.0 (99.7)	0.1 (0.3)
Navy beans	83.7	95.1	22.8	1.6	36.2	36.2 (100.0)	0.0 (0.0)
Black-eyed peas	90.6	96.5	24.4	2.7	32.6	32.4 (99.4)	0.2 (0.6)
Split peas	90.0	96.8	26.1	2.5	33.1	31.3 (94.6)	1.8 (5.4)
Northern beans	89.2	95.3	27.5	4.0	41.1	37.9 (92.2)	3.2 (7.8)
Cereal grains							
Barley	90.3	98.6	12.7	2.8	17.0	12.0 (70.6)	5.0 (29.4)
Corn	86.8	98.6	12.8	4.9	19.6	16.0 (81.6)	3.6 (18.4)
White rice	87.9	99.4	9.1	1.6	1.5	1.2 (80.0)	0.3 (20.0)
Brewer's rice	92.2	99.2	9.6	1.9	2.1	1.5 (71.4)	0.6 (28.6)
Brown rice	87.7	98.6	10.2	4.0	5.7	4.3 (75.4)	1.4 (24.6)
Wheat	94.2	97.7	18.1	3.2	17.0	14.7 (86.5)	2.3 (13.5)
Millet	88.5	98.8	11.2	4.8	5.4	3.1 (57.4)	2.3 (42.6)
Oats	90.0	96.7	14.2	6.9	37.7	33.9 (89.9)	3.8 (10.1)
Sorghum	94.6	98.6	11.1	4.3	4.6	4.2 (91.3)	0.4 (8.7)
Flours							
Corn	92.1	99.4	11.2	2.6	2.8	2.8 (100.0)	0.0 (0.0)
Wheat	91.1	98.3	17.2	3.1	12.1	8.5 (70.2)	3.6 (29.8)
Brown rice	89.1	98.8	7.6	4.2	5.1	3.4 (66.7)	1.7 (33.3)
Potato	94.4	95.3	9.8	1.5	2.1	1.1 (52.4)	1.0 (47.6)
Soy	94.5	92.9	54.5	5.2	15.4	14.7 (95.5)	0.7 (4.5)
Barley	91.0	97.9	11.4	3.8	22.9	20.1 (87.8)	2.8 (12.2)
Sorghum	91.9	99.6	10.6	2.0	1.3	1.1 (84.6)	0.2 (15.4)
Grain-based food products							
Macaroni	89.2	99.0	15.9	2.7	5.6	3.4 (60.7)	2.2 (39.3)
Spaghetti	90.4	99.2	15.5	2.6	5.6	3.7 (66.1)	1.9 (33.9)
Corn meal	89.6	99.7	7.7	1.9	4.4	4.3 (97.7)	0.1 (2.3)
Rice bran	92.1	89.4	16.9	3.6	28.0	27.6 (98.6)	0.4 (1.4)
Rolled oats	91.1	97.9	14.2	9.1	10.0	6.6 (66.0)	3.4 (34.0)
Hominy grits	88.7	99.4	8.4	2.2	11.4	7.9 (69.3)	3.5 (30.7)
Reference substrates							
Corn starch	91.2	99.8	0.6	0.9	0.0	0.0	0.0
Potato starch	90.2	99.9	0.2	0.03	0.0	0.0	0.0
Amylomaize	88.7	99.7	0.9	1.5	5.3	3.2 (60.4)	2.1 (39.6)

[1] DM = dry matter; OM = organic matter; CP = crude protein; TDF = total dietary fiber; S = soluble fiber; I = insoluble fiber.
[2] Numbers in parentheses are soluble (S) or insoluble (I) fiber concentrations expressed as a percentage of TDF.

DM, OM and CP concentrations were similar among the reference substrates. Corn and potato starch contained low fat concentrations. Corn starch and potato starch contained no TDF. Although 5.3% TDF was detected in the amylomaize, this is probably RS rather than fiber.

Starch fractions. Concentrations of starch fractions of substrates are presented in **Table 3**. FG concentrations were low for all substrates, as expected.

The concentrations of RDS, SDS and RS in the legume group varied widely. RDS concentrations were lowest for red kidney beans and highest for split peas. SDS concentrations varied more than twofold. RS concentrations generally constituted the highest proportion of the starch fractions of legumes. Ring et al. (1988) reported that leguminous starches displayed a C-type pattern of crystallinity. This type of starch is more resistant to hydrolysis than that with an A-type crystallinity pattern and helps explain why legumes have high amounts of RS.

Gee and Johnson (1985) found that there was a relationship between the "half-time starch hydrolysis" (time taken to achieve 50% hydrolysis of the original starch of the substrate) and the dietary fiber content of certain foods. Their data indicate that legumes such as peas and red kidney beans all had higher half-time hydrolysis rates (60.0 and 58.0 min, respectively), whereas white bread and white rice had much lower values (19.5 and 2.1 min, respectively). In their study, dietary fiber content averaged 27.8% for peas and red kidney beans and only 3.1% for white bread and white rice. McBurney et al. (1988) also found that SCFA production from ileal effluent was significantly correlated with dietary fiber isolates but not whole foods. The authors concluded that dietary fiber isolates, rather than whole foods, could provide the closest estimation of colonic SCFA production. Another possible reason for the higher RS concentrations in legumes could be the relationship between starch and protein. Tovar et al. (1990) found that when red kidney beans were preincubated with pepsin, there was an increase in their susceptibility to amylolytic attack.

TS values of legumes obtained by adding FG, RDS, SDS and RS components closely paralleled those reported from the determination of starch using the method of Thivend et al. (1972), attesting to the accuracy of the Muir and O'Dea (1993) method for quantifying starch fractions. A possible explanation for the higher concentration of TS for substrates such as black beans and black-eyed peas using the Thivend et

TABLE 3

Starch fractions of selected food and feed ingredients

Substrate	% FG[1]	% RDS	% SDS	% RS	TS	Thivend
			g/100 g dry matter			
Legumes						
Black beans	0.1 (0.2)	7.5 (17.5)	8.4 (19.6)	26.9 (62.7)	42.9	46.8
Red kidney beans	0.1 (0.2)	4.3 (10.1)	13.7 (32.2)	24.6 (57.7)	42.6	42.9
Lentils	0.1 (0.2)	16.4 (30.8)	11.4 (21.4)	25.4 (47.7)	53.3	51.9
Navy beans	0.1 (0.2)	6.5 (13.2)	16.8 (34.1)	25.9 (52.5)	49.3	50.8
Black-eyed peas	0.1 (0.2)	18.5 (34.3)	18.5 (34.3)	17.7 (32.8)	53.9	57.0
Split peas	0.1 (0.2)	22.3 (34.5)	17.8 (27.5)	24.5 (37.9)	64.7	65.6
Northern beans	0.1 (0.2)	10.9 (21.8)	10.9 (21.8)	28.0 (56.1)	49.9	46.7
Cereal grains						
Barley	0.1 (0.2)	24.9 (45.1)	12.1 (21.9)	18.2 (33.0)	55.2	54.7
Corn	0.2 (0.3)	37.1 (47.6)	15.6 (20.0)	25.2 (32.3)	77.9	80.1
White rice	0.1 (0.1)	32.0 (33.6)	48.9 (51.4)	14.1 (14.8)	95.1	93.0
Brewer's rice	0.0 (0.0)	68.4 (79.4)	14.3 (16.6)	3.5 (4.1)	86.2	83.7
Brown rice	0.0 (0.0)	28.7 (32.5)	44.7 (50.7)	14.8 (16.8)	88.2	87.8
Wheat	0.1 (0.2)	29.9 (58.9)	7.3 (14.4)	13.6 (26.8)	50.8	52.9
Millet	0.1 (0.1)	35.9 (41.6)	37.7 (43.7)	12.6 (14.6)	86.2	90.9
Oats	0.2 (0.5)	35.8 (82.5)	0.3 (0.7)	7.2 (16.6)	43.4	46.5
Sorghum	0.0 (0.0)	29.2 (36.9)	13.9 (17.6)	36.1 (45.6)	79.2	77.8
Flours						
Corn	0.1 (0.1)	73.2 (86.8)	0.0 (0.0)	11.0 (13.0)	84.3	90.8
Wheat	0.0 (0.0)	38.1 (55.4)	29.0 (42.2)	1.7 (2.5)	68.8	73.4
Rice	0.0 (0.0)	57.7 (66.4)	27.6 (31.8)	1.6 (1.8)	86.9	89.3
Potato	0.1 (0.1)	75.5 (93.2)	3.8 (4.7)	1.7 (2.1)	81.0	77.9
Soy	0.1 (1.8)	2.2 (40.0)	2.7 (49.1)	0.6 (10.9)	5.5	8.2
Barley	0.0 (0.0)	37.7 (54.2)	30.6 (44.0)	1.2 (1.7)	69.5	75.6
Sorghum	0.2 (0.2)	63.5 (70.8)	24.6 (27.4)	1.6 (1.8)	89.7	84.8
Grain-based food products						
Macaroni	0.3 (0.4)	60.0 (79.9)	8.9 (11.9)	6.0 (8.0)	75.1	77.2
Spaghetti	0.0 (0.0)	48.9 (67.0)	20.9 (28.6)	3.3 (4.5)	73.0	82.7
Corn meal	0.2 (0.2)	49.3 (56.3)	33.0 (37.7)	5.0 (5.7)	87.5	95.5
Rice bran	0.0 (0.0)	0.1 (0.4)	25.1 (88.1)	3.4 (11.9)	28.5	27.5
Rolled oats	0.0 (0.0)	42.5 (75.9)	4.8 (8.6)	8.5 (15.2)	56.0	60.1
Hominy grits	0.1 (0.2)	36.8 (56.4)	20.4 (31.2)	8.0 (12.3)	65.3	70.9
Reference substrates						
Corn starch	0.0 (0.0)	71.8 (70.0)	22.6 (22.0)	8.1 (7.9)	102.5	101.5
Potato starch	0.0 (0.0)	27.2 (27.9)	3.3 (3.4)	66.9 (68.7)	97.4	99.3
Amylomaize	0.0 (0.0)	30.3 (30.1)	18.2 (18.1)	52.0 (51.7)	100.5	99.8

[1] FG = free glucose; RDS = rapidly digestible starch; SDS = slowly digestible starch; RS = resistant starch; TS = total starch = (FG × 0.9) + RDS + SDS + RS; Thivend = total starch as measured by the Thivend et al. (1972) method. Numbers in parentheses are FG, RDS, SDS and RS expressed as a percentage of the TS.

al. (1972) method may be the inclusion of sucrose in the measurement. This method enzymatically converts sucrose into monosaccharides and allows for their recovery in the supernatant. The Muir and O'Dea (1993) method does not account for this conversion, so sucrose is not part of the starch value.

Cereal grains varied widely in percentage starch found in each of the starch fractions. RDS and SDS concentrations represented the majority of the TS in the cereal group. Cereal grains have an A-type crystalline form, which is the starch structure least resistant to hydrolysis (Ring et al. 1988). This crystalline form leads to more of the starch being categorized as RDS and SDS. RDS concentrations as a percentage of TS varied from 32.5 to 82.5%. White rice contained the highest concentration of SDS (51.4%) as a percentage of TS. Raw cereals are partially inaccessible to digestion due to the physical form of the cereal itself (Englyst et al. 1992b). Structures like the pericarp and seed coat may impede the efficiency of amylase digestion of starch in cereal grains.

RS concentrations were highest for sorghum and lowest for oats. Four categories of RS have been defined (Brown 1996). The first category (RS1) includes starch granules that are physically inaccessible and can be found in whole or partially milled grains and legumes. The second category (RS2) refers to native starch granules, whereas the third category (RS3) refers to retrograded starch that is formed during processing. The fourth category of RS (RS4) was only recently described and includes chemically modified starches resistant to enzymatic hydrolysis to some degree.

Flours also varied widely in percentage starch found in each of the starch fractions. Approximately 95% of the TS in flours is RDS and SDS combined. RS concentrations were highest for corn and soy and lowest for barley. Englyst et al. (1992a) reported that white wheat flour contained 49% RDS, 48% SDS and 3% RS as a percentage of TS. Our wheat flour contained 55.4% RDS, 42.2% SDS and 2.5% RS as a percentage of TS, agreeing closely with the values of Englyst et al. (1992a). RS concentrations were low for the flour group as a whole. Cereal flours display an A-type crystalline pattern, which is more readily hydrolyzed than raw cereals that are not as highly processed as flours. Therefore, cereal flours contain more RDS and SDS than RS.

The nutrient profile of cereal grains and their corresponding flours varied considerably. Grain flours are made up pri-

marily of two components: protein and starch. Cereal grains, in contrast, contain the pericarp, aleurone layers and germ portions of the grain that provide lipid and fiber (Hoseney 1994). Cereal grains are processed and milled to flours, thereby altering the chemical composition of the flour compared with the cereal grain. Even DM concentrations varied when cereal grains were compared with their flour counterparts. Except for barley, flours were numerically higher in OM. CP concentrations of flours were 1–3 percentage units lower than that for ground grains. Total dietary fiber concentrations of flours, except for barley, were numerically lower compared with their ground grain counterparts. This reduction in TDF points to how the processing of grains alters their fiber content through removal of the pericarp, aleurone layers and germ. Of interest is how the processing of cereals to flours affects the starch fraction profile. The combined RDS and SDS concentrations of cereal grains were ~74% of TS versus, flours, which were 95% of TS. The RS concentrations were, on average, five times higher in the cereal grains than in the flours.

For the grain-based food products, RDS concentrations, expressed as a percentage of TS, were highest for macaroni and rolled oats; intermediate for spaghetti, corn meal and hominy grits; and lowest for rice bran. SDS concentrations varied, with corn meal having the highest concentration and rolled oats having the lowest. Prepared grain products contained moderate levels of RS (mean 9.6% as a percentage of TS). Hermansen et al. (1986) postulated that starch in foods like spaghetti is more slowly digested because of the densely packed starch in the food. During pasta production, pasta is kneaded and extruded, leading to a tight, entrapped starch granule (Colonna et al. 1990). Again, food ingredients like rice bran with high TDF (28.0%) may experience a lower amount of starch hydrolysis as a result of its fiber content. Corn meal contained the highest concentration of TS, whereas rice bran contained the lowest.

The reference substrates varied widely in their starch fractions. RDS values were highest for corn starch and similar for potato starch and amylomaize. SDS values were similar for corn starch and amylomaize and lower for potato starch. As a percentage of TS, potato starch had the highest RS concentration and corn starch had the lowest. Englyst et al. (1992a) found that raw potato starch contained 75% RS as a percentage of TS. Starches from tubers such as potatoes tend to exhibit B-type crystallinity patterns that are highly resistant to digestion (Englyst et al. 1992a). Amylomaize contains mostly amylose, which has been shown to lower not only digestibility but also blood insulin and glucose values in humans (Behall et al. 1995).

A common characteristic of all foods and feeds studied is that RS is a component of each. This starch fraction is not hydrolyzed and enzymatically digested in the small intestine but rather serves as a substrate for fermentation by microflora either in the ileum and/or large bowel.

In vitro experiment 1

Ileal bacteria. Fermentative events in the nonruminant occur as a result of bacterial activity in the colon and possibly in the ileum of the small intestine. Ruseler-van Embden et al. (1992) found >25 different species of bacteria residing in the small intestine of dogs. Murray et al. (2000) found the following colony-forming units (CFU)/mL of ileal effluent after isolation and plating: 4.2×10^8 total anaerobes, 7.1×10^5 total aerobes, 1.3×10^6 *Escherichia coli*, 1.7×10^8 *Clostridium perfringens*, 1.8×10^8 *Bifidobacteria* and 3.3×10^6 *Lactobacillus*. Finegold et al. (1970) found that in the human ileostomate, there were 10^7–10^8 colonies/g of ileal contents. These values confirm that there may be a substantial bacterial population residing in the small intestine of both dogs and humans. It is uncertain whether ileal microbes are indigenous to this site or whether they emanate from the cecum, finding their way via the ileocecal valve into the small intestine. The contents of the small intestine normally flow rapidly, possibly becoming static for an appreciable period only in the distal small intestine (Drasar and Hill 1974).

IDS and TDS concentrations. IDS concentrations for the legume group were statistically highest ($P < 0.05$) for black-eyed peas and split peas, next highest for lentils and navy beans and lowest for northern beans, black beans and red kidney beans (**Table 4**). Bjorck et al. (1992) reported that the small intestinal digestibility by rats of a cooked and canned pea product was 70%. As a percentage of TS (i.e., IDS/TS), our ileal digestibility value for split peas (45.7%) was lower and may be due to the raw, unprocessed nature and high RS content of this substrate. Key et al. (1995) also found that as the concentration of cooked haricot beans in the diet of rats increased from 0 to 450 g/kg, ileal digestibility decreased from 87 to 69% for the haricot bean–containing diet.

TDS concentrations were lowest ($P < 0.05$) for black beans, red kidney beans and northern beans and highest ($P < 0.05$) for black-eyed peas and split peas. Biliaderis et al. (1981) found that wrinkled peas contained 55.4% amylose as a percentage of TS, whereas beans contained higher amounts of amylose (mean 59.2%). Higher amylose concentrations in starches are believed to lower digestibility (Borchers 1962). This could explain why the peas displayed higher TDS concentrations and the beans displayed lower TDS concentrations. Goodlad et al. (1992) found that as the proportion of peas doubled from 250 to 500 g/kg in the diet of rats, total tract digestibility was reduced ($P < 0.05$) from 94 to 91%. The TDS concentrations were low for the bean group as a whole, with a possible explanation being the physical entrapment of the starch within fibrous, thick-walled parenchyma cells (Wursch et al. 1986). Also, antinutrients (e.g., enzyme inhibitors, lectins and tannins) have been found in legumes, and that could reduce the digestibility of legume starches. RS and TDF concentrations also were high for the legume group and could affect starch digestion in these substrates.

Starch utilized by the microflora in the large bowel (percent TDS − percent IDS) was numerically highest for split peas and lowest for northern beans.

For the cereal grains group, IDS concentrations were highest ($P < 0.05$) for brewer's rice and lowest for oats. As a percentage of TS, starch in oats and barley was completely digested at the ileum. Englyst and Cummings (1985), using human ileostomates, found that raw oat starch hydrolysis was complete in the small intestine. Barriers to amylase digestion apparently do not impede the starch in oats. Of interest is how white rice and brown rice differ with respect to IDS values. O'Dea et al. (1981) found that relative rates of starch hydrolysis in an in vitro system correlated very closely with in vivo peak glucose responses in humans. In vitro rates of starch hydrolysis (percent hydrolyzed/30 min) for ground brown rice and white rice were 68.2 and 71.8%, respectively. O'Dea et al. (1981) suggest that fiber might act indirectly to slow carbohydrate absorption, restricting access of hydrolytic enzymes to starch from an unrefined source like brown rice. Our brown rice source was higher in TDF content and lower in IDS than white rice. Two other grains have been shown to have structural differences that may contribute to resistance to digestion. Hosney (1994) suggested that the protein-starch matrix of

TABLE 4

In vitro ileal digestible starch (IDS) and total digestible starch (TDS) concentrations of selected food and feed ingredients[1,2,3]

Substrate	IDS	TDS	TDS-IDS
		%	
Legumes			
Black beans	16.4[c] (35.0)	22.3[c] (47.6)	5.9[c]
Red kidney beans	15.0[d] (35.0)	21.7[c] (50.6)	6.7[b,c]
Lentils	20.6[b] (39.7)	32.8[b] (63.2)	12.2[a,b]
Navy beans	20.6[b] (40.6)	33.7[b] (66.3)	13.1[a]
Black-eyed peas	30.0[a] (52.6)	44.4[a] (77.9)	14.4[a]
Split peas	30.0[a] (45.7)	44.5[a] (67.8)	14.5[a]
Northern beans	17.0[c] (36.4)	20.3[c] (43.5)	3.3[c]
SEM	0.33	1.93	1.72
Cereal grains			
Barley	54.7[d] (100.0)	52.3[e] (95.6)	−2.4[h]
Corn	59.4[c] (74.2)	74.2[c] (92.6)	14.8[b]
White rice	69.0[b] (74.2)	80.0[b] (86.0)	11.0[d]
Brewer's rice	73.2[a] (87.5)	79.1[b] (94.5)	5.9[f]
Brown rice	61.3[c] (69.8)	74.3[c] (84.6)	13.0[c]
Wheat	52.8[d] (99.8)	47.1[f] (89.0)	−5.7[i]
Millet	68.9[b] (75.8)	86.4[a] (95.0)	17.5[a]
Oats	46.5[e] (100.0)	46.5[e] (100.0)	0.0[g]
Sorghum	52.8[d] (67.9)	62.4[d] (80.2)	9.6[e]
SEM	1.07	0.71	0.92
Flours			
Corn	82.3[a] (90.6)	90.8[a] (100.0)	8.5[a,b]
Wheat	62.7[d] (85.4)	73.4[f] (100.0)	10.7[a]
Rice	78.6[b] (88.0)	88.7[b] (99.3)	10.1[a]
Potato	70.7[c] (90.8)	77.6[d] (99.6)	6.9[b,c]
Soy	2.4[e] (29.3)	8.2[g] (100.0)	5.8[b,c]
Barley	69.9[c] (92.5)	75.2[e] (99.5)	5.3[c]
Sorghum	84.8[a] (100.0)	84.8[c] (100.0)	0.0[d]
SEM	0.82	0.33	0.82
Grain-based food products			
Macaroni	73.7[c] (95.5)	76.7[c] (99.4)	3.0[c]
Spaghetti	75.7[b] (91.5)	82.6[b] (99.9)	6.9[b]
Corn meal	83.9[a] (87.9)	92.3[a] (96.6)	8.4[a]
Rice bran	27.5[f] (100.0)	27.5[f] (100.0)	0.0[d]
Rolled oats	60.1[e] (100.0)	60.1[e] (100.0)	0.0[d]
Hominy grits	70.9[d] (100.0)	63.2[d] (89.1)	−7.7[e]
SEM	0.14	0.75	0.31
Reference substrates			
Corn starch	95.0[a] (93.6)	101.5[a] (100.0)	6.5[c]
Potato starch	34.5[c] (34.7)	64.0[b] (64.5)	29.5[a]
Amylomaize	42.5[b] (42.6)	59.8[c] (59.9)	17.3[b]
SEM	0.74	0.38	1.00

[1] IDS determined by subtracting (free glucose × 0.9) from (total glucose/original sample weight) present in supernate after 15 h of digestion. Numbers in parentheses are IDS concentrations expressed as a percentage of total starch as determined by the Thivend et al. (1972) method.

[2] TDS determined by subtracting [(total glucose/original sample weight) × 0.9] in the remaining sample from the percent total starch as determined by the Thivend et al. (1972) method. Numbers in parentheses are TDS concentrations expressed as a percentage of total starch as determined by the Thivend et al. (1972) method.

[3] Means in a column within substrate category not sharing superscript letters differ ($P < 0.05$).

sorghum and corn grains was quite strong, making hydrolysis and digestion more difficult.

TDS concentrations for cereals varied from a high ($P < 0.05$) for millet to a low ($P < 0.05$) for oats and barley. TDS concentrations were high, indicating continued digestion of starch by the microflora once it reached the large bowel. Moore et al. (1980) fed plant-based diets containing one of three grain sources (rice, oats or corn) to dogs. Total tract starch digestibility for the uncooked oat diet (93.8%) was lowest, intermediate for the uncooked corn diet (94.3%) and highest for the uncooked rice diet (98.6%). Our values were 92.6% for corn, 86.0% for white rice and 100.0% for oats. The dog diets in the Moore et al. (1980) study were extruded; this leads to increased susceptibility to amylase and greater starch digestion.

Cereal starch utilization by microflora in the large bowel varied. Millet had the highest ($P < 0.05$) and wheat had the lowest ($P < 0.05$) digestibility values. Of interest is how fermentable each substrate is if any appreciable amount reaches the large bowel. According to Hosney (1994), millet, sorghum and corn starch granules appear to be similar. In our study, their fermentative capabilities were similar, with millet having the highest value.

IDS concentrations for flours were lowest ($P < 0.05$) for soy, which has very low starch concentrations, but higher for wheat, barley, potato and brown rice. The highest ($P < 0.05$) concentrations were noted for corn and sorghum. IDS concentrations were high for most flours. With low TDF and RS concentrations in the flours, there appears to be less of a barrier to digestion of starch. Our wheat flour had a lower IDS concentration compared with all other flours with the exception of soy. (Snow and O'Dea 1981) assayed different flours (rice, barley, rye, white [bleached wheat flour] and wheat) to determine their in vitro starch hydrolysis capacity. After 30 min of hydrolysis, all flours were similar in percent starch hydrolyzed (mean 16.1%) except for wheat flour. The authors postulated that an amylase inhibitor may have affected the hydrolysis rate of the wheat flour. Also, wheat starch can contain nonstarch polysaccharides (Topping et al. 1993).

The flour that had the lowest ($P < 0.05$) TDS concentration was soy, whereas corn had the highest ($P < 0.05$) TDS value. All flours were virtually completely digested when TDS concentrations were compared. The flours used were primarily composed of RDS and SDS (mean 95.1%), and as a result of processing, most barriers to digestion are overcome. Murray et al. (1999) found that the starch component of canine diets containing high-starch flours as the main source of carbohydrate was nearly completely digested (>99%).

Starch utilization by microflora (percent TDS − percent IDS) varied numerically in the flour group from a low for sorghum to a high for wheat. Microflora fermented virtually all available remaining starch. Even though the wheat flour IDS concentration was relatively low, large bowel microflora appeared to ferment the remaining starch well. The wheat amylase inhibitor mentioned by Snow and O'Dea (1981) appeared to have no effect on the microflora once the wheat starch was placed in an environment simulating the large bowel.

For the grain-based food products, IDS was lowest for rice bran and highest ($P < 0.05$) for corn meal. Expressed as a percentage of TS, rice bran, rolled oat and hominy grit starches were completely digested at or before the ileum. Macaroni and spaghetti were well digested at the ileum (95.5 and 91.5% as a percentage of TS, respectively), but certain factors can reduce their susceptibility to amylolytic attack. Colonna et al. (1990) found that high-temperature drying of pasta may result in high levels of protein cross-linking, leading to a greater encapsulation of starch and thus decreasing its susceptibility to amylase. There also can be differences ($P < 0.05$) between the digestion of macaroni and spaghetti, as noted in our study. Granfeldt and Bjorck (1991) tested mac-

aroni and spaghetti glucose responses in 10 human subjects. Spaghetti resulted in a glycemic index score of 60.5, whereas macaroni resulted in a score of 78.0. Macaroni had a lower product thickness and a greater surface area that allowed easier access to amylase. Rolled oats were completely digested at the ileum. This corroborates the results of Heaton et al. (1988), where insulin responses were measured in humans fed certain cereal products (corn, wheat or rolled oats). Rolled oats resulted in a higher peak insulin response compared with oat flour. Decreasing the particle size of both corn and wheat seemed to increase digestion rate, but this was not the case for oat products.

When grain-based food products were compared, TDS concentrations were different ($P < 0.05$) among substrates. The highest ($P < 0.05$) TDS value was found for corn meal. Rice bran, rolled oats and hominy grits were completely digested proximal to the terminal ileum. The processing and cooking of rice bran and rolled oats affect their digestion. As mentioned previously, rolling oats appeared to disrupt the structural integrity of the grain, leaving it accessible to enzymatic attack. Processing of the rice kernel through a milling machine produces rice bran and polished rice. The compositions of rice and rice bran vary greatly due to this processing. Rice bran is composed of the aleurone layer and some parts of the endosperm and germ of the rice kernel after milling.

Starch utilization by microflora (percent TDS − percent IDS) again varied for the grain-based food products. Corn meal was highest ($P < 0.05$) compared with all other substrates. A larger percentage of starch was fermented in the large bowel for spaghetti compared with macaroni. This relates to the greater amount of starch escaping digestion in the small intestine, making spaghetti more efficacious if the goal is to supply the large bowel with more starch.

Of the reference substrates, IDS concentrations were lowest ($P < 0.05$) for potato starch, intermediate for amylomaize and highest ($P < 0.05$) for corn starch. High concentrations of RS in potato starch cause its digestion to be limited in the small intestine. Mathers et al. (1997) fed either a raw potato or corn starch diet to rats and found that the digestibility of the corn starch diet was 99% at the ileum, whereas only 28% of the potato starch diet was digested at the ileum. Native potato starch granules are composed of a B-type crystalline pattern. These granules exist as a layer of large blocklets that appear to confer resistance to enzymatic hydrolysis (Gallant et al. 1992). Amylomaize was more digestible than potato starch, possibly due to its lower concentration of RS.

TDS concentrations were lowest ($P < 0.05$) for amylomaize, intermediate for potato starch and highest ($P < 0.05$) for corn starch. Total tract digestibility of potato starch fed to rats at 240 g/kg of the diet was 80%, whereas corn starch at 240 g/kg was 100% (Mathers et al. 1997).

Starch utilization by microflora in the large bowel (percent TDS − percent IDS) was greatest ($P < 0.05$) for potato starch, pointing to its high fermentative capacity. Of interest is that although potato starch was lower in IDS, it was higher in TDS compared with amylomaize. Lajvardi et al. (1993) fed rats either a cooked potato starch, arrowroot starch, high amylose corn starch or raw potato starch diet. Raw potato starch was found to be the most fermentable starch of the four tested. Only raw potato starch was found to significantly prolong gastrointestinal transit time, possibly allowing this substrate a longer time to ferment in the large bowel.

In vitro experiment 2

OMD. This experiment was conducted to determine whether ileal fermentation events, independent of hydrolytic digestion events, affected the disappearance of OM for a widely divergent group of substrates. Although data were collected at 0-, 2.5-, 5- and 7.5-h time periods, only those collected at 7.5 h are reported because they were judged to be most relevant from a biological perspective (i.e., data at the 5- and 7.5-h time points were similar; 7.5 h is about the length of time chyme would be available to ileal microbes).

OMD of substrates is reported in **Table 5**. All substrate × time interactions were significant at $P < 0.05$. After correction for solubility, OMD was very low for the legume group as a whole. Solubilization of the substrates at the 0-h fermentation time was high (13–17%), resulting in lower corrected OMD values. Red kidney beans and black beans had the lowest ($P < 0.05$) OMD values of all legumes tested. Schweizer et al. (1990) found, using ileostomates fed a white kidney bean flake–containing diet, that ~10% of the bean starch was not absorbed from the small intestine. Tovar et al. (1992) postulated that the high amylose-to-amylopectin ratio, the physical insulation of starch by thick-walled cells and the presence of amylase inhibitors resulted in a reduction in digestibility of leguminous starches. These physicochemical characteristics of legumes act as direct inhibitors of α-amylase and, thus, starch breakdown.

Solubility of cereal grains in the in vitro medium generally was much lower than was the case for legumes. OMD was greatest ($P < 0.05$) for oats and lowest for corn. Again, the starch in certain cereals may be inaccessible due to the physical form of the cereal, resulting in digestion responses lower than expected (Englyst et al. 1992b). Cell walls and encapsulation of starch in a protein matrix of whole grains greatly affect digestion by reducing access of amylase to the starch itself.

Flours as a group were very digestible by ileal microbes. Potato and soy flours had extremely high solubility values. Rice and corn had the highest ($P < 0.05$) OMD values compared with other flours, and wheat flour had the lowest ($P < 0.05$). Interestingly, the two former flours had among the lowest solubility values. Wheat flour was two to three times lower in OMD than all other flours. Murray et al. (2000) also reported a low OMD at 7.5 h for wheat flour (1.9%). In this case, protein may encapsulate the starch granules, thereby reducing the digestibility of the starch (Annison and Topping 1994).

Of particular interest is how processing affects substrate disappearance. For example, barley flour was approximately five times more digestible compared with barley grain. Heaton et al. (1988) compared particle size effects of wheat, corn and oats on human in vivo plasma insulin responses and on in vitro rate of starch digestion by pancreatic amylase. Insulin responses were as follows: whole grains < cracked grains < coarse flour < fine flour. In vitro starch hydrolysis by amylase was faster for grains of smaller particle size. Larger food particles have a lower surface-to-volume ratio, and this might reduce the access of enzymes to the interior of the particle as might the presence of intact cell walls. Processing affects the physical nature of cereals, causing the disruption of the cell matrix and increasing starch digestion.

Grain-based food products ranged in OMD from a low for macaroni to a high for rolled oats. Knudsen et al. (1993) stated that oat bran, a rich source of dietary fiber containing β-glucans, is an easily fermentable energy source for microflora. The

TABLE 5

Zero hour solubilities, organic matter disappearance (OMD) and total short-chain fatty acid (SCFA) and lactate concentrations at 7.5 h of in vitro fermentation of selected food and feed ingredients using canine ileal fluid as inoculum[1]

Substrate	Solubility[2]	Corrected OMD[3] at 7.5 h	Total SCFA[4]	Lactate
	%		*mmol/g OM at 7.5 h*	
Legumes				
Black beans	14.2	1.8	7.24	0.04
Red kidney beans	15.2	0.2	7.28	0.05
Lentils	12.5	5.3	8.46	0.05
Navy beans	13.6	3.5	6.79	0.02
Black-eyed peas	15.4	3.4	8.35	0.06
Split peas	13.3	8.1	8.72	0.06
Northern beans	17.4	4.7	7.73	0.05
SEM	1.0	1.0	0.16	0.004
Cereal grains				
Barley	9.5	7.2	8.13	0.10
Corn	10.6	2.7	5.18	0.04
White rice	0.9	3.8	4.72	0.03
Brewer's rice	0.8	8.8	5.84	0.04
Brown rice	4.6	5.4	4.82	0.04
Wheat	2.8	8.9	6.54	0.01
Millet	2.7	15.4	5.48	0.04
Oats	9.0	19.0	7.87	0.07
Sorghum	0.0	8.4	4.70	0.02
SEM	1.1	1.1	0.17	0.01
Flours				
Corn	6.7	35.6	3.64	0.26
Wheat	18.0	11.7	4.59	0.01
Rice	5.9	37.1	2.93	0.26
Potato	58.5	21.7	10.10	0.51
Soy	30.2	25.2	6.55	0.10
Barley	13.6	33.3	4.66	0.30
Sorghum	5.9	28.0	2.45	0.17
SEM	0.9	0.9	0.12	0.01
Grain-based food products				
Macaroni	11.7	13.1	4.39	0.05
Spaghetti	9.8	18.3	4.75	0.07
Corn meal	2.3	22.4	2.27	0.14
Rice bran	13.3	22.0	3.70	0.14
Rolled oats	2.9	59.1	6.04	0.39
Hominy grits	0.0	17.6	2.08	0.07
SEM	1.1	1.1	0.11	0.01
Reference substrates				
Corn starch	0.0	32.5	3.58	0.25
Potato starch	0.0	3.9	0.64	0.02
Amylomaize	0.0	12.9	0.81	0.04
SEM	1.0	1.0	0.07	0.004

[1] The interaction of substrate × time was significant ($P < 0.05$) for OMD, total SCFA and lactate. The LSD values for separating substrate means are 2.95 × SEM.
[2] Solubility of substrates in in vitro medium at 0 h at 39°C.
[3] Values have been corrected for solubility.
[4] Total SCFA = acetate + propionate + butyrate.

process of rolling would make the fiber more accessible to microbial enzymes during the fermentation process.

OMD was greatest ($P < 0.05$) among reference substrates for corn starch, intermediate for amylomaize and lowest ($P < 0.05$) for potato starch. Potato starch contained the highest concentrations of RS, which influenced its digestion.

Data indicate that small intestinal bacteria ferment cereal grains and flours differently. The flour group had relatively high OMD values (mean 27.5%), whereas the cereal group had relatively low OMD values (mean 8.8%). This relates to the greater amount of processing that resulted in production of the flours. The cereal grain, as a result of this processing, loses TDF and RS components, as was found in this study. The lower concentrations of TDF and RS in flours lead to increased susceptibility to both enzymatic and microbial digestion.

Organic acid production. SCFA and lactate production data at the 7.5-h fermentation time are reported in **Table 5**. All substrate × time interactions were significant at $P < 0.05$.

Among leguminous substrates, the greatest ($P < 0.05$) total production of SCFA was for split peas, and the lowest was for navy beans. The high concentrations of total SCFA as a result of pea fermentation point to the ability of this substrate to be more rapidly fermented than beans. Bjorck and Siljestrom (1992) found that 90% of a pea product that reached the large bowel of a rat was fermented. The lower amylose content of peas could lead to higher fermentability by microflora, whether ileal or large bowel in origin. Tovar et al. (1992) reported that lentils contained more potentially available starch than did red kidney beans, corroborating the higher total SCFA concentration.

Lactate production was similar for all legumes. The largest amount of lactate produced was for split peas and black-eyed peas, whereas the lowest lactate production was for navy beans.

Among cereals, barley and oat fermentation resulted in the greatest ($P < 0.05$) total SCFA concentrations. The lowest ($P < 0.05$) total SCFA concentrations were for corn, white rice, brown rice and sorghum. Lactate production was greatest ($P < 0.05$) for barley compared with all other cereal grains.

Butyrate concentrations found in oats and barley (data not shown) were numerically higher compared with the cereal grains group (mean 0.66 mmol/g OM) as a whole. The presence of β-glucans, a soluble dietary fiber found in both oats and barley, may have stimulated butyrate production by ileal microflora.

Potato flour resulted in the highest ($P < 0.05$) total SCFA production compared with all other flours. Murray et al. (2000) also found that potato flour was numerically highest in total SCFA production when comparing six different flours incubated in inoculum containing ileal microorganisms. Processing was suggested as responsible for the increased susceptibility of potato flour to fermentation. The lowest ($P < 0.05$) total SCFA production was for sorghum and corn flours.

Flour fermentation resulted in generally higher lactate concentrations than for the other groups. Average lactate production for flours was 0.23 mmol/g OM. Zentek (1995) performed in vitro studies using canine ileal chyme to measure the fermentative capabilities of different substrates. He postulated that ileal fermentation of carbohydrates favored the growth of lactobacilli, which produce lactate as a major metabolic end-product. The high starch levels resulting from extensive processing of flours may have created a favorable environment for the selection of lactobacilli and subsequent production of lactate.

Rolled oats resulted in the highest ($P < 0.05$) total SCFA production compared with all other grain-based food products. Yiu et al. (1987) found raw oat starch to be highly digestible because of the disruption of starch granules due to oat processing. Rolling the oats leads to this disruption of the starch granules in the oat grain. Also, lactate production was highest ($P < 0.05$) for rolled oats, again relating to the high degree of processing and subsequent fermentative capacity of rolled oats.

Total SCFA production for the reference substrates was highest ($P < 0.05$) for corn starch compared with all other substrates. Zentek (1995), using canine ileal chyme, found that after 24 h of in vitro fermentation, corn starch resulted in higher concentrations of total SCFA compared with potato starch (7.11 versus 5.80 μmol/mL of fermentation broth, respectively). This is comparable to our SCFA and lactate data, in which corn starch had the highest ($P < 0.05$) concentrations and potato starch had the lowest. Although both are composed of starch, potato starch contains a much higher concentration of RS (66.9%) than corn starch (8.1%), possibly leading to a reduction in the fermentation of potato starch.

The response criteria used in this experiment to test differences among substrates included OMD and organic acid production. Organic acid production appears to be the more accurate criterion for the determination of fermentative activity, because OMD values are obtained using a gravimetric method with its attendant difficulties. High solubility values in relation to OMD do not appear to equate to high total SCFA concentrations. For example, the average solubility value for the flour group was 19.8% and total SCFA concentrations were only 4.99 mmol/g OM. The cereal grains group, on the other hand, averaged 4.5% solubility but had a total SCFA concentration of 5.92 mmol/g OM. Likewise, there were no statistically significant correlations between OMD and total SCFA concentrations (data not shown).

Of interest to many researchers is the potential fermentation of RS. Although starch is fermentable and believed to favor butyrate production, the data are not entirely consistent (Topping and Clifton 2000). Our data do not point to increased concentrations of butyrate from the fermentation of RS. For example, legumes had high concentrations of RS (mean 24.7%), whereas butyrate concentrations averaged 0.77 mmol/g OM. Flours, low in RS concentrations (mean 2.8%), had similar butyrate concentrations (mean 0.67 mmol/g OM) as the legume group (data not shown).

What is the contribution of ileal bacteria to starch disappearance compared with that resulting from any residual digestive enzymes present in ileal chyme? Using the same ileal in vitro model, Murray et al. (2000) found that fermenting substrates in the presence of sodium azide–treated ileal bacteria resulted in no total SCFA for the first 5 h and minimal amounts at 7.5 h. This points to the minimal effect of residual digestive enzymes on starch disappearance using this in vitro model.

In conclusion, starch and fiber fractions in foods and feeds affect starch digestion in the gastrointestinal tract as assessed using in vitro models. It should be noted that the emphasis of this work was the effect of starch and fiber fractions on intestinal microbial digestion. Gut motility, digestive enzymes and other aspects of gut function will affect digestion in vivo. Greater knowledge of the precise chemical composition and digestive capabilities of starch fractions in foods and feeds will allow for more precise dietary formulations for both humans and companion animals, with implications in both performance and health arenas.

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PubMed

Format: Abstract

J Anim Sci. 1999 Aug;77(8):2180-6.

Evaluation of selected high-starch flours as ingredients in canine diets.

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Author information

Abstract

Cereal grains represent 30 to 60% of the DM of many companion animal diets. Once incorporated into a diet, the starch component of these grains can provide an excellent source of ME. However, crystallinity and form of starch are variable and can cause incomplete digestion within the gastrointestinal tract. Diets fed in this experiment included one of six high-starch flours as the main source of carbohydrate. The flours originated from barley, corn, potato, rice, sorghum, and wheat. The diets were extruded and kibbled. Starch fraction concentrations of flours consisted of nearly 100% rapidly digestible starch (RDS) and slowly digestible starch (SDS) combined. Starch fraction concentrations of diets paralleled concentrations in flours. Flours varied widely in concentrations of CP, fat, starch, and total dietary fiber. Ileal OM and CP digestibilities were lowest for the potato flour treatment (74 and 64%, respectively). Ileal and total tract starch digestibilities were different (P<.05) among treatments; however, the starch component of all diets was nearly completely digested (>99%). Total tract digestibility of DM and OM was lowest for sorghum (80 and 84%, respectively) compared to all other diets. Crude protein digestibility was highest for corn (87%). Wet fecal weights tended (P<.08) to be greatest for dogs fed the barley treatment (175 g/d). However, dry fecal weights (dried at 55 degrees C) were greatest for dogs consuming the sorghum diet (51 g/d). Fecal scores were consistently greater (i.e., looser stools) for the barley treatment. Any of these flours could be used without negative effects on digestion at either the ileum or in the total tract. Fecal consistency data for dogs consuming the barley treatment indicate that diets containing large amounts (>50%) of barley may not be advantageous for dog owners who house their animals indoors for most of the day.

PMID: 10461997

[Indexed for MEDLINE]

MeSH terms, Substance

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Journal of
Animal Physiology and Animal Nutrition

DOI: 10.1111/j.1439-0396.2011.01203.x

ORIGINAL ARTICLE

Fibre analysis and fibre digestibility in pet foods – a comparison of total dietary fibre, neutral and acid detergent fibre and crude fibre*

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Keywords
carbohydrates, cat, dog, methods, nitrogen-free extract, fibre

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*Supported by Fundação de Amparo à Pesquisa do Estado de São Paulo, São Paulo, Brazil (FAPESP; process 03/07496-0 and 01/08639-3), and Mogiana Alimentos (Guabi), Campinas, Brazil.

Received: 19 June 2011;
accepted: 20 June 2011

Summary

Six dry dog foods and six dry cat foods with different carbohydrate sources were investigated in digestion trials. Food and faecal samples were analysed for CF, TDF and starch. In dogs, also neutral detergent fibre (aNDFom) and acid detergent fibre (ADFom) were analysed. N-free extract (NfE) was calculated for CF, and similarly for all other fibre analyses. Linear regressions were calculated between fibre intake and faecal fibre excretion. True digestibility was calculated from the regression coefficients [true digestibility in % = (1 − regression coefficient)*100], with the intercept of the equation representing excretion of material of non-food origin. Crude fibre analyses gave the lowest values, and TDF the highest, while ADFom and aNDFom were in between. Variation between diets was lowest in CF and highest in TDF. Total dietary fibre, aNDFom and ADFom in food were positively correlated. Crude fibre in food did not correlate with any other method. The NfE analogue for TDF was closest to the starch content. Methods of fibre analyses in faeces did not agree very well with each other. Crude fibre had the lowest apparent digestibility, followed by ADFom, TDF and aNDFom. For all fibre analyses, there was a significant correlation between fibre intake and faecal fibre excretion. True digestibility was close to zero for CF, with a high uniformity in both species. In dogs, true digestibility of aNDFom was 53%, of ADFom 26% and of TDF 37%; in cats, true digestibility of TDF was 31%. Except for CF, the intercept of the regression equations suggest that faecal excretion of some material of non-food origin is analysed as fibre. A combination of TDF and CF analyses might give good information on the content of total (TDF), unfermentable (CF) and partially fermentable fibre (TDF-CF) in pet foods.

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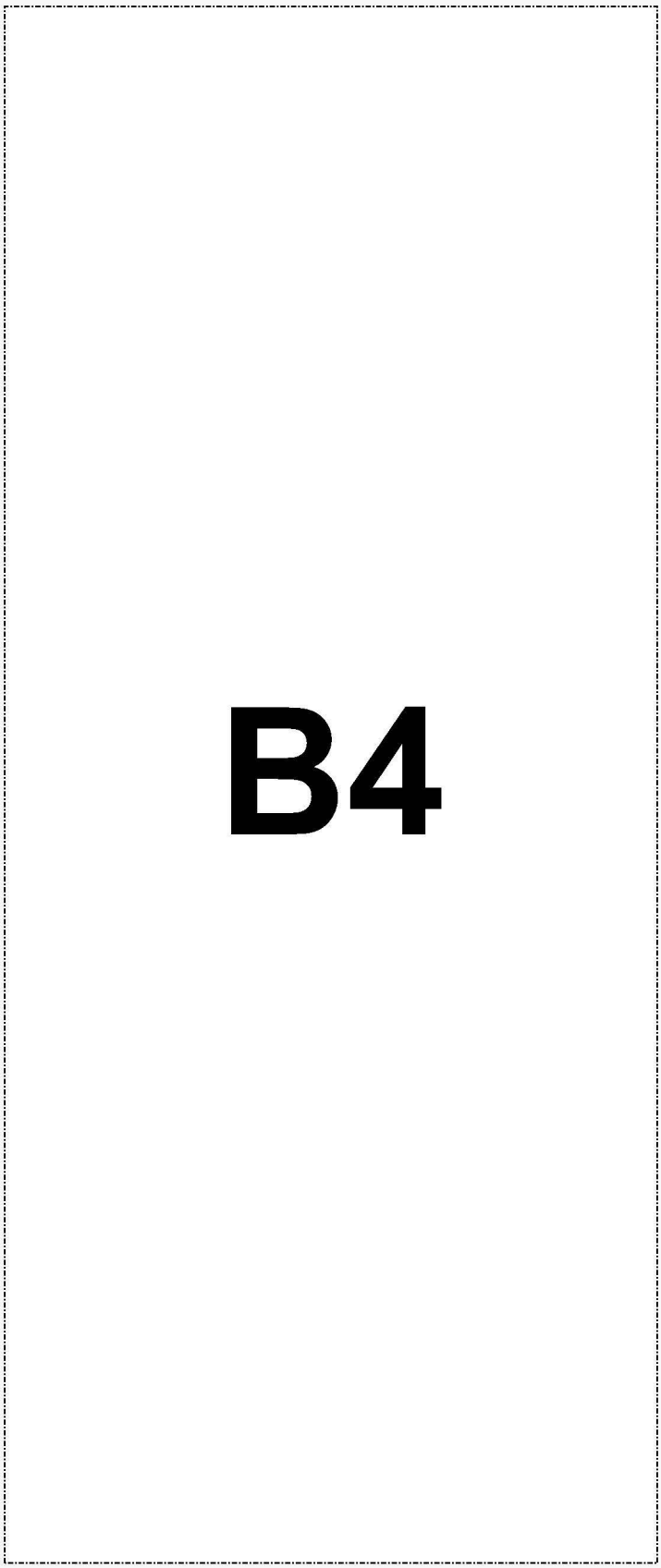

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Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997–2001)

Andrea J. Fascetti, VMD, PhD, DACVN, DACVIM; John R. Reed, DVM, MS, DACVIM;
Quinton R. Rogers, PhD, DACVN; Robert C. Backus, DVM, PhD

Objective—To determine signalment, history, clinical signs, blood and plasma taurine concentrations, electrocardiographic and echocardiographic findings, treatment, and outcome of dogs with low blood or plasma taurine concentrations and dilated cardiomyopathy (DCM).

Design—Retrospective study.

Animals—12 client-owned dogs with low blood or plasma taurine concentrations and DCM.

Procedure—Medical records were reviewed, and clinical data were obtained.

Results—All 12 dogs were being fed a commercial dry diet containing lamb meal, rice, or both as primary ingredients. Cardiac function and plasma taurine concentration improved with treatment and taurine supplementation. Seven of the 12 dogs that were still alive at the time of the study were receiving no cardiac medications except taurine.

Conclusions and Clinical Relevance—Results suggest that consumption of certain commercial diets may be associated with low blood or plasma taurine concentrations and DCM in dogs. Taurine supplementation may result in prolonged survival times in these dogs, which is not typical for dogs with DCM. Samples should be submitted for measurement of blood and plasma taurine concentrations in dogs with DCM, and taurine supplementation is recommended while results of these analyses are pending. (*J Am Vet Med Assoc* 2003;223:1137–1141)

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Assessment of protein and amino acid concentrations and labeling adequacy of commercial vegetarian diets formulated for dogs and cats

Kayo Kanakubo, BVSc; Andrea J. Fascetti, VMD, PhD; Jennifer A. Larsen, DVM, PhD

Objective—To determine measured crude protein (CP) and amino acid (AA) concentrations and assess labeling adequacy of vegetarian diets formulated for dogs and cats.

Design—Cross-sectional study.

Sample—13 dry and 11 canned vegetarian diets for dogs and cats.

Procedures—Concentrations of CP and AAs were determined for each diet. Values were compared with the Association of American Feed Control Officials (AAFCO) Dog and Cat Food Nutrient Profiles. Product labels were assessed for compliance with AAFCO regulations.

Results—CP concentration (dry-matter basis) ranged from 19.2% to 40.3% (median, 29.8%). Minimum CP concentrations for the specified species and life stage were met by 23 diets; the remaining diet passed appropriate AAFCO feeding trials. Six diets did not meet all AA minimums, compared with the AAFCO nutrient profiles. Of these 6 diets, 1 was below AAFCO minimum requirements in 4 AAs (leucine, methionine, methionine-cystine, and taurine), 2 were below in 3 AAs (methionine, methionine-cystine, and taurine), 2 were below in 2 AAs (lysine and tryptophan), and 1 was below in 1 AA (tryptophan). Only 3 and 8 diets (with and without a statement of calorie content as a requirement, respectively) were compliant with all pet food label regulations established by the AAFCO.

Conclusion and Clinical Relevance—Most diets assessed in this study were not compliant with AAFCO labeling regulations, and there were concerns regarding adequacy of AA content. Manufacturers should ensure regulatory compliance and nutritional adequacy of all diets, and pets fed commercially available vegetarian diets should be monitored and assessed routinely. (*J Am Vet Med Assoc* 2015;247:385–392)

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From this month's *AJVR*

Electrocardiogram reference intervals for clinically normal wild-born chimpanzees (*Pan troglodytes*)

Rebeca Atencia et al

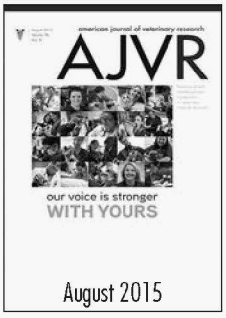
Objective—To generate reference intervals for ECG variables in clinically normal chimpanzees (*Pan troglodytes*).

Animals—100 clinically normal (51 young [< 10 years old] and 49 adult [≥ 10 years old]) wild-born chimpanzees.

Procedures—Electrocardiograms collected between 2009 and 2013 at the Tchimpounga Chimpanzee Rehabilitation Centre were assessed to determine heart rate, PR interval, QRS duration, QT interval, QRS axis, P axis, and T axis. Electrocardiographic characteristics for left ventricular hypertrophy (LVH) and morphology of the ST segment, T wave, and QRS complex were identified. Reference intervals for young and old animals were calculated as mean ± 1.96•SD for normally distributed data and as 5th to 95th percentiles for data not normally distributed. Differences between age groups were assessed by use of unpaired Student *t* tests.

Results—Reference intervals were generated for young and adult wild-born chimpanzees. Most animals had sinus rhythm with small or normal P wave morphology; 24 of 51 (47%) young chimpanzees and 30 of 49 (61%) adult chimpanzees had evidence of LVH as determined on the basis of criteria for humans.

Conclusions and Clinical Relevance—Cardiac disease has been implicated as the major cause of death in captive chimpanzees. Species-specific ECG reference intervals for chimpanzees may aid in the diagnosis and treatment of animals with, or at risk of developing, heart disease. Chimpanzees with ECG characteristics outside of these intervals should be considered for follow-up assessment and regular cardiac monitoring. (*Am J Vet Res* 2015;76:688–693)



August 2015

See the midmonth issues of *JAVMA* for the expanded table of contents for the *AJVR* or log on to avmajournals.avma.org for access to all the abstracts.

Taurine and Carnitine in Canine Cardiomyopathy

Article *in* Veterinary Clinics of North America Small Animal Practice · December 2006

DOI: 10.1016/j.cvsm.2006.08.010 · Source: PubMed

1 author:

Sherry L Sanderson
University of Georgia
26 PUBLICATIONS **309** CITATIONS

SEE PROFILE

Vet Clin Small Anim 36 (2006) 1325–1343
VETERINARY CLINICS
SMALL ANIMAL PRACTICE

Taurine and Carnitine in Canine Cardiomyopathy

Sherry Lynn Sanderson, DVM, PhD

Department of Physiology and Pharmacology, University of Georgia, College of Veterinary Medicine, 501 DW Brooks Drive, Athens, GA 30602, USA

Dilated cardiomyopathy (DCM) is one of the most common acquired cardiovascular diseases in dogs [1–4]. Although few studies of the prevalence of DCM in the overall population of dogs have been reported, estimates range from 0.5% to 1.1% [5,6]. Only degenerative valvular disease and, in some regions of the world, heartworm infection are more common causes of cardiac morbidity and mortality in dogs. DCM is seen most commonly in large and giant breeds of dogs, although its frequency seems to be increasing in medium-sized breeds, such as the English and American cocker spaniels [4–8]. It has been reported rarely in small and miniature breeds of dogs [9].

DCM is particularly challenging to veterinarians because the cause is often unknown and can vary among dog breeds [10]. Because most cases of DCM in dogs are classified as idiopathic, most therapies can be classified as "Band-Aid therapies" that palliate the effects of this disease for a short duration but do little to address the primary disease process. Therefore, DCM is almost always a progressive disease, and most dogs will eventually succumb to their disease. Survival times in dogs with DCM are variable and can be influenced by several factors, including breed. However, the prognosis for survival of dogs with DCM remains poor, with reported survival rates of 17.5% at 1 year and 7.5% at 2 years [11–13]. Until recently, reported cases of DCM reversal in dogs were very rare.

With advancements in echocardiology, diagnostic capabilities in canine cardiology have improved dramatically over the past 2 decades. Therapeutic advances have made surprisingly little progress. Symptomatic treatment is the standard care and outcome remains poor.

Recently, more promising therapies for dogs with DCM have resulted from a clearer understanding of the importance of biochemistry and nutrition in managing this disease. Nutrition is now widely accepted as an important adjunct to medical therapy in dogs with DCM.

E-mail address: sanderso@vet.uga.edu

0195-5616/06/$ – see front matter
doi:10.1016/j.cvsm.2006.08.010

vetsmall.theclinics.com

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B6

Date Performed: 09/11/2018 09:48 PM

Patient Info:
ID: B6
Name: B6
Owner: B6
Provider: 26

Species: Canine
Breed: Great Dane
Birthdate: B6
Sex: MN

Clinic:
B6

IVLS-20180911_213512_74864.pdf

GLU	B6	74-143 mg/dL	B6
CREA		0.5-1.8 mg/dL	
BUN		7-27 mg/dL	
BUN/CREA			
PHOS		2.5-6.8 mg/dL	
CA		7.9-12.0 mg/dL	
TP		5.2-8.2 g/dL	
ALB		2.3-4.0 g/dL	
GLOB		2.5-4.5 g/dL	
ALB/GLOB			
ALT		10-125 U/L	
ALKP		23-212 U/L	
GGT		0-11 U/L	
TBIL		0.0-0.9 mg/dL	
CHOL		110-320 mg/dL	
AMYL		500-1500 U/L	
LIPA		200-1800 U/L	
Na		144-160 mmol/L	
K		3.5-5.8 mmol/L	
Na/K			
Cl		109-122 mmol/L	
Osm Calc		m	
RBC		5.65-8.87 M/µL	
HCT		37.3-61.7 %	
HGB		13.1-20.5 g/dL	

MCV		61.6-73.5fL
MCH		21.2-25.9pg
MCHC		32.0-37.9g/dL
RDW		13.6-21.7%
%RETIC		%
RETIC		10.0-110.0K/µL
RETIC-HGB		22.3-29.6pg
WBC		5.05-16.76K/µL
%NEU		%
%LYM		%
%MONO		%
%EOS		%
%BASO		%
NEU		2.95-11.64K/µL
LYM		1.05-5.10K/µL
MONO		0.16-1.12K/µL
EOS		0.06-1.23K/µL
BASO		0.00-0.10K/µL
nRBC		
PLT		148-484K/µL
MPV		8.7-13.2fL
PDW		9.1-19.4fL
PCT		0.14-0.46%

B6

B6

From: B6
To: Jones, Jennifer L; Andrea Fascetti
CC: Guag, Jake
Sent: 4/1/2019 11:34:02 PM
Subject: Re: Heads up: Vet-LIRN (FDA) shipped 800.267 samples

Hi Dr. Jones,

I will correct the mislabels and get back to you tomorrow.

Thanks,
B6

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Sent: Monday, April 1, 2019 4:30 AM
To: Andrea Fascetti; B6
Cc: Guag, Jake
Subject: RE: Heads up: Vet-LIRN (FDA) shipped 800.267 samples

Good morning Andrea and B6
I was reviewing the results and needed some clarification of the results for 2 cases. The results you sent show plasma amino acid values for cv-09 but not cv-14. However, I did not send any plasma for cv-09. I did send plasma for cv-14 (attached inventory sheet). Can you please clarify which set of plasma values belong to cv-14?
Thank you in advance and have a wonderful week,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Andrea Fascetti <ajfascetti@ucdavis.edu>
Sent: Saturday, March 23, 2019 1:30 PM
To: B6
Cc: Guag, Jake <Jake.Guag@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Re: Heads up: Vet-LIRN (FDA) shipped 800.267 samples

Hello Jen and Jake- Please see attached file with your results. Thanks for the heads-up on the species. We have to know in case someone in the lab comes in contact with the blood (especially through a cut). Our occupational health and safety folks then have us file a report and follow up on those cases to ensure vaccination status etc.

We will bill according to your comments below.

Have a nice weekend.

Andrea

On Mar 21, 2019, at 10:51 AM, B6 wrote:

Hi Jake,

May you help to confirm the samples are for dogs or cats? I could not find the information

Thanks,
B6

From: Guag, Jake <Jake.Guag@fda.hhs.gov>
Sent: Tuesday, March 12, 2019 8:53 AM
To: B6
Cc: Jones, Jennifer L
Subject: Heads up: Vet-LIRN (FDA) shipped 800.267 samples

Hi Joshua,
Hope you are well. We shipped 800.267 samples on dry ice to you.
Box#1 has urine samples its tracking number is 1ZA4420T0194520315 with UPS.
Box#2 has whole blood and serum samples and its tracking number is 1ZA4420T0192121929 with UPS. Both boxes are expected to arrive your location tomorrow (Mar. 13th, 2019)

Please charge the urine sample analysis under AA contract.
Please provide invoice for the blood and serum analysis.

Thank you
Jake

Jake Guag, MPH, CPH
Biologist (FDA/CVM/OR/Vet-LIRN)
8401 Muirkirk Road
Laurel, Maryland 20708
Email: jake.guag@fda.hhs.gov
Tel: 240-402-0917

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
(508) 839-5395

All Medical Records

Client:
Address: B6

Patient: B6
Breed: Doberman Pinscher
DOB: B6

Species: Canine
Sex: Female (Spayed)

Home Phone:
Work Phone:
Cell Phone: B6

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
intestinal foreign material, vomiting

SOAP Text Mar 8 2015 7:14AM B6

3/8/2015 7:33:38 AM NEW VISIT (ER)
Doctor: B6
Presenting complaint: vomit x 10 this AM

B6

Objective (O)

B6

Client: B6
Patient:

B6

Diagnostics Completed:
AXR (2 view): foreign material (midabdomen on lateral, overlapping L3 on VD), no obstructive pattern, stomach is not distended
NOVA:
PCV/TS:

Assessment (A)
A1: GI foreign object - r/o unobstructive v obstructive
A2: B6

Plan (P)
P1:
P2:
P3:
P4:
P5:
P6:

B6

Communication Summary: Discussed presence of foreign object in intestines. Hopefully this can move along with hydration. B6

B6

Additional requests submitted: none

Estimate given: $ B6

3/8/2015 8:52:32 AM
Prescribed -
Instructions

B6

3/8/2015 8:52:50 AM
Prescribed -
Instructions

B6

TS (FHSA): 6.8
PCV **: 54

SOAP Text Mar 8 2015 10:01AM B6

3/8/2015 B6, DVM
Presenting complaint: vomit x 10 this AM

B6

Client: B6
Patient:

Visit is a referral: No

B6

Diagnostics Completed:

B6

Assessment (A)
A1:
A2: B6

Plan (P)
P1:
P2:
P3:
P4:
P5:
P6:
P7:

B6

B6

Prescribed -
Instructions - B6
B6

Prescribed -
Instructions B6
BW 31 kg, AR5 - Expires: 3/8/2016 6 Refills

SOAP Text Mar 9 2015 1:13PM - B6

2 yo SF Dobberman Pinscher was presented early yesterday morning Sunday 03/08/2015 for severe acute vomiting.

Vomitted once overnight and given B6 ; no vomiting since. Urinating well; no defecation yet. Still NPO.

B6

B6

B6

SOAP Text Mar 10 2015 1:55PM B6

2 yo SF Dobberman Pinscher was presented Sunday 03/08/2015 for severe acute vomiting. Vomited once since admit. Started refeeding last night and has been eating ravenously.

S/O: overall unchanged with no significant findngs

B6

B6

Initial Complaint:

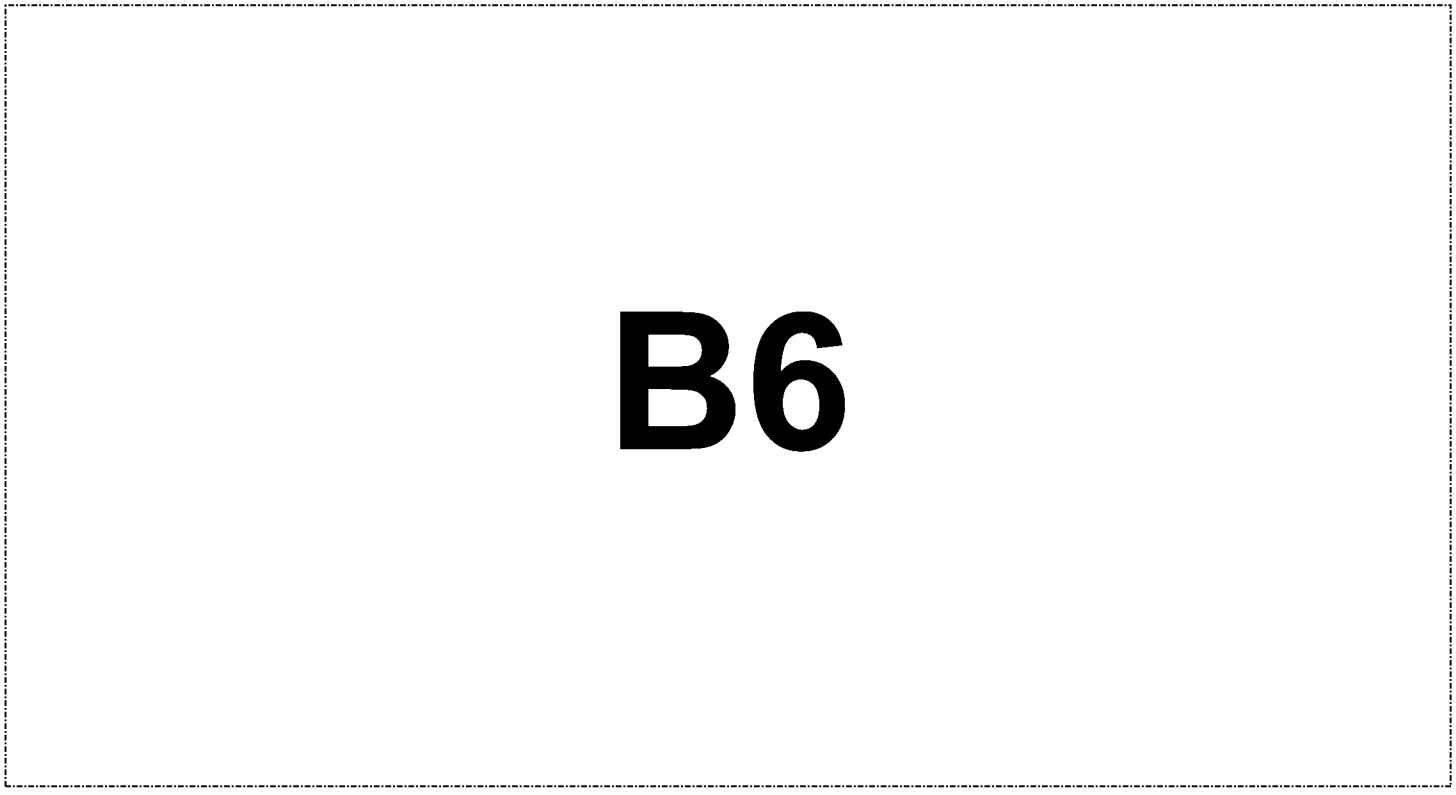
Emergency

Client: B6
Patient: B6

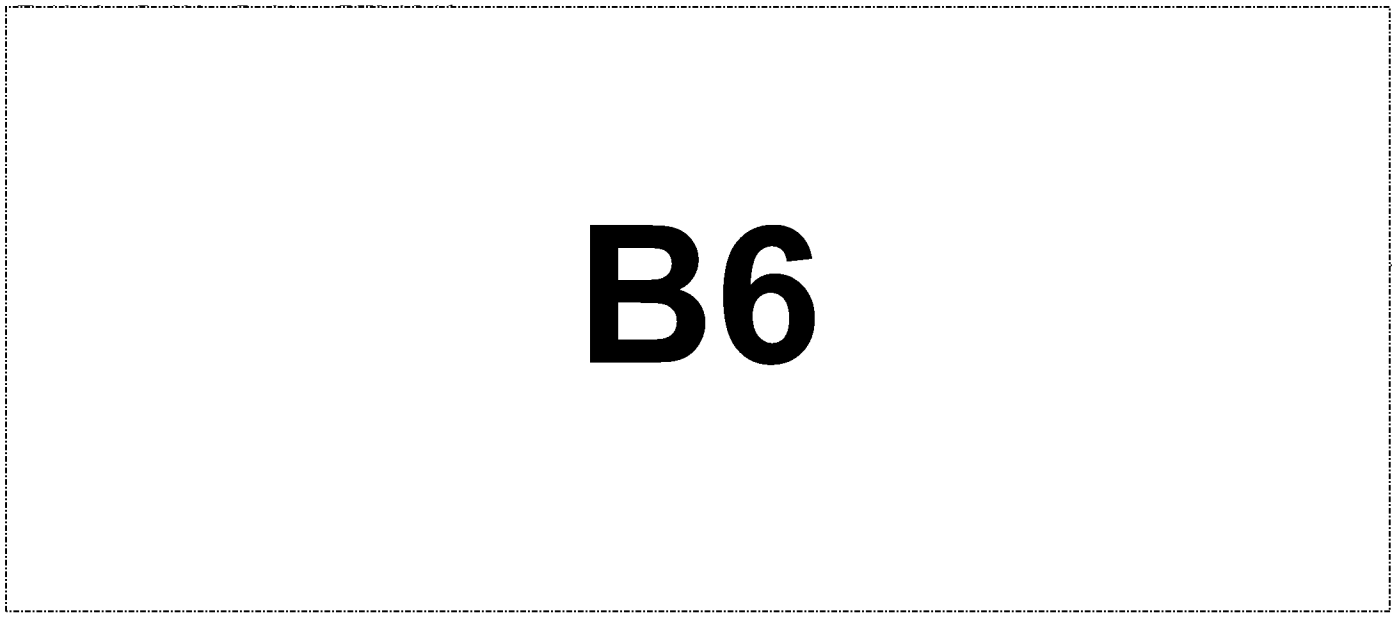
SOAP Text Sep 21 2015 5:20PM - B6

9/21/2015 5:20:18 PM NEW VISIT (ER)
Doctor:
Student: B6

Presenting complaint: Left carpal pad laceration



Objective (O)



Client: B6
Patient:

Assessment (A)
A1: Carpal pad lacerations
A2: Hx of HBC
A3: Hx of fever of unknown origin
A4: Hx of intestinal FB

Plan (P)
1.
2.
3.
4.

B6

Communication Summary:

B6

Estimate given: $ Deposit collected: $

9/21/2015 7:06:22 PM
Prescribed - B6
Instructions

Initial Complaint:
New - B6 - DCM protocol

Disposition/Recommendations

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
(508) 839-5395

Client:	B6
Veterinarian:	
Patient ID:	314074
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Doberman Pinscher
Sex:	Female (Spayed)
Age:	B6 Years Old

Lab Results Report

Nova Full Panel-ICU **3/8/2015 8:55:00 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
nCA	B6	0 - 0	mmol/L
FiO2		0 - 0	%
BEb		0 - 0	mmol/L
TCO2 (POC)		0 - 0	mmol/L
GAP		0 - 0	mmol/L
BEecf		0 - 0	mmol/L
CREAT (POC)		0.2 - 2.1	mg/dL
NOVA SAMPLE		0 - 0	
MG (POC)		0.1 - 0.4	mmol/L
CA/MG		0 - 0	mol/mol
HCT (POC)		38 - 48	%
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
SO2%		94 - 100	%
nMG		0 - 0	mmol/L
CL(POC)		109 - 120	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
K (POC)		3.6 - 4.8	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
HB (POC)		12.6 - 16	g/dL
A		0 - 0	mmIg

Client:
Patient: B6

NA (POC)	B6	140 - 154	mmol/L
PO2		80 - 100	mmHg
PCO2		36 - 44	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

Nova Full Panel-ICU **3/8/2015 9:01:30 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

Nova Full Panel-ICU **3/9/2015 9:50:00 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
MCH(ADVIA)	B6	21.3 - 25.9	pg
MCHC(ADVIA)		31.9 - 34.3	g/dL
WBC (ADVIA)		4.4 - 15.1	K/uL
MCV(ADVIA)		64.5 - 77.5	fL
MPV (ADVIA)		8.29 - 13.2	fl
RDW (ADVIA)		11.9 - 15.2	
HCT(ADVIA)		39 - 55	%
PLT(ADVIA)		173 - 486	K/uL
RBC(ADVIA)		5.8 - 8.5	M/uL
HGB(ADVIA)		13.3 - 20.5	g/dL

Nova Full Panel-ICU **3/9/2015 9:50:00 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
CALCIUM2	B6	9.4 - 11.3	mg/dL
D.BILIRUBIN		0 - 0.1	mg/dL
T BILIRUBIN		0.1 - 0.3	mg/dL
NA/K		29 - 40	
SODIUM		140 - 150	mEq/L
CREATININE		0.6 - 2	mg/dL
ALK PHOS		12 - 127	U/L
GLOBULINS		2.3 - 4.2	g/dL
T. PROTEIN		5.5 - 7.8	g/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
I BILIRUBIN		0 - 0.2	mg/dL
ALT		14 - 86	U/L
OSMOLALITY (CALCULATED)		291 - 315	mmol/L
CHLORIDE		106 - 116	mEq/L

Client:
Patient: B6

AST	B6	9 - 54	U/L
UREA		8 - 30	mg/dL
POTASSIUM		3.7 - 5.4	mEq/L
CHOLESTEROL		82 - 355	mg/dL
GLUCOSE		67 - 135	mg/dL
ALBUMIN		2.8 - 4	g/dL
A/G RATIO		0.7 - 1.6	

Nova Full Panel-ICU **3/9/2015 9:50:00 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
EOS%	B6	0 - 16	%
RBC MORPHOLOGY		0 - 0	
No morphologic abnormalities			
SEGS%		43 - 86	%
LYMPHS (ABS)ADVIA		1 - 4.8	K/uL
MONOS (ABS)ADVIA		0.1 - 1.5	K/uL
SEGS (AB)ADVIA		2.8 - 11.5	K/ul
EOS (ABS)ADVIA		0 - 1.4	K/uL
LYMPHS%		7 - 47	%
MONOS%		1 - 15	%
WBC MORPHOLOGY		0 - 0	
No Morphologic Abnormalities			

Nova Full Panel-ICU **3/9/2015 9:50:00 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
VWF:AG	B6	0 - 0	%

Nova Full Panel-ICU **3/9/2015 10:22:42 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

B6

stringsoft

Printed Tuesday, October 09, 2018

Client: B6
Patient:

Emergency Form: PACS

TUFTS UNIVERSITY
Foster Hospital for Small Animals
Hospital for Large Animals
200 Westboro Road,
N. Grafton, MA 01536

EMERGENCY SERVICES

This form must be submitted to accounting within 24 hours of overtime incurred for treatment of emergency cases to ensure timely entry on bill. Emergency fees will not be posted to patient's account. **This form must be completed in full or it will not be accepted.**

Doctor or Technician name: B6, DVM

Client name: B6 Animal name: B6

Date of services 8 Mar 2015 Case #: ~~306953~~ 314074 Client #:

TECHNICIAN

S1X2 Surgery
M8X2 Ophthalmology
A1X2 Anesthesia
M1D9 Intensive Care
R1X2 Radiology

Procedure:

Overtime hours incurred:

Time paged/called:

Arrived:

Start surgery/procedure:

End surgery/procedure:

Left building:

CLINICIAN Equine Farm Small

SAH

Surgery	Anesthesia
S1X3 Surgeon	A1X3 Anesthesiologist
S1X3 Resident	A1X3 Resident

LAH

Surgery	Anesthesia
S1X5 Surgeon	A1X6 Anesthesiologist<4hrs
S1XA Surgeon w/sx<4hrs	A1X7 Anesthesiologist>4hrs
S1XB Surgeon w/sx>4hrs	A1X3 Resident
S1X3 Resident	

LAH & SAH

Medicine	Pathology
M1X1 Resident	P1X1 Pathologist
M1X4 Clinician < 4 hrs	P1X1 Resident
M1X5 Clinician > 4 hrs	G1X1 Ambulatory

RADIOLOGY Equine Farm X Small

R1X5 ER Radiologist:
R1X1 ER Resident:
R1X3 Celiogram:
R1X4 Cysto/Urethogram:
R1X6 Myelogram:
R1X7 Ultrasound:
R1X8 Intrav/Urogram (IVU):
R1X9 Upper Gastro-I/G (L):

Ophthalmology Equine Farm Small

M8X4 Ophthalmologist 1 hr:
M8X5 Ophthalmologist 2 hrs:
M8X6 Ophthalmologist 3 hrs:
M8X7 Ophthalmologist 4 hrs:

X R1XH Radiologist (PACS)

B6

B6

Supervisor Signature

Print Name

Form #255 C (Rev. 12/11/12) **WHITE-Accounting** **YELLOW-Payroll** **PINK-Employee**

Client: B6
Patient:

Diet history 10-2-18

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet.

Pet's name B6 Owner's name B6 Today's date 10/02/18

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)

Example Poor _____ Excellent

Poor _____ Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
☐ Seems to prefer different foods than usual ☐ Other: _____

3. Over the last few weeks, has your pet (check one):
☐ Lost weight ☐ Gained weight ☒ Stayed about the same weight ☐ Don't know

4. Please list below ALL pet foods, people food, treats, snacks, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

Food (include specific product and flavor) **Form** **Amount** **How often?** **Fed since**

Examples are shown in the table – please provide enough detail that we could go do the store and buy the exact same food

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2015*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
Taste of the Wild	dry	1 cup	3x day	Nov 2013
Purina Pro Weight manage.	dry	1 cup	3x day	Sep 2018
various veggies (fresh)	treat		daily	Nov 2013
K9 Granola Factory	treat	5-10	daily	Nov 2013
Raw marrow Bones	treat	1	1x week	2015

*Any additional diet information can be listed on the back of this sheet.

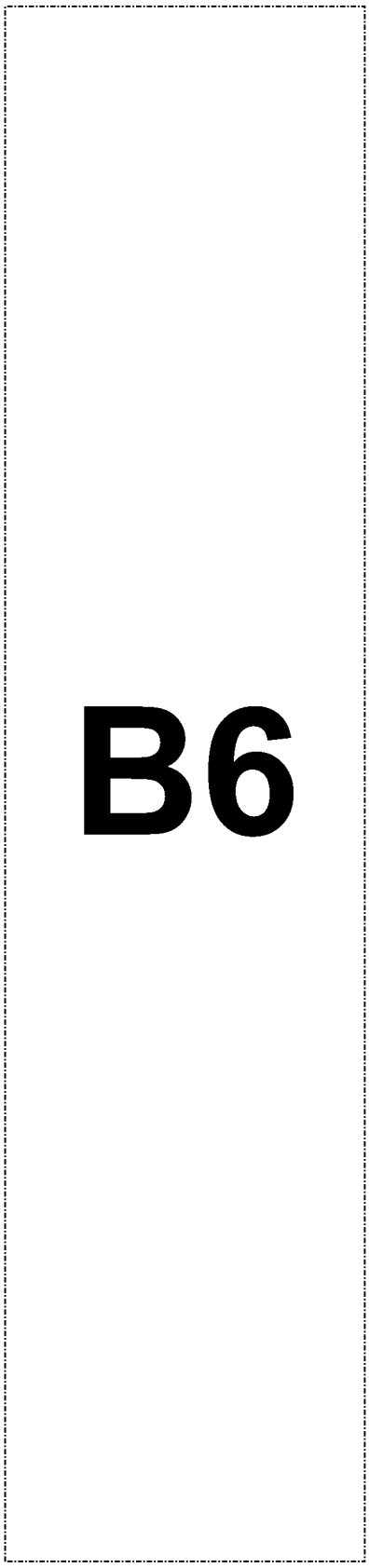
5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☒ No		
Carnitine	☐ Yes ☒ No		
Antioxidants	☐ Yes ☒ No		
Multivitamin	☐ Yes ☒ No		
Fish oil	☐ Yes ☒ No		
Coenzyme Q10	☐ Yes ☒ No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

6. How do you administer pills to your pet?
☐ I do not give any medications
☐ I put them directly in my pet's mouth without food
☒ I put them in my pet's dog/cat food
☐ I put them in a Pill Pocket or similar product
☐ I put them in foods (list foods): _____

Vitals Results

3/8/2015 7:00:15 AM	Nursing note
3/8/2015 8:04:09 AM	Temperature (F)
3/8/2015 8:04:41 AM	Heart Rate (/min)
3/8/2015 8:04:59 AM	Respiratory Rate
3/8/2015 8:05:10 AM	Weight (kg)
3/8/2015 9:01:51 AM	Notes
3/8/2015 9:02:21 AM	Quantify IV fluids (mls)
3/8/2015 9:05:28 AM	Eliminations
3/8/2015 9:08:07 AM	Respiratory Rate
3/8/2015 9:08:24 AM	Heart Rate (/min)
3/8/2015 1:14:46 PM	Respiratory Rate
3/8/2015 1:14:56 PM	Quantify IV fluids (mls)
3/8/2015 1:15:08 PM	Eliminations
3/8/2015 3:03:56 PM	Heart Rate (/min)
3/8/2015 5:10:06 PM	Quantify IV fluids (mls)
3/8/2015 5:10:59 PM	Respiratory Rate
3/8/2015 5:16:36 PM	Eliminations
3/8/2015 7:53:39 PM	Temperature (F)
3/8/2015 9:14:21 PM	Quantify IV fluids (mls)
3/8/2015 9:26:23 PM	Eliminations
3/8/2015 9:28:24 PM	Nursing note
3/8/2015 9:34:23 PM	Respiratory Rate
3/8/2015 9:34:35 PM	Heart Rate (/min)
3/8/2015 11:25:05 PM	Cage or Walk notes
3/9/2015 12:41:08 AM	Cage or Walk notes
3/9/2015 1:21:29 AM	Quantify IV fluids (mls)
3/9/2015 1:21:47 AM	Eliminations
3/9/2015 1:22:15 AM	Cage or Walk notes
3/9/2015 1:24:43 AM	Respiratory Rate
3/9/2015 4:31:18 AM	Heart Rate (/min)
3/9/2015 5:42:34 AM	Respiratory Rate
3/9/2015 5:51:30 AM	Quantify IV fluids (mls)
3/9/2015 5:51:40 AM	Eliminations
3/9/2015 8:26:27 AM	Eliminations
3/9/2015 11:56:11 AM	Temperature (F)
3/9/2015 11:56:23 AM	Heart Rate (/min)
3/9/2015 11:56:50 AM	Quantify IV fluids (mls)
3/9/2015 11:57:02 AM	Respiratory Rate



Client: B6
Patient:

Vitals Results

3/9/2015 1:27:57 PM	Eliminations
3/9/2015 3:32:11 PM	Quantify IV fluids (mls)
3/9/2015 3:35:18 PM	Respiratory Rate
3/9/2015 3:35:30 PM	Heart Rate (/min)
3/9/2015 3:37:40 PM	Temperature (F)
3/9/2015 5:27:01 PM	Eliminations
3/9/2015 7:04:35 PM	Eliminations
3/9/2015 7:07:59 PM	Weight (kg)
3/9/2015 7:08:08 PM	Temperature (F)
3/9/2015 7:08:44 PM	Quantify IV fluids (mls)
3/9/2015 7:14:28 PM	Heart Rate (/min)
3/9/2015 7:14:36 PM	Respiratory Rate
3/9/2015 9:09:44 PM	Amount eaten
3/9/2015 11:42:29 PM	Heart Rate (/min)
3/9/2015 11:42:36 PM	Respiratory Rate
3/9/2015 11:42:45 PM	Eliminations
3/9/2015 11:43:13 PM	Quantify IV fluids (mls)
3/10/2015 3:38:41 AM	Quantify IV fluids (mls)
3/10/2015 3:43:03 AM	Heart Rate (/min)
3/10/2015 3:43:09 AM	Respiratory Rate
3/10/2015 3:43:19 AM	Eliminations
3/10/2015 5:09:16 AM	Amount eaten
3/10/2015 7:01:03 AM	Heart Rate (/min)
3/10/2015 7:01:09 AM	Weight (kg)
3/10/2015 7:01:19 AM	Respiratory Rate
3/10/2015 7:01:25 AM	Temperature (F)
3/10/2015 7:01:36 AM	Eliminations
3/10/2015 7:02:01 AM	Quantify IV fluids (mls)
3/10/2015 11:38:03 AM	Heart Rate (/min)
3/10/2015 11:39:59 AM	Respiratory Rate
3/10/2015 11:40:05 AM	Quantify IV fluids (mls)
3/10/2015 11:40:13 AM	Eliminations
3/10/2015 1:43:47 PM	Amount eaten
9/21/2015 5:20:19 PM	Heart Rate (/min)
9/21/2015 5:20:20 PM	Temperature (F)
9/21/2015 5:20:21 PM	Respiratory Rate
9/21/2015 5:20:22 PM	Weight (kg)
10/2/2018 3:58:13 PM	Weight (kg)

B6

Patient History

03/08/2015 06:47 AM	Purchase
03/08/2015 07:00 AM	Vitals
03/08/2015 07:51 AM	UserForm
03/08/2015 07:54 AM	Treatment
03/08/2015 07:54 AM	Purchase
03/08/2015 08:03 AM	UserForm
03/08/2015 08:04 AM	Treatment
03/08/2015 08:04 AM	Vitals
03/08/2015 08:04 AM	Vitals
03/08/2015 08:04 AM	Vitals
03/08/2015 08:05 AM	Vitals
03/08/2015 08:08 AM	UserForm
03/08/2015 08:10 AM	Purchase
03/08/2015 08:55 AM	Purchase
03/08/2015 08:59 AM	Purchase
03/08/2015 08:59 AM	Purchase
03/08/2015 09:01 AM	Labwork
03/08/2015 09:01 AM	Vitals
03/08/2015 09:02 AM	Treatment
03/08/2015 09:02 AM	Treatment
03/08/2015 09:02 AM	Vitals
03/08/2015 09:05 AM	Purchase
03/08/2015 09:05 AM	Purchase
03/08/2015 09:05 AM	Treatment
03/08/2015 09:05 AM	Vitals
03/08/2015 09:07 AM	Prescription
03/08/2015 09:08 AM	Treatment
03/08/2015 09:08 AM	Treatment
03/08/2015 09:08 AM	Vitals
03/08/2015 09:08 AM	Purchase
03/08/2015 09:08 AM	Treatment
03/08/2015 09:08 AM	Vitals
03/08/2015 09:09 AM	Prescription
03/08/2015 09:18 AM	Treatment
03/08/2015 09:50 AM	Purchase
03/08/2015 09:51 AM	Purchase
03/08/2015 01:07 PM	Treatment
03/08/2015 01:07 PM	Treatment
03/08/2015 01:14 PM	Treatment
03/08/2015 01:14 PM	Vitals
03/08/2015 01:14 PM	Treatment
03/08/2015 01:14 PM	Vitals
03/08/2015 01:15 PM	Treatment
03/08/2015 01:15 PM	Vitals

B6

Patient History

03/08/2015 03:03 PM	Treatment
03/08/2015 03:03 PM	Vitals
03/08/2015 05:10 PM	Treatment
03/08/2015 05:10 PM	Vitals
03/08/2015 05:10 PM	Treatment
03/08/2015 05:10 PM	Vitals
03/08/2015 05:11 PM	Treatment
03/08/2015 05:16 PM	Treatment
03/08/2015 05:16 PM	Treatment
03/08/2015 05:16 PM	Vitals
03/08/2015 07:53 PM	Treatment
03/08/2015 07:53 PM	Vitals
03/08/2015 09:13 PM	Purchase
03/08/2015 09:14 PM	Treatment
03/08/2015 09:14 PM	Vitals
03/08/2015 09:26 PM	Treatment
03/08/2015 09:26 PM	Treatment
03/08/2015 09:26 PM	Treatment
03/08/2015 09:26 PM	Vitals
03/08/2015 09:28 PM	Vitals
03/08/2015 09:34 PM	Treatment
03/08/2015 09:34 PM	Vitals
03/08/2015 09:34 PM	Treatment
03/08/2015 09:34 PM	Vitals
03/08/2015 11:25 PM	Vitals
03/09/2015 12:41 AM	Vitals
03/09/2015 01:21 AM	Treatment
03/09/2015 01:21 AM	Vitals
03/09/2015 01:21 AM	Treatment
03/09/2015 01:21 AM	Vitals
03/09/2015 01:22 AM	Treatment
03/09/2015 01:22 AM	Treatment
03/09/2015 01:22 AM	Vitals
03/09/2015 01:24 AM	Treatment
03/09/2015 01:24 AM	Vitals
03/09/2015 01:33 AM	Treatment
03/09/2015 01:36 AM	Treatment
03/09/2015 01:39 AM	Treatment
03/09/2015 04:31 AM	Treatment
03/09/2015 04:31 AM	Vitals
03/09/2015 05:39 AM	Treatment
03/09/2015 05:39 AM	Treatment
03/09/2015 05:42 AM	Treatment
03/09/2015 05:42 AM	Vitals
03/09/2015 05:51 AM	Treatment

B6

Client: B6
Patient:

Patient History

03/09/2015 05:51 AM	Vitals
03/09/2015 05:51 AM	Treatment
03/09/2015 05:51 AM	Vitals
03/09/2015 08:26 AM	Vitals
03/09/2015 09:10 AM	UserForm
03/09/2015 09:11 AM	Purchase
03/09/2015 09:11 AM	Purchase
03/09/2015 09:42 AM	Purchase
03/09/2015 09:44 AM	Treatment
03/09/2015 09:49 AM	Purchase
03/09/2015 09:49 AM	Purchase
03/09/2015 09:49 AM	Purchase
03/09/2015 10:22 AM	Labwork
03/09/2015 10:22 AM	Treatment
03/09/2015 10:39 AM	Prescription
03/09/2015 10:39 AM	Prescription
03/09/2015 10:40 AM	Purchase
03/09/2015 10:49 AM	Purchase
03/09/2015 11:40 AM	Treatment
03/09/2015 11:55 AM	Treatment
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Vitals
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Vitals
03/09/2015 11:56 AM	Treatment
03/09/2015 11:56 AM	Vitals
03/09/2015 11:57 AM	Treatment
03/09/2015 11:57 AM	Vitals
03/09/2015 01:27 PM	Treatment
03/09/2015 01:27 PM	Vitals
03/09/2015 02:06 PM	Purchase
03/09/2015 03:32 PM	Treatment
03/09/2015 03:32 PM	Vitals
03/09/2015 03:34 PM	Treatment
03/09/2015 03:35 PM	Treatment
03/09/2015 03:35 PM	Vitals
03/09/2015 03:35 PM	Treatment
03/09/2015 03:35 PM	Vitals
03/09/2015 03:37 PM	Vitals

B6

Client: B6
Patient:

Patient History

03/09/2015 04:47 PM	UserForm
03/09/2015 05:27 PM	Treatment
03/09/2015 05:27 PM	Vitals
03/09/2015 06:52 PM	Prescription
03/09/2015 06:53 PM	Prescription
03/09/2015 07:04 PM	Treatment
03/09/2015 07:04 PM	Vitals
03/09/2015 07:04 PM	Treatment
03/09/2015 07:07 PM	Treatment
03/09/2015 07:07 PM	Vitals
03/09/2015 07:08 PM	Treatment
03/09/2015 07:08 PM	Vitals
03/09/2015 07:08 PM	Treatment
03/09/2015 07:08 PM	Vitals
03/09/2015 07:14 PM	Treatment
03/09/2015 07:14 PM	Vitals
03/09/2015 07:14 PM	Treatment
03/09/2015 07:14 PM	Vitals
03/09/2015 09:09 PM	Treatment
03/09/2015 09:09 PM	Vitals
03/09/2015 09:13 PM	Purchase
03/09/2015 11:42 PM	Treatment
03/09/2015 11:42 PM	Vitals
03/09/2015 11:42 PM	Treatment
03/09/2015 11:42 PM	Vitals
03/09/2015 11:42 PM	Treatment
03/09/2015 11:42 PM	Vitals
03/09/2015 11:43 PM	Treatment
03/09/2015 11:43 PM	Vitals
03/09/2015 11:44 PM	Treatment
03/10/2015 03:38 AM	Treatment
03/10/2015 03:38 AM	Vitals
03/10/2015 03:43 AM	Treatment
03/10/2015 03:43 AM	Vitals
03/10/2015 03:43 AM	Treatment
03/10/2015 03:43 AM	Vitals
03/10/2015 03:43 AM	Treatment
03/10/2015 03:43 AM	Vitals
03/10/2015 05:09 AM	Treatment
03/10/2015 05:09 AM	Vitals
03/10/2015 07:01 AM	Treatment

B6

Client: B6
Patient:

Patient History

03/10/2015 07:01 AM	Vitals
03/10/2015 07:01 AM	Treatment
03/10/2015 07:01 AM	Vitals
03/10/2015 07:01 AM	Treatment
03/10/2015 07:01 AM	Vitals
03/10/2015 07:01 AM	Treatment
03/10/2015 07:01 AM	Vitals
03/10/2015 07:01 AM	Treatment
03/10/2015 07:01 AM	Vitals
03/10/2015 07:02 AM	Treatment
03/10/2015 07:02 AM	Vitals
03/10/2015 09:11 AM	Purchase
03/10/2015 09:11 AM	Purchase
03/10/2015 11:38 AM	Treatment
03/10/2015 11:38 AM	Vitals
03/10/2015 11:39 AM	Treatment
03/10/2015 11:39 AM	Vitals
03/10/2015 11:40 AM	Treatment
03/10/2015 11:40 AM	Vitals
03/10/2015 11:40 AM	Treatment
03/10/2015 11:40 AM	Vitals
03/10/2015 12:12 PM	Purchase
03/10/2015 12:12 PM	Treatment
03/10/2015 01:33 PM	UserForm
03/10/2015 01:43 PM	Treatment
03/10/2015 01:43 PM	Vitals
09/21/2015 05:17 PM	UserForm
09/21/2015 05:20 PM	Vitals
09/21/2015 05:20 PM	Vitals
09/21/2015 05:20 PM	Vitals
09/21/2015 05:20 PM	Vitals
09/21/2015 05:24 PM	Prescription
09/21/2015 05:24 PM	Prescription
09/21/2015 05:49 PM	Prescription
09/21/2015 07:16 PM	Purchase
09/21/2015 07:16 PM	Purchase
09/21/2015 07:18 PM	Purchase
09/21/2015 07:28 PM	Prescription
09/05/2018 08:11 AM	Appointment
09/20/2018 01:47 PM	Appointment
10/02/2018 03:53 PM	UserForm
10/02/2018 03:54 PM	UserForm
10/02/2018 03:55 PM	UserForm
10/02/2018 03:55 PM	Treatment

B6

Client: B6
Patient:

Patient History

10/02/2018 03:58 PM	Vitals
10/02/2018 04:25 PM	Purchase
10/02/2018 04:25 PM	Purchase
10/02/2018 04:59 PM	UserForm
10/02/2018 05:25 PM	Purchase

B6

Client: B6
Patient:

Research cbc/chem 4/26/2019

Tufts Cummings School Of Veterinary Medicine

200 Westboro Road
North Grafton, MA 01536

Name/DOB: B6
Patient ID:
Phone number:
Collection Date: 4/26/2019 4:57 PM
Approval date: 4/26/2019 5:57 PM

Sex: CM
Age: 2
Species: Canine
Breed: Pit Bull

Provider: Dr. Lisa Freeman
Order Location: Foster Hospital for Small Animals
Sample ID: 1904260155

CBC, Comprehensive, Sm Animal (Research)

		Ref. Range/Males
SMACHUNSKI	B6	
WBC (ADVIA)		4.40-15.10 K/uL
RBC (Advia)		5.80-8.50 M/uL
Hemoglobin (ADVIA)		13.3-20.5 g/dL
Hematocrit (Advia)		39-55 %
MCV (ADVIA)		64.5-77.5 fL
MCH (ADVIA)		21.3-25.9 pg
CHCM		
MCHC (ADVIA)		31.9-34.3 g/dL
RDW (ADVIA)		11.9-15.2
Platelet Count (Advia)		173-486 K/uL
04/26/19 5:54 PM	platelets per 100x field (estimated count of 200,000-500,000/ul)	
Mean Platelet Volume (Advia)	B6	8.29-13.20 fl
04/26/19 5:30 PM	Platelet clumps (if present) and sample age (greater than 4 hours) can result in a falsely increased MPV.	
Platelet Crit	B6	0.129-0.403 %
04/26/19 5:30 PM	Platelet Crit is invalid when clumped platelets are present. Interpretation of PltCt is unclear in species other than canines.	
PDW		
Reticulocyte Count (Advia)	B6	0.20-1.60 %
Absolute Reticulocyte Count (Advia)		14.7-113.7 K/uL
CHr		
MCVr		

Microscopic Exam of Blood Smear (Advia)

		Ref. Range/Males
SMACHUNSKI	B6	
Seg Neuts (%)		43-86 %
Lymphocytes (%)		7-47 %
Monocytes (%)		1-15 %
Eosinophils (%)		0-16 %
Seg Neutrophils (Abs) Advia		2.800-11.500 K/ul
Lymphs (Abs) Advia		1.00-4.80 K/uL
Mono (Abs) Advia		0.10-1.50 K/uL
Eosinophils (Abs) Advia		0.00-1.40 K/uL
WBC Morphology		
RBC Morphology		

Research Chemistry Profile - Small Animal (Cobas)

Sample ID: 1904260155/1
This report continues... (Final)

Reviewed by: _____

Tufts Cummings School Of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

Name/DOB:
Patient ID: **B6**
Phone number:
Collection Date: 4/26/2019 4:57 PM
Approval date: 4/26/2019 5:57 PM

Sex: CM
Age: 2
Species: Canine
Breed: Pit Bull

Provider: Dr. Lisa Freeman
Order Location: Foster Hospital for Small Animals
Sample ID: 1904260155

Research Chemistry Profile - Small Animal (Cobas) (cont'd)

SMACHUNSKI	B6	Ref. Range/Males
Glucose		67-135 mg/dL
Urea		8-30 mg/dL
Creatinine		0.6-2.0 mg/dL
Phosphorus		2.6-7.2 mg/dL
Calcium 2		9.4-11.3 mg/dL
Magnesium 2+		1.8-3.0 mEq/L
Total Protein		5.5-7.8 g/dL
Albumin		2.8-4.0 g/dL
Globulins		2.3-4.2 g/dL
A/G Ratio		0.7-1.6
Sodium		140-150 mEq/L
Chloride		106-116 mEq/L
Potassium		3.7-5.4 mEq/L
tCO2(Bicarb)		14-28 mEq/L
AGAP		8.0-19.0
NA/K		29-40
Total Bilirubin		0.10-0.30 mg/dL
Alkaline Phosphatase		12-127 U/L
GGT		0-10 U/L
ALT		14-86 U/L
AST		9-54 U/L
Creatine Kinase		22-422 U/L
Cholesterol		82-355 mg/dL
Triglycerides		30-338 mg/dl
Amylase		409-1250 U/L
Osmolality (calculated)		291-315 mmol/L

Sample ID: 19042601552
END OF REPORT (Final)

Reviewed by: _____
Page 2

Client: B6
Patient:

Idexx NT-proBNP 4/26/2019

IDEXX Reference Laboratories

Client: B6 Patient: B6

IDEXX VetConnect 1-888-433-9987

Client: B6
Patient:
Species: CANINE
Breed: AMERICAN_PIT_BU
Gender: MALE NEUTERED
Age: 2Y

Date: B6
Requisition #: 1A
Accession #:
Ordered by: B6

TUFTS UNIVERSITY
200 WESTBORO RD
NORTH GRAFTON, Massachusetts 01536
508-839-5395

Account #88933

CARDIOPET proBNP - CANINE

Test	Result	Reference Range		Low	Normal	High
CARDIOPET proBNP - CANINE	B6	0 - 900 pmol/L	HIGH		B6	

Comments:

B6

Please note: Complete interpretive comments for all concentrations of Cardiopet proBNP are available in the online directory of services. Serum specimens received at room temperature may have decreased NT-proBNP concentrations.

Page 1 of 1

Client: B6
Patient:

Diet Hx 4/26/2019

B6

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 4/26/19

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)

Example: **Poor**_____**Excellent**

Poor_____**Excellent**

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
☐Eats about the same amount as usual ☐Eats less than usual ☐Eats more than usual
☐Seems to prefer different foods than usual ☒Other I have reduced his intake because of switching to Grain Foods

3. Over the last few weeks, has your pet (check one)
☐Lost weight ☒Gained weight ☐Stayed about the same weight ☐Don't know

1. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats and that you have fed in the last 2 years.

Please provide enough detail that we could go to the store and buy the exact same food - examples are shown in the table

Food (include specific product and flavor)	Form	Amount	How often?	Dates fed
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2016-present*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*June -Aug 2016*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Sept 2016-present*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2018-present*
NUTRA SOURCE PUREVITA VENISON + RED LENTILS	DRY	2 CUPS	2 X DAY	AUG 2018 - MAR 2019
NATURAL BALANCE VENISON + SWEET POTATO	CAN	3 TBLS	2 X DAY	AUG 2018 - MAR 2019
NATURAL BALANCE VENISON + SWEET POTATO	TREAT	6 TREATS/BAG	6 A DAY	AUG 2018 - MAR 2019
NATURAL BALANCE SWEET POTATO + FISH	TREAT	SAME	6 A DAY	AUG 2018 - MAR 2019
NUTRA SOURCE CHICKEN + RICE FORMULA	DRY*	1.5 CUPS	2 X DAY	MAR 2019 - PRESENT
" "	CAN	1.5 TBLS	2 X DAY	MAR 2019 - PRESENT
PUPPERONI DOG TREATS	TREAT	1/2	1 X DAY	MAR 2019 - PRESENT
MILK BONE SMALL MORSELS	TREAT	4	1 X DAY	MAR 2019 - PRESENT
PIG EARS	TREAT	1	1 X WEEK	MAR 2019 - PRESENT
FEMUR OR KNUCKLE BONE	TREAT	1	1 X MONTH	MAR 2019 - PRESENT

*Any additional diet information can be listed on the back of this sheet

2. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐Yes ☐No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☒Yes ☐No	GNC	2000 MG
Carnitine	☐Yes ☐No		
Antioxidants	☐Yes ☐No		
Multivitamin	☐Yes ☐No		
Fish oil	☐Yes ☐No		
Coenzyme Q10	☐Yes ☐No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

3. How do you administer pills to your pet?
☐ I do not give any medications
☐ I put them directly in my pet's mouth without food
☒ I put them in my pet's dog/cat food
☐ I put them in a Pill Pocket or similar product
☐ I put them in foods (list foods):_____

Dear Doctors,

Please see the accompanying cardiology report for our mutual patient. Thank you for the referral and your continued support of B6. Please contact me if you need any more information regarding this patient. As I am only at B6 once to twice per month, email (see below) is the best mode of communication for me.

B6

Consulting Cardiologist: B6

Client: B6
Patient: (2yo MN pit bull)

Examination Date: 3/14/19

CARDIOLOGY EXAMINATION

HISTORY: Cough x 2 weeks, decreased appetite. Admitted yesterday for monitoring/echo. Started o B6 (rDVM) 50mg SQ q 8 h B6 . Taurine drawn/not yet submitted. ECG 100 bpm NSF. TFAST suspect DCM. rDVM rads in record.

MEDICATIONS:

DIET: grain free pork and pea

WEIGHT: 27 kg

PHYSICAL EXAMINATION:

Sedate. BCS 4/9. Adequate hydration

Mm color: pink, CRT: 1.5 sec

Chest conformation: normal

Heart rate: 100/minute. Rhythm: regular. PMI: Left apex.

Murmurs: Grade III/VI left apical systolic murmur

Pulmonary auscultation: clear

Femoral pulse quality: moderate, synchronous

Other Comments: Moderate diffuse muscle atrophy. Sedated wit B6 .2mg/kg IV with great effect.

ECHOCARDIOGRAM

Two-dimensional description:

The left atrium is moderately to severely enlarged. The mitral valve leaflets are normal thickness. The left ventricular chamber is severely dilated with normal to thin walls and significantly reduced wall motion. The aortic valve leaflets and aortic root are normal. The right atrium and right ventricle are moderately enlarged. Remainder of the right heart appears normal. No masses or effusions noted.

Cardiac rhythm during study appeared regular.

2-D measurements:

LA (cm)	Ao (cm)	LA/Ao
B6		

M-mode measurements:

IVSd (cm)	LVIDd (cm)	LVFWd (cm)	FS (%)	LA (cm)	Ao (cm)	LA/Ao
B6						

IVSs (cm)	LVIDs (cm)	LVFWs (cm)
B6		

Doppler findings:

B6

Consulting Cardiologist: B6

B6

ECHOCARDIOGRAPHIC DIAGNOSIS:
1. Dilated cardiomyopathy (severe left atrial and left ventricular enlargement; moderate right atrial and right ventricular enlargement; severely reduced left ventricular wall motion)
2. Mild mitral and trace tricuspid regurgitations – likely from annular stretch secondary to #1

RADIOGRAPHIC FINDINGS: 2 view thorax, rDVM: The cardiac silhouette is severely and globally enlarged. The pulmonary vasculature is moderately dilated. There is a moderate to severe bilateral caudodorsal interstitial pattern consistent with congestive heart failure.

**** FINAL REPORT ******
FINAL DIAGNOSIS:
1. Dilated cardiomyopathy (severe left atrial and left ventricular enlargement; moderate right atrial and right ventricular enlargement; severely reduced left ventricular wall motion) – R/O nutritional (taurine deficiency or secondary to grain free/pork based diet) vs familial vs hypothyroidism
2. Mild mitral and trace tricuspid regurgitations – likely from annular stretch secondary to #1
3. Congestive heart failure (pulmonary edema), 3/13/19

DIAGNOSTIC RECOMMENDATIONS:

B6

THERAPEUTIC RECOMMENDATIONS:

B6

FOLLOW UP SCHEDULE:
10-14 days for recheck exam, renal panel, CXR.
3 months for echocardiogram

*There is a chance that some of B6 cardiac disease may be reversible if this is secondary to nutritional cause. However, even some patients with diet-induced DCM can have irreversible cardiac changes. Thus, prognosis is variable and will be determined based on followup testing.

Consulting Cardiologist: B6

Consulting Cardiologist: B6

Consulting Cardiologist: B6

Client: B6
Patient:

B6 thyroid panel 3/14/2019

B6

B6

Accession No. B6
Received 03/14/2019
Reported 03/16/2019 04:32 AM

Owner	Pet Name	Species	Breed	Sex	Pet Age	Chart#
B6	B6	Canine	Other	CM	3Y	53241

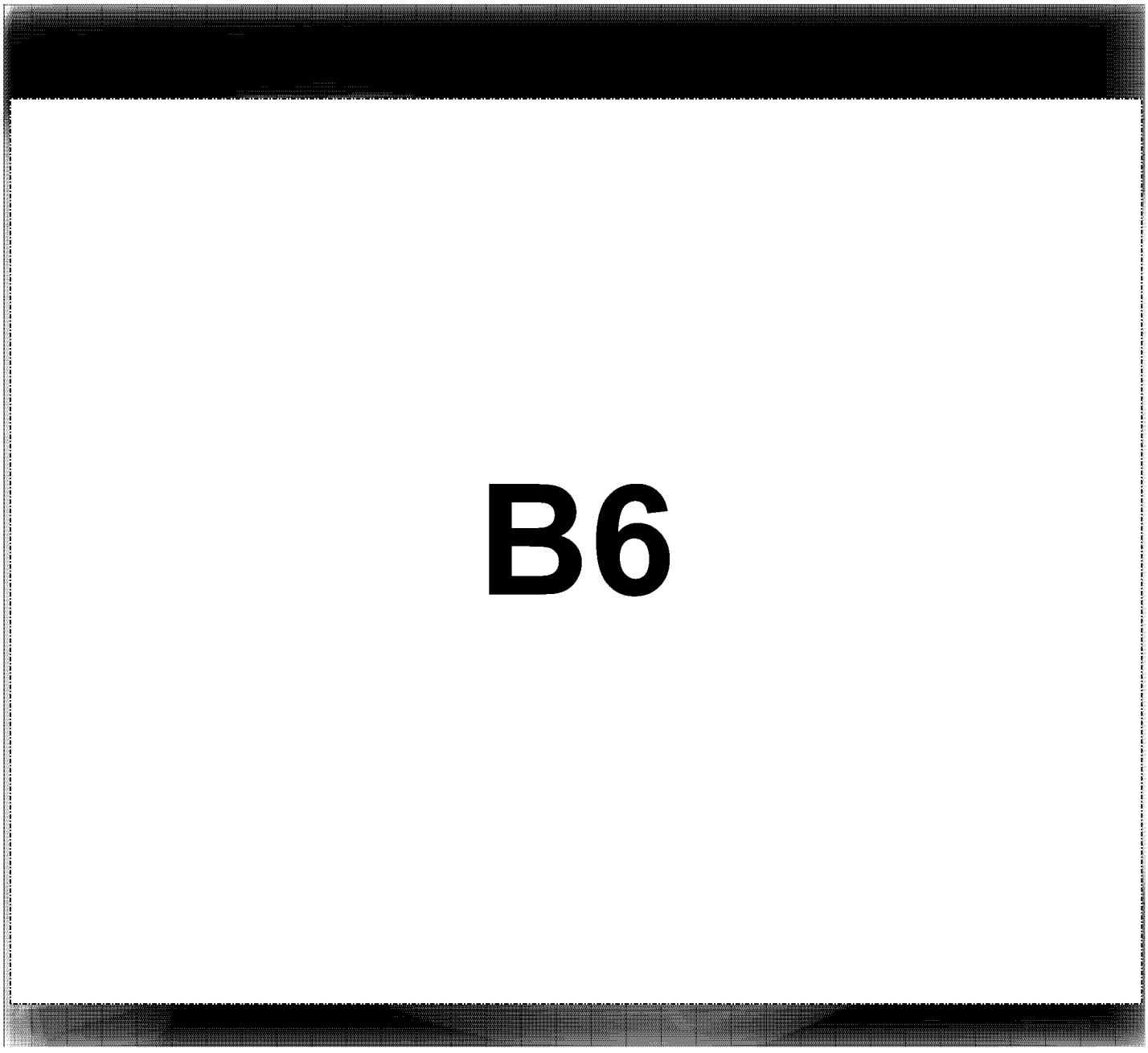
Test Requested	Results	Reference Range	Units
T4			
T4	B6	0.8-3.5	µg/dL
FREE T4 BY EQUILIBRIUM DIALYSIS			
Free T4 (Dialysis)		8-40	pmol/L
TSH			
TSH		0 - 0.60	ng/mL

While many dogs with primary hypothyroidism have elevated cTSH concentrations, up to one third of affected dogs have normal or low cTSH concentrations, for reasons that are unclear. In those cases where TSH concentrations are normal and hypothyroidism is still strongly suspected, consider performing a free T4 and/or thyroglobulin autoantibodies.

Client:
Patient: B6

Vitals Results

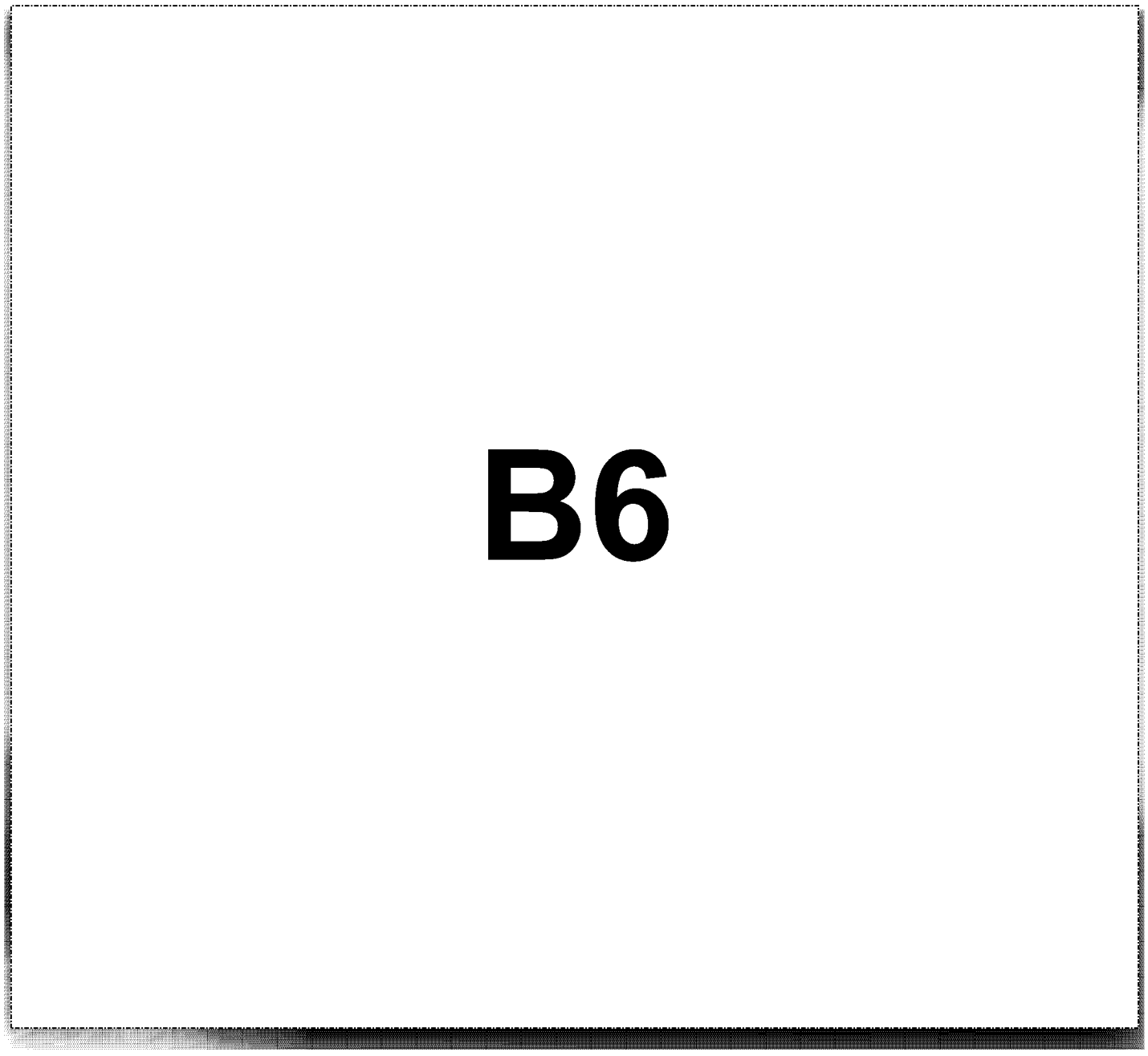
4/26/2019 2:52:48 PM	Weight (kg)	32.0000



Medical Record Image

B6

Medical Record Image



Client: B6
Patient:

ECG from Cardio

B6

4/26/2019 4:27:10 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

12 Lead; Standard Placement

Client: B6
Patient:

ECG from Cardio

B6

4/26/2019 4:27:45 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

12-Lead: Standard Placement

Client: B6
Patient:

ECG from Cardio

B6

4/26/2019 4:28:13 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

12 Lead: Standard Placement

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
(508) 839-5395

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Treeing Walker Coonhound
Sex:	Male (Neutered)
Age:	B6

Lab Results Report

Chemistry 21 (Cobas) 6/7/2019 2:48:19 PM **Accession ID:** B6

Test	Results	Reference Range	Units
PHOSPHORUS	B6	2.6 - 7.2	mg/dL
GLUCOSE		67 - 135	mg/dL
A/G RATIO		0.7 - 1.6	
OSMOLALITY (CALCULATED)		291 - 315	mmol/L
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
CALCIUM2		9.4 - 11.3	mg/dL
ALBUMIN		2.8 - 4	g/dL
AST		9 - 54	U/L
POTASSIUM		3.7 - 5.4	mEq/L
ALK PHOS		12 - 127	U/L
CHOLESTEROL		82 - 355	mg/dL
UREA		8 - 30	mg/dL
T. PROTEIN		5.5 - 7.8	g/dL
NA/K		29 - 40	
COMMENTS (CHEMISTRY)		0 - 0	
CREATININE		0.6 - 2	mg/dL
ALT		14 - 86	U/L
T BILIRUBIN		0.1 - 0.3	mg/dL

Client:
Patient: B6

GLOBULINS	B6	2.3 - 4.2	g/dL

stringsoft

Printed Monday, June 10, 2019

Vitals Results

6/7/2019 2:04:56 PM	Weight (kg)	37.3000

Patient History

06/07/2019 01:55 PM	UserForm
06/07/2019 01:57 PM	Purchase
06/07/2019 02:04 PM	Vitals
06/07/2019 02:04 PM	Vitals
06/07/2019 02:08 PM	Treatment
06/07/2019 02:35 PM	UserForm
06/07/2019 02:36 PM	Purchase
06/07/2019 02:47 PM	Purchase
06/07/2019 03:33 PM	Prescription

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

Discharge Instructions

Patient
Name: B6
Species: Canine
Tricolor Male (Neutered) Treeing Walker Coonhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
☑ John E. Rush DVM, MS, DACVIM (Cardiology), DACVECC
B6

Cardiology Resident: B6

Cardiology Technician:
B6

Student: B6

Admit Date: 6/7/2019 1:52:55 PM
Discharge Date: 6/7/2019

Diagnoses: Chronic valvular disease with mitral regurgitation, history of congestive heart failure with pulmonary edema and ascites.

Clinical Findings: Thank you for bringing B6 to Tufts for a one week recheck. B6 had a recent episode of heart failure and still had residual fluid in his abdomen during his last visit. You report he has been tolerating his medications very well and has been eating wonderful since last visit! You also noticed his belly has gotten smaller since last visit.

On physical exam today, B6 was bright and alert. He lost about 2kg (4.4lb). As expected, his murmur is unchanged since his last visit. His pulses were good today. We took a quick look at B6 belly with the ultrasound to check for fluid in his abdomen (ascites). B6 ascited has almost completely resolved, indicating that the medications are working great for him!

We have submitted a chemistry panel to recheck B6 kidney values to make sure he is tolerating the spironolactone well. You should hear back with these results in the next 1-2 business days. Depending on the values, we may consider increase the frequency of the B6 to twice a day.

Monitoring at Home:

***You can evaluate the fluid in his belly by using a malleable measuring tape around the same part of his abdomen every other day. If you notice significant increases in size, this may also mean that you should give an extra dose of furosemide. * Please let us know if additional doses are given.**

We would like you to monitor B6 breathing rate and effort at home, ideally during sleep or at a time of rest. The doses of drugs will be adjusted based on the breathing rate and effort. In general, most dogs with heart failure that is well controlled have a breathing rate at rest of less than 35 breaths per minute. In addition, the breathing effort, noted by the amount of belly wall motion used for each breath, is fairly minimal if heart failure is controlled. An increase in breathing rate or effort will usually mean that you should give an extra dose of B6 If difficulty breathing is not improved within 30-60 minutes after giving extra B6 then we recommend that a recheck exam be scheduled and/or that B6 be evaluated by an emergency clinic. There are instructions for monitoring breathing, and a form to help keep track of breathing rate and drug doses, on the Tufts HeartSmart web site (http://vet.tufts.edu/heartsmart/at-home-monitoring/).

We also want you to watch for weakness or collapse, a reduction in appetite, worsening cough, or distention of the belly as these findings indicate that we should do a recheck examination.

Diet Suggestions: Continue B6 on his early cardiac diet. He is on the thinner side right now so we recommend increasing his food from 4 cups a day to 5 cups a day.

Recommended Medications:

B6

Recheck Visits: B6 has an appointment recheck scheduled for the study he is participating in at 2pm on August 23rd with B6

Thank you for entrusting us with B6 care. Please contact our Cardiology liaison at (508)-887-4696 or email us at cardionet@tufts.edu for scheduling and non-emergent questions or concerns.

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:
Please check with your primary veterinarian to purchase the recommended diet(s). If you wish to purchase your food from us, please call 7-10 days in advance (508-887-4629) to ensure the food is in stock. Alternatively, veterinary diets can be ordered from online retailers with a prescription/veterinary approval.

Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

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Cummings
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AT TUFTS UNIVERSITY

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http://vetmed.tufts.edu/

Nutritional Tips for Pets with Heart Disease

Low sodium, high quality pet treats

Notes:

1. Most other dog treats are high in sodium.
2. If your pet has other medical conditions, these treats may not be appropriate. Talk to your veterinarian if you have questions or make an appointment with the Nutrition Service.

Product	Calories per treat
Dogs	
Hill's Science Diet Baked Light Biscuits with Real Chicken Small Dog Treat	8
Hill's Science Diet Baked Light Biscuits with Real Chicken Medium Dog Treat	34
Hill's Science Diet Soft Savories Peanut Butter & Banana, Beef & Cheddar, or Chicken & Yogurt Dog Treat	25-27, depending on flavor
Hill's Ideal Balance Soft-Baked Naturals with Chicken & Carrots, Duck & Pumpkin, or Beef & Sweet Potato Dog Treat	12-13, depending on flavor
Purina Beyond Natural Salmon Dog Biscuit Treat with Oats or Chicken & Barley	27-29, depending on flavor
Purina Alpo Variety Snaps Little Bites (beef, chicken, liver, lamb or beef, bacon, cheese, peanut butter)	16
Purina Alpo Variety Snaps Big Bites (beef, chicken, liver, lamb)	58
Royal Canin Original Canine treat	5
Cats	
Royal Canin Original Feline treat	2
Fancy Feast Duos Natural Rotisserie Chicken Cat treat	2
Fancy Feast Duos Tuna with Accents of Parsley Cat treat	2

Taste enhancers to can make your pet's food tastier to increase food intake

Safe and effective appetite stimulants are now available for dogs and cats. Please talk to your veterinarian if your pet is not eating well, not eating ideal foods, or is losing weight.

Notes:

1. All foods in this list should be prepared without salt
2. These taste enhancers should be added in small amounts. If your pet eats too much of them, they will unbalance the diet and increase your pet's risk for nutritional deficiencies

Dogs

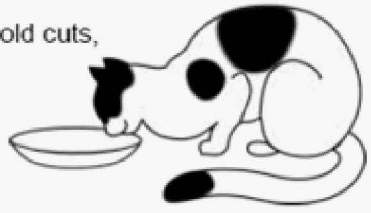
- Honey or maple syrup
- Homemade chicken, beef, or fish broth (made without salt; avoid all deli meats and rotisserie chicken). Avoid store bought broths because even the low sodium brands are too high in sodium.
- Sugar (brown or white) – Domino pourable light brown sugar is a good option
- Vanilla or fruit yogurt – One option that dogs seem to like is Yoplait Custard Yogurt (caramel or vanilla flavors). If you try other brands, just be sure the sodium is less than 100 mg per 100 calories (the Yoplait is 95 mg per 170 calories which comes out to 56 mg sodium per 100 calories). Also avoid yogurts with artificial sweeteners.
- Maple syrup. Low salt brands include Log Cabin All Natural, Maple Grove Farm 100% pure maple syrup, or Stop and Shop Original Syrup
- Applesauce (be sure they have less than 50 mg sodium per serving)
- Ketchup (no salt added). Examples include Hunts or Heinz no salt added
- Pasta sauce (no salt added). Examples: Francesco Rinaldi no salt added or Enrico's no salt added)
- Frosted Mini Wheats Original – these can be crumbled on his food
- Lean meats, cooked (chicken, turkey, beef, or fish) – not deli/sandwich meats/cold cuts, rotisserie chicken, and any canned fish or meat
- Eggs, cooked

Dogs (continued)

- Homemade chicken, beef, or fish broth (even low sodium store-bought broths are too high in sodium). Avoid all canned soups unless labeled as no salt added
- Low-salt breakfast cereal - the label should read, "very low sodium food" or contain less than 20 mg sodium per serving. A good option is Frosted Mini Wheats Original or Little Bites Original
- Fresh vegetables/fruit. Examples include carrots, green beans, apple, orange, banana (avoid grapes, raisins, onions, garlic)
- Low sodium canned dog foods

Cats

- Lean meats, cooked (chicken, turkey, beef, or fish) – not sandwich meats/cold cuts, canned tuna, or rotisserie chicken
- Eggs, cooked
- Homemade chicken, beef, or fish broth (even low sodium store-bought broths are too high in sodium)
- Low sodium canned cat foods



Foods to avoid

- Fatty foods (meat trimmings, cream, ice cream)
- Baby food
- Pickled foods
- Bread
- Pizza
- Condiments (ketchup, soy sauce, barbecue sauce, etc – unless they are unsalted or no salt added)
- Sandwich meats/cold cuts (ham, corned beef, salami, sausages, bacon, hot dogs)
- Rotisserie chicken
- Most cheeses, including "squirtable" cheeses
- Processed foods (such as, potato mixes, rice mixes, macaroni and cheese)
- Canned vegetables (unless "no salt added")
- Potato chips, packaged popcorn, crackers, and other snack foods
- Soups (unless homemade without salt)
- Most commercial pet treats

Tips for administering medications

Foods commonly used to administer your pet's pills can provide a large amount of additional salt to your pet's diet. Preferable ways to give medications include:

- Have one of our staff show you how to give medications without using food
- Insert medications into one of the following foods:

Dogs or cats

- Low-sodium canned pet food
- Home-cooked meat such as chicken or hamburger (made without salt); not lunch meats
- Whipped cream (Reddi Wip)
- Marshmallows
- Greenies Pill Pockets
  - Dog chicken, hickory smoke, or peanut butter flavors; cat chicken or salmon flavor
  - Avoid grain-free duck and pea which is high in sodium
  - Try to use the smallest size possible (ideally, the cat sized Pill Pockets, even for dogs) and as few as possible to avoid excessive salt.
    - Caution: Not all similar products from other companies are low in sodium .

Dogs

- Soft fruit, such as banana, orange, melon, or strawberries (avoid grapes)
- Peanut butter (only if labeled as "no salt added") – examples include Smucker's Natural Creamy Peanut Butter with No Salt Added or Teddie All Natural Smooth Unsalted Butter
- Frosting (should be less than 75 mg/serving and contain no artificial sweeteners or xylitol). Examples include Duncan Hines whipped vanilla frosting, Betty Crocker whipped vanilla frosting)

You may find our Petfoodology post called, "Pill-popping pets" helpful for additional ideas: http://vetnutrition.tufts.edu/2018/09/foods_for_giving_pills/

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

Patient ID: B6
Kris Canine
B6 Male (Neutered) Treeing Walker Coonhound
Tricolor

Cardiology Appointment Report

Date: 6/7/2019

Attending Cardiologist:
John E. Rush DVM, MS, DACVIM (Cardiology), DACVECC

B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

Presenting Complaint: Recheck. DMVD with decreased contractile function and recent history of CHF (5/22/19). Persistent mild to moderate ascites during last visit 5/29/19.

Concurrent Diseases:
Blindness- unknown etiology (saw optho but declined further diagnostics)

General Medical History:
Appetite back to normal, taking medications no problem, less restless, belly seems less distended than last visit. Looks thinner than he was prior to CHF

History of splenic hematoma.
Had loose bowel movements recently but also had change in diet.
Flaky skin
Blind

Diet and Supplements:
Royal canin early cardiac- 4 cups a day

Cardiovascular History:
Prior CHF diagnosis? Y
Prior heart murmur? Y- III
Prior ATE? N

Prior arrhythmia? N
Monitoring respiratory rate and effort at home? Y averaging 33
Cough? N
Shortness of breath or difficulty breathing? N
Syncope or collapse? N
Sudden onset lameness? N
Exercise intolerance? N

Current Medications Pertinent to CV System:

B6

Cardiac Physical Examination:

B6

Muscle condition:

- ☐ Normal
- ☑ Mild muscle loss
- ☐ Moderate cachexia
- ☐ Marked cachexia

Cardiovascular Physical Exam:

Murmur Grade:

- ☐ None
- ☐ I/VI
- ☑ II/VI
- ☑ III/VI
- ☐ IV/VI
- ☐ V/VI
- ☐ VI/VI

Murmur location/description: left apical systolic

Jugular vein:

- ☑ Bottom 1/3 of the neck
- ☐ 1/2 way up the neck

- [ ] Middle 1/3 of the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [x] Good
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [x] None
- [ ] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [x] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
CMVD;
Hx of CHF;
Hx of ascites;

Diagnostic plan:
- [ ] Echocardiogram
- [x] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [x] Other tests: fluid check

Echocardiogram Findings:
General/2-D findings: *fluid check*
There is very mild ascites visualized. No pericardial effusion or b-lines seen.

Assessment and recommendations:
Findings consistent with marked improvement on abdominal fluid and, since patient is clinically better with good appetite and energy level, recommend maintain current medications doses and frequency. Since blood work revealed increase in kidney values B6 will be kept SID instead of increasing to BID. Clients oriented to measure belly twice a week and keep counting respiratory rate. Recommend start fish oil since patient has moderate cachexia. Recheck kidney values and echocardiogram in 2 months, sooner if clinical signs occur such as decreased appetite, lethargy, abdominal distension, or dyspnea.

Final Diagnosis:
DMVD with PHTN;
Reduced contractile function.

Heart Failure Classification Score:
ISACHC Classification:

- ☐ Ia
- ☐ Ib
- ☐ II
- ☑ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☐ B2
- ☑ C
- ☐ D

IDEXX

B6

PET OWNER: B6
SPECIES: Canine
BREED: Labrador Retriever
GENDER: Female
AGE: 6 Years
PATIENT ID: B6

B6

ACCOUNT #: B6
ATTENDING VET: B6

LAB ID: B6
ORDER ID:
COLLECTION DATE: 2/26/18
DATE OF RECEIPT: 2/27/18
DATE OF RESULT: 3/9/18

IDEXX Services: B6

IDEXX SDMA

B6

Jan '18 Feb '18

Creatinine

B6

Jan '18 Feb '18

BUN

B6

Jan '18 Feb '18

Chemistry

2/27/18 (Order Received)
3/9/18 9:58 AM (Last Updated)

1/23/18

TEST	RESULT	REFERENCE VALUE	1/23/18
IDEXX SDMA	a	0 - 14 µg/dL	
Creatinine		0.5 - 1.5 mg/dL	
BUN		9 - 31 mg/dL	
BUN:Creatinine Ratio			
Phosphorus		2.5 - 6.1 mg/dL	
Calcium		8.4 - 11.8 mg/dL	
Sodium		142 - 152 mmol/L	
Potassium		4.0 - 5.4 mmol/L	
Na:K Ratio	B6	28 - 37	B6
Chloride		108 - 119 mmol/L	
TCO2 (Bicarbonate)		13 - 27 mmol/L	
Anion Gap		11 - 26 mmol/L	
Total Protein		5.5 - 7.5 g/dL	
Albumin		2.7 - 3.9 g/dL	
Globulin		2.4 - 4.0 g/dL	
Alb:Glob Ratio		0.7 - 1.5	

Chemistry (continued)

TEST	RESULT	REFERENCE VALUE	
Cholesterol	B6	131 - 345 mg/dL	B6
Hemolysis Index			
Lipemia Index			

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.

Therapeutics/Toxicology

2/27/18 (Order Received)
3/9/18 9:58 AM (Last Updated)

TEST	RESULT	REFERENCE VALUE	
Serum Iron		73 - 245 ug/dL	B6
Ferritin	B6	89 - 489 ng/mL	
TIBC	a	270 - 530 ug/dL	

a Referral test performed at Kansas State University.

From: B6
To: Jones, Jennifer L
Sent: 8/25/2018 1:12:49 PM
Subject: RE: 800.267-FDA Case Investigation for B6 and B6 (EON-308715)

Hi Dr. Jones,
Dr. Freeman has taken care of submitting an official report for B6 h, and I have asked my secretary to send you B6 full records. Please let me know if you don't receive them early next week, or have any additional questions.
Best,

B6

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Thursday, August 23, 2018 11:51 AM
To: B6
Subject: 800.267-FDA Case Investigation for B6 and B6 (EON-308715)

Good morning B6
Thank you for submitting your consumer complaint to FDA. I'm sorry to hear about B6 illness.
As part of our investigation, we'd like to request:

- **Full Medical Records**
  - Please email (preferred) or fax (301-210-4685) a copy of B6 **entire** medical history (not just this event), including any referral diagnostics.
- **Have you submitted a report for B6** I was forwarded the medical records and told from Dr. Lisa Freeman that you may have submitted a complaint. I cannot seem to locate it within our system.

I attached a copy of our Vet-LIRN network procedures. The procedures describe how Vet-LIRN operates and how veterinarians help with our case investigations.
Please respond to this email so that we can initiate our investigation.
Thank you kindly,
Dr. Jones

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From:	Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To:	Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David
Sent:	10/25/2018 11:54:09 AM
Subject:	B6 ase-FW: Taste of the Wild High Prairie: Lisa Freeman - EON-369325
Attachments:	2057945-report.pdf; 2057945-attachments.zip

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

From: PFR Event <pfreventcreation@fda.hhs.gov>
Sent: Thursday, October 25, 2018 7:53 AM
To: Cleary, Michael * <Michael.Cleary@fda.hhs.gov>; HQ Pet Food Report Notification <HQPetFoodReportNotification@fda.hhs.gov>; B6
Subject: Taste of the Wild High Prairie: Lisa Freeman - EON-369325

A PFR Report has been received and PFR Event [EON-369325] has been created in the EON System.

A "PDF" report by name "2057945-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2057945-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-369325
ICSR #: 2057945
EON Title: PFR Event created for Taste of the Wild High Prairie; 2057945

AE Date	02/20/2018	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Naturally

Breed	Great Dane		
Age	9 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2057945
Product Group: Pet Food
Product Name: Taste of the Wild High Prairie
Description: DCM, CHF, atrial fibrillation WB taurine = B6 Dog's diet previously submitted to FDA Note: this may be a duplicate submission
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Died Naturally
Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Taste of the Wild High Prairie		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6

To view this PFR Event, please click the link below:
https://eon.fda.gov/eon//browse/EON-369325

To view the PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction!viewReport.jspa?decorator=none&e=0&issueType=12&issueId=386247

==========

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Jones, Jennifer L
CC: Reimschuessel, Renate
Sent: 7/20/2018 11:01:57 PM
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

PS – I have food samples for B6 and B6

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Freeman, Lisa
Sent: Friday, July 20, 2018 6:32 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

Hi Jen and Renate
I'll get permission from all 3 owners and send records. I might wait another week before calling B6 and B6 owners based on updates below.
Lisa

Updates:
For B6, WB taurine was B6 On B6 We talked to owner: B6 was having trouble breathing, they were planning to pts today but he died at home yesterday.

For B6, taurine came back normal (plasma = B6 WB= B6. Owner left a message that B6 died on B6 so no repeat echo. We're calling the vet to see if we can find out any additional info.

For B6, owner told us on B6 He collapsed twice on B6 once at home and again at B6 where we had him put to sleep
No autopsy done. Not sure if I sent before but his taurine was plasma B6 and WB B6

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Sent: Friday, July 20, 2018 8:47 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

Good morning Lisa,
Yes, we got the reports you previously submitted and recorded the information for our database. Will you please forward any medical records for:

- B6, are you able to send any updates on the Taurine testing or echocardiogram (if done?)
- B6 -Also was an autopsy done?

Thank you in advance and for your time to report all the cases!
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD &DRUG ADMINISTRATION

From: Freeman, Lisa [mailto:Lisa.Freeman@tufts.edu]
Sent: Friday, July 20, 2018 8:06 AM
To: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

Dear Renata and Jennifer
That seems reasonable. I was never contacted about the other cases that I submitted. There was some confusion about the way I submitted them so I want to be sure you actually got them (B6, B6). I'm sure you're all getting slammed with reports (and there will probably be even more coming now) but just wanted to check to be sure they got recorded.
Thanks
Lisa

From: Reimschuessel, Renate [mailto:Renate.Reimschuessel@fda.hhs.gov]
Sent: Friday, July 20, 2018 7:55 AM
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

Dear Lisa
Thanks for gathering the information.
I think, since we are getting so many reports since our CVM update, we should pass on the B6 case as it is not clear-cut.

I think Jen is more familiar with the B6 case, so I'll let her respond regarding that one.
Thank you again for all your work on this investigation.
rr

Renate Reimschuessel V.M.D. Ph.D. Director Vet-LIRN
Phone 1- 240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Freeman, Lisa [mailto:Lisa.Freeman@tufts.edu]
Sent: Thursday, July 19, 2018 5:59 PM
To: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.267-FDA Case Investigation for B6 (EON-358523)

Dear Renate
In looking back through this case, I'm not sure this is a completely clear-cut one. The dog has degenerative mitral valve disease and CHF but also has reduced cardiac contractility so might be a combination.
Do you still want me to collect the info below?

Also, I have an update on B6 who died at home last week. I do have food from the owner if you want that.
Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Sent: Tuesday, July 17, 2018 11:48 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>
Subject: 800.267-FDA Case Investigation for B6 (EON-358523)

Dear Dr. Freeman,
Thank you for submitting your consumer complaint to FDA. I'm sorry to hear about B6 illness.
As part of our investigation, we'd like to request:

- **Full Medical Records**
  - Please email (preferred) or fax (301-210-4685) a copy of B6 **entire** medical history (not just this event), including any referral diagnostics.
- **Phone interview** about B6 diet and environmental exposures
  - Please confirm permission to contact the owner.
  - The interview generally lasts 30 minutes.

I attached a copy of our Vet-LIRN network procedures. The procedures describe how Vet-LIRN operates and how veterinarians help with our case investigations.
Please respond to this email so that we can initiate our investigation.

Thank you kindly, especially for submitting multiple cases,
Dr. Reimschuessel

Renate Reimschuessel V.M.D. Ph.D.
Director: Vet-LIRN
(Veterinary Laboratory Investigation and Response Network)
Center For Veterinary Medicine, FDA,
8401 Muirkirk Road, Laurel, MD 20708
Phone 1- 240-402-5404 Fax 301-210-4685
EMAIL : renate.reimschuessel@fda.hhs.gov

Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

Phish-Pharm
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ToolsResources/Phish-Pharm/default.htm

Aquaculture

http://www.fda.gov/AnimalVeterinary/ScienceResearch/ResearchAreas/ucm130892.htm

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

Foster Hospital for Small Animals

55 Willard Street

North Grafton, MA 01536

(508) 839-5395

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	2477624

Patient:	B6
Species:	Canine
Breed:	Great Dane
Sex:	Male
Age:	B6 Years Old

Lab Results Report

Chemistry 21 (Cobas) 6/5/2018 11:07:21 AM **Accession ID:** B6

Test	Results	Reference Range	Units
GLUCOSE		67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
T. PROTEIN		5.5 - 7.8	g/dL
ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE	B6	106 - 116	mEq/L
POTASSIUM		3.7 - 5.4	mEq/L
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
D.BILIRUBIN		0 - 0.1	mg/dL
I BILIRUBIN		0 - 0.2	mg/dL
ALK PHOS		12 - 127	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CHOLESTEROL		82 - 355	mg/dL
OSMOLALITY (CALCULATED)		291 - 315	mmol/L
COMMENTS (CHEMISTRY)		0 - 0	
Slight hemolysis,Slight lipemia			

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

Radiology Request & Report

Patient
Name: B6
Species: Canine
Fawn Male Great Dane
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: B6
Date of request: 2/20/2018

Attending Clinician: B6 VM (SAM Rotating Intern) **Student:**

Date of exam: 2/20/18

Patient Location: Ward/Cage: ICU Weight(lbs) 0.00

- ☑ Inpatient
- ☐ Outpatient Time:
- ☐ Waiting
- ☐ Emergency

Sedation
- ☐ BAG
- ☐ OBAG
- ☐ 1/2 dose OBAG
- ☐ DexDomitor/Butorphanol
- ☐ Anesthesia to sedate/anesthetize

Examination Desired: CXR (do standing in large animal)

Presenting Complaint and Clinical Questions you wish to answer:
Emergency

Pertinent History: collapse episode, dx with DCM, CHF, and A-fib

Findings:

B6

Conclusions:
- Generalized cardiomegaly with mild to moderate left atrial enlargement. No clear evidence of cardiogenic pulmonary edema on this limited exam.

Radiologists

Primary: B6, DVM
Reviewing: B6, DVM, DACVR

Dates
Reported: 2/20/18
Finalized: 2/21/18

Client: B6
Patient:

Chem 3/14/19

Tufts Cummings School Of Veterinary Medicine

200 Westboro Road
North Grafton, MA 01536

DUPLICATE

Name/DOB: B6
Patient ID:
Phone number:
Collection Date: 3/14/2019 4:02 PM
Approval date: 3/14/2019 6:30 PM

Sex: CM
Age: 9
Species: Canine
Breed: Doberman Pinscher

Provider: B6
Order Location: V320559: Investigation into
Sample ID: 1903140161

Research Chemistry Profile - Small Animal (Cobas)

B6

DNOYES	Ref. Range/Males
Glucose	67-135 mg/dL
Urea	8-30 mg/dL
Creatinine	0.6-2.0 mg/dL
Phosphorus	2.6-7.2 mg/dL
Calcium 2	9.4-11.3 mg/dL
Magnesium 2+	1.8-3.0 mEq/L
Total Protein	5.5-7.8 g/dL
Albumin	2.8-4.0 g/dL
Globulins	2.3-4.2 g/dL
A/G Ratio	0.7-1.6
Sodium	140-150 mEq/L
Chloride	106-116 mEq/L
Potassium	3.7-5.4 mEq/L
tCO2(Bicarb)	14-28 mEq/L
AGAP	8.0-19.0
NA/K	29-40
Total Bilirubin	0.10-0.30 mg/dL
Alkaline Phosphatase	12-127 U/L
GGT	0-10 U/L
ALT	14-86 U/L
AST	9-54 U/L
Creatine Kinase	22-422 U/L
Cholesterol	82-355 mg/dL
Triglycerides	30-338 mg/dl
Amylase	409-1250 U/L
Osmolality (calculated)	291-315 mmol/L
Comments (Chemistry)	

Sample ID: 1903140161/1
REPRINT: Orig. printing on 3/14/2019 (Final)

Reviewed by: _____

Client: B6
Patient:

Diet Hx 3/14/19

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name B6 Owner's name : B6 Today's date: 3/14/19

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: *Poor* ——— *Excellent*

   Poor ——— Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☐Eats about the same amount as usual ☒Eats less than usual ☐Eats more than usual
   ☒Seems to prefer different foods than usual ☐Other ———

3. Over the last few weeks, has your pet (check one)
   ☐Lost weight ☐Gained weight ☒Stayed about the same weight ☐Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

   Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2018*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
~~Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult~~	~~dry~~	~~1 ½ cup~~	~~2x/day~~	~~Jan 2018~~
Salmon / Rice		2C	2x day	Nov 2018
Chicken / Rice				Dec. 2018
Beef / Rice				Jan. 2019
Dr. Marty's Nature Diet -		2C	2x day	Feb - (10 days)
People food - eating - sweet potatoes (doesn't want rice anymore)				Feb 11, 2019
Loves salmon - sweet potatoes		1½c	2x day	
appetite dropped off a bit -				
Still eating a diet of people food -				

*Any additional diet information can be listed on the back of this sheet – I can mail a date/time/exact foods daily- diary- I keep for B6 since he got home.

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or fatty outlet supplements)? ☐Yes ☒No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☐Yes ☐No		
Carnitine	☐Yes ☐No		
Antioxidants	☐Yes ☐No		
Multivitamin	☐Yes ☐No		
Fish oil	☐Yes ☐No		
Coenzyme Q10	☐Yes ☐No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

6. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food
   ☒ I put them in a Pill Pocket or similar product I use the chicken or Peanut Butter Pill pockets – He never takes them in the AM – I always hv. 2 put pill pocket down throat at PM He eats them
   ☐ I put them in foods (list foods): ———

Client: B6
Patient:

Diet Hx 3/14/19

When we took B6 home initially he refused to eat!
We tried the dry food and Hills Canned food as prescribed -
He ate NOTHING! we tried to give him his old food - he refused
By the 4th day I got worried - tried chicken breast - No!
He refused to eat - I could get him to take
ice cubes & drink water only -
B6 prescribed the medicine "entyce".
By the 5th day home - and after the Entyce - he finally
ate 2 can of urgent care hills diet it smelled like
cat food & came in the same small can -

* He then rejected the prescribed diet of dog food again
and began eating - Salmon/Rice or chicken/Rice/or
Beef/Rice/ or Scrambled eggs! Then my husband
ordered Dr. Marty's - for about [3 or 10 days 2 weeks] he ate this
then he began rejecting them and is regularly eating

People food - Chicken - carrots, potatoes - Beef
Salmon - he no longer wants
rice - 2C - 2x daily

In the past 3 days 3/11/19 - his appetite has
dropped off - he is only eating 1x a day
almost 2½ - 3C People food -
I keep a detailed hand written record from the day B6 came home with
exactly what he has eaten/how many times he pees/or poops -/his walks/
I can collect Mail to you

Notes from owner 3/14/19

MEMORANDUM

TO; B6

TUFTS UNIVERSITY - Cummings School of Veterinary Medicine

Re: B6 - Cummings Patient ID No: B6 Doberman Pinscher b. B6

EXPERIENCE WITH PROTOCOL FOR DILATED CARDIOMYOPATHY (DCM)

RESEARCH REVIEW VOLUNTEER

Antecedents - On Sunday, 11\4\2018, B6 came running back to me retrieving a tennis ball and let out a yelp for no apparent reason . He dropped the ball and walked around somewhat disoriented - an apparent hypoxic event. We brought him into the house and kept a close watch on him with no signs of distress. The next morning when he seemed somewhat lethargic, I put a stethoscope on him and was surprised that his heart rate was very rapid. I also detected a gurgle in his abdomen. We took him to our local vet B6, diagnosed him as having DCM and recommended that he be taken to Tufts. As we had had him at Tufts before, we immediately agreed and our vet made contact with Tufts and told us that they would be expecting us.

I might also note, retrospectively that approximately six months earlier, he was running in the backyard and let out an "idiopathic yelp", but without any disorientation or unusual behavior.

In the intervening six months and perhaps some months before he had numerous incidents of head tremors which were described by our vet as benign and idiopathic - but perhaps are not idiopathic and may be symptomatic of cardiovascular output issues.

B6 was admitted to Tufts on 11.05.2018 and spent 1-1/2 days in the ICU with our interfacing with Dr. B6 A medicinal regime was put in place (with minor modifications over the first few weeks in consultation with B6 The current dosages are as follows:

B6

We left Tufts with a prognosis of a 4-8 month potential survival with reasonable quality of life, but with sudden death a possibility at any time. We were also told that while DCM can be managed for an indeterminate period it is not a reversible condition.

His heart rate remained very high B6 for most of the first two months as did his resting respiration rate (mid 20's to mid 30's). Over the past two months his respiration rate has been quite

normal and his heart rate has not been visibly rapid (although I was surprised at the heart rate shown on the Kardia ecg app when I recorded it today at B6.

BEHAVIORAL CHANGES.

There have been numerous behavioral changes.

1. He sleeps a lot more than pre-incident.

2. His appetite has diminished considerably and B6 has had to be very creative to assure adequate nutrition. We started him out on the diet recommended by the Nutrition Dept consisting of Purina Pro Plan Adult Weight Management and Hill's Science Diet Adult Beef & Barley Entree. He basically refused this diet after our trying various ways to entice him to eat this. He also refused his prior diet of Earthborn Holistic Adult Weight Management Kibbles and Wellness grain free Beef, Chicken, Lamb, or Turkey. He kept losing weight and after consulting with B6, he suggested we feed him whatever it takes to maintain body mass. We started out with roasted chicken and rice. Whatever we fed him he seemed to lose interest in rather quickly. At one point we resorted to Hills Science Urgent Care a/d to stimulate his appetite. We now tend to feed him baked salmon, hamburger, steak, turkey, pork, halibut, etc. It is generally difficult to get him to eat other that at our dinner hour when he indicates he'll have the same thing we are having. We have also had some intermittent success with Dr. Marty's freeze dried raw meat, fish, poultry and eggs.

This is a dog that lived for food and exercise. He ate anything that we put in front of him with gusto and always had his head on my arm at meal time. He always wanted a dog biscuit when he came in from outside. Now he often has no interest in such a treat or will refuse 3 choices hoping to get what might be his current favorite.

3. We have had and continue to have considerable trouble with diarrhea. He'll be good for a few days then bad for a few days - but quite difficult to permanently stabilize.

4. He is not as assertive as he was pre-treatment as instead of bounding out the door and running around the property being a watchdog, he now walks out the door and waits to be sure I am with him.

QUALITY OF LIFE

I would say that once his respiration stabilized and his apparent heart rate appeared non burdensome, he has had a good quality of life. He thoroughly enjoys his walks and we take him out for 15 minute to 45 minute walks when the weather is reasonably comfortable. On colder days, if he stops walking due to me chatting with somebody, he will start shivering after a few minutes; but as long as he is moving he is fine. When a vehicle pulls into the driveway he goes into watch dog mode and barks loudly - although he misses some of the delivery trucks that do not ring the bell (which he never missed before). He maintains his very gentle charming self when not sleeping and enjoys a little ball playing in the house. He bounds up to the second floor bedroom as if everything is just fine.

MANAGEMENT

The two biggest management issues have been (1) diet and diarrhea and (2) frequent urination around the clock. B6 stays up with him until 12:00 - 2:00 a.m. and I get the graveyard shift with a wake-up generally between 2:00 and 4:00 a.m. where I accompany him outside for five to ten minutes with perhaps a wind chill of 10 degrees below zero. This is a feature of the B6 which has kept his lungs clear and his respiratory rate comfortable.

QUESTIONS

We are most interested in your evaluation and any suggestions that you might have for us.

Would any of the supplements that are prescribed for humans such as CoQ10, magnesium or arginine be of any value?

Would a raw food diet be of any benefit?

We are very grateful for the B6 days we have had with our pal. We were not sure he would last until we got back to B6 when we left Cummings. B6 was very responsive to any questions and suggested modifications to the protocol based on conditions presented once we were home. All the staff that we interacted with at Tufts were top notch.

Client: B6
Patient: B6

IDEXX BNP - 3/14/2019

IDEXX Reference Laboratories

Client: B6 Patient: B6

IDEXX VetConnect 1-888-433-9987

Client: B6
Patient: B6
Species: CANINE
Breed: DOBERMAN_PINSCH
Gender: MALE NEUTERED
Age: 9Y

Date: B6
Requisition #: 1A
Accession #: B6
Ordered by: B6

TUFTS UNIVERSITY
200 WESTBORO RD
NORTH GRAFTON, Massachusetts 01536
508-839-5395

Account #88933

CARDIOPET proBNP - CANINE

Test	Result	Reference Range	Low	Normal	High
CARDIOPET proBNP - CANINE	B6	0 - 900 pmol/L	HIGH	B6	

Comments:

1. B6

Please note: Complete interpretive comments for all concentrations of Cardiopet proBNP are available in the online directory of services. Serum specimens received at room temperature may have decreased NT-proBNP concentrations.

Page 1 of 1

03/19/2019 14:10 B6 B6 PAGE 01/06

B6

Attention:
B6
Phone: B6
Fax: B6

In regards to our 3/19/2019 visit with:
PATIENT: B6 Canine
ACCT NO: B6
OWNER:

Patient Medical History:
B6 is a 9y CM dobie who is evaluated today for inappetance that is likely induced by his current cardiac medications, as it has begun to improve since adjusting medications 4-5 days ago. He is currently happily eating a variety of human products and his people plan to start introducing some of the dog foods previously recommended by the nutrition department at Tufts. His DCM is being managed by cardiology at Tufts as well and a thyroid panel, leptospirosis panel are currently pending. Based on those results the plan is to check an amiodarone level provided the abdominal ultrasound he was sent here for does not reveal any underlying cause for his appetite. He was diagnosed with DCM and hospitalized for this about 4 months ago.

B6

Treatment Plan:

B6

Client Instructions:
We love your sweet boy and are happy not to have seen anything concerning in his abdomen today! We agree with the suspicion that his cardiac medications have led to the reduced appetite which has already started to improve. We discussed the concern for deficiencies in his current diet of a variety of healthy human food and you have reached out to the nutritionist at Tufts to discuss a supplement. You are also cautiously optimistic that he will eat some dog food with his improvement and will start to try and introduce the diets recommended by Tufts.

Please continue with his cardiac medications as previously directed.

Please let B6 know how things are going with him and if there is anything else we can help with for his care!

Thank you for letting us assist you in B6 care.

Sincerely,
B6 DVM DACVIM

Attachments: u/s report, discharge instruction

Transcription: B6 Edits: B6

If B6 is scheduled to return to B6 for further services, please forward any new medical history and lab work to B6 or fax to B6

03/19/2019 14:10 B6 B6 PAGE 03/06

B6

Sonographic Evaluation - Abdomen

Patient: B6
Owner:
Account Number: B6

Date: B6

Procedure Performed by: B6 DVM DACVIM

B6

Medical Discharge Instructions

B6

B6

Patient Update:

B6 is a 9y CM dobie who is evaluated today for inappetance that is likely induced by his current cardiac medications as it has begun to improve since adjusting medications 4-5 days ago. He is currently happily eating a variety of human products and his people plan to start introducing some of the previously recommended dog foods by the nutrition department at Tufts. His DCM is being managed by cardiology at Tufts as well and a thyroid panel, leptospirosis panel are currently pending. Based on those results the plan is to check an amiodarone level provided the abdominal ultrasound he was sent here for does not reveal any underlying cause for his appetite. He was diagnosed with DCM and hospitalized for this about 4 months ago.

B6

Discharge Instructions:

We love your sweet boy and are happy not to have seen anything concerning in his abdomen today! We agree with the suspicion that his cardiac medications have led to the reduced appetite which has already started to improve. We discussed the concern for deficiencies in his current diet of a variety of healthy human food and you have reached out to the nutritionist at Tufts to discuss a supplement. You are also cautiously optimistic that he will eat some dog food with his improvement and will start to try and introduce the diets recommended by Tufts.

B6 B6

Please continue with his cardiac medications as previously directed.

Please let B6 know how things are going with him and if there is anything else we can help with for his care!

Please call our office at B6 if you have any questions or concerns before your next scheduled progress exam. If you have a medical emergency outside of our normal office hours, please contact your regular veterinarian, or consult the list of emergency clinics below.

B6 DVM, DACVIM

B6

B6 B6

B6

Urinalysis

Date: B6

Doctor: B6

Cysto ☒

Catheter ☐

Freecatch ☐

B6

B6 (Dog)
Breed: Doberman Pinscher
Color: Black & Tan
Sex: Neutered Male Wt: 88.7 lbs
Birthday: B6 Age: 9y

Gross Examination: Color: Straw Appearance: Clear

Pellet: _____ Specific Gravity: 1.014

Strip Reading:

Urobili (mg/dL): ☒ normal ☐ 2 ☐ 4 ☐ 8

Glucose (mg/dL): ☒ negative ☐ 50 ☐ 100 ☐ 250 ☐ 500 ☐ 1000

Ketone (mg/dL): ☒ negative ☐ trace ☐ 15(+) ☐ 40(++) ☐ 80(+++) ☐ 160(++++)

Bilirubin: ☒ negative ☐ + ☐ ++ ☐ +++

Protein (mg/dL): ☐ negative ☒ trace ☐ 30(+) ☐ 100(++) ☐ 300(+++) ☐ 2000(++++)

Blood: ☒ negative Non-Hemolyzed ☐ trace ☐ moderate
Hemolyzed ☐ trace ☐ small(+) ☐ moderate (++) ☐ large(+++)

pH: ☐ 5 ☒ 6 ☐ 6.5 ☐ 7 ☐ 8 ☐ 9

Sediment Analysis: WBC: none RBC: none Bacteria: none

Casts: none

Crystals: rare amorph

Epithelium: none

Notes: _____

B6 SCANNED

03/21/2019 3:39:07 PM -0400 B6 PAGE 1 OF 1

B6

B6
B6

REPORT OF LABORATORY EXAMINATION

Client: B6

Owner: B6

3-7181 SM

Rcvd Date: 3/19/2019 3:40:00 PM
Admitted By: B6
Ordered By: N/A
Encounter: 02617248
CR#: AP

Animal: B6
Species: Canine
Age: 8 years
Tag/Reg ID:
Other ID:

MRN: 37181
Breed: Doberman Pinscher
Gender: Male, Castrated

Pending Order Summary

Received Date	Order Name	Status
03/18/2019	Endocrinology Interpretation	Ordered

Endocrinology

Endocrine Results

Collected Date/Time (If Provided)	03/18/2019 11:00:00		
Procedure		Ref Range	Units
Total Thyroxine (TT4) (RIA)	B6	[11-60]	nmol/L
Total Triiodothyronine (TT3) (RIA) *		[0.8-2.1]	nmol/L
Free T4 by dialysis (RIA)		[6-42]	pmol/L
T4 Autoantibody (RIA)		[0-20]	%
T3 Autoantibody (RIA)		[0-10]	%
Thyroid Stimulating Hormone (CLIA)		[0.00-0.58]	ng/mL
Thyroglobulin Autoantibody (ELISA) *		[0-35]	%

B6

L = Low Result; H = High Result; @ = Critical Result; ^ = Corrected Result; * = Interpretive Data; # = Result Footnote

Print Date/Time: 3/21/2019 3:39 PM

Page 1 of 1

B6 3/22

B6

Final Report

B6

Case#: B6
Accessioned: 03/20/19
Report Generated: 03/20/19 @ 3:35 PM by AS1
Results Last Modified: 03/20/19 @ 3:35 PM

37181 SM

Case ID	Owner	Coordinator
B6	B6	B6

Breed	Species	Sex / Fixed	Age
Doberman Pinscher	Canine (dog)	Male - Neutered /	B6 Years

Microbiology

Lepto Titer Verified: 03/20/19 3:27 PM by B6

Animal	L autumn	L brat	L can	L grip	L hard	L ict	L pom
B6							

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

Patient ID: B6
B6 Canine
B6 Years Old Male (Neutered) Doberman Pinscher
Black/Tan

Cardiology Appointment Report
ENROLLED IN DCM DIET STUDY

Date: B6

Attending Cardiologist:
☐ John E. Rush DVM, MS, DACVIM (Cardiology), DACVECC
B6

Cardiology resident:
B6

Cardiology Technician:
B6

Presenting Complaint:
recheck DCM

Concurrent Diseases:
B6

B6

B6

Muscle condition:

- ☐ Normal
- ☑ Mild muscle loss
- ☑ Moderate cachexia
- ☐ Marked cachexia

Cardiovascular Physical Exam:

Murmur Grade:

- ☑ None
- ☐ I/VI
- ☐ II/VI
- ☐ III/VI
- ☐ IV/VI
- ☐ V/VI
- ☐ VI/VI

Jugular vein:

- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [x] Good
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia: slow afib?
- [ ] None
- [ ] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [x] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
-DCM

Diagnostic plan:
- [ ] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

B6

Mitral inflow:
- [x] E waves present only –Afib

B6

B6

Assessment and recommendations:

Findings consistent with mild improvement in contractile function and decrease in LA size. It is unclear whether it is secondary to better control of ventricular rate, better management of DCM with pimobendan, or diet-induced DCM with improvement on systolic function.

Blood work revealed marked azotemia B6 increased liver values (T Bili B6 and cholesterol also elevated B6 dL). Liver enzymes and cholesterol elevation coud be secondary to amiodarone hepatic +/- thyroid toxicity, with concurrent overzealous diuresis; however the combination of elevated kidney and liver values could also be consistent with leptospirosis. Recommend B6 B6

B6

Final Diagnosis:

Dilated cardiomyopathy with atrial fibrillation - r/o primary DCM vs. diet induced DCM.
Azotemia - rule out secondary to furosemide vs primary renal disease vs infection
Elevated LFT - rule out amiodarone toxicity vs primary hepatopathy vs infection (leptospirosis v other)

Heart Failure Classification Score:

ISACHC Classification:

- ☐ Ia
- ☐ Ib
- ☑ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☐ B2
- ☑ C
- ☐ D

M-Mode		
IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Max LA		cm
TAPSE		cm
EPSS		cm
M-Mode Normalized		
IVSdN	B6	(0.290 - 0.520)
LVIDdN		(1.350 - 1.730)
LVPWdN		(0.330 - 0.530)
IVSsN		(0.430 - 0.710)
LVIDsN		(0.790 - 1.140) !
LVPWsN		(0.530 - 0.780)
2D		
SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
IVSd		cm
LVIDd		cm
EDV(Teich)		ml
LVPWd		cm
IVSs		cm
LVIDs		cm
ESV(Teich)		ml
EF(Teich)		%
ESV(Cube)		ml
EF(Cube)		%

%FS	B6	%
SV(Teich)		ml
SI(Teich)		ml/m
SV(Cube)		ml
SI(Cube)		ml/m
LVPWs		cm
LV Major		cm
LV Minor		cm
Sphericity Index		
LVLd LAX		cm
LVAd LAX		cm
LVEDV A-L LAX		ml
LVEDV MOD LAX		ml
LVLs LAX		cm
LVAs LAX		cm
LVESV A-L LAX		ml
LVESV MOD LAX		ml
HR		BPM
EF A-L LAX		%
LVEF MOD LAX		%
SV A-L LAX		ml
SV MOD LAX		ml
CO A-L LAX		l/min
CO MOD LAX		l/min
R-R		ms
HR		BPM
CO A-L LAX		l/min
CO MOD LAX		l/min

Doppler		
E'	B6	m/s
S'		m/s
IVRT		ms
AV Vmax		m/s
AV maxPG		mmHg

Cummings Veterinary Medical Center at Tufts University

Foster Hospital for Small Animals

55 Willard Street
North Grafton, MA 01536
(508) 839-5395

All Medical Records

Client: B6
Address:

Patient: B6
Breed: Doberman
DOB: B6

Species: Canine
Sex: Female (Spayed)

Home Phone: B6
Work Phone: ( ) -
Cell Phone: B6

Referring Information

B6

Client: B6
Patient:

Initial Complaint:
Cardiology Study Appointment

SOAP Text Aug 20 2018 1:58PM - B6

Initial Complaint:
Recheck - B6 - DCM study

SOAP Text Dec 12 2018 12:23PM - B6

Disposition/Recommendations

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
(508) 839-5395

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Doberman
Sex:	Female (Spayed)
Age:	B6

Lab Results Report

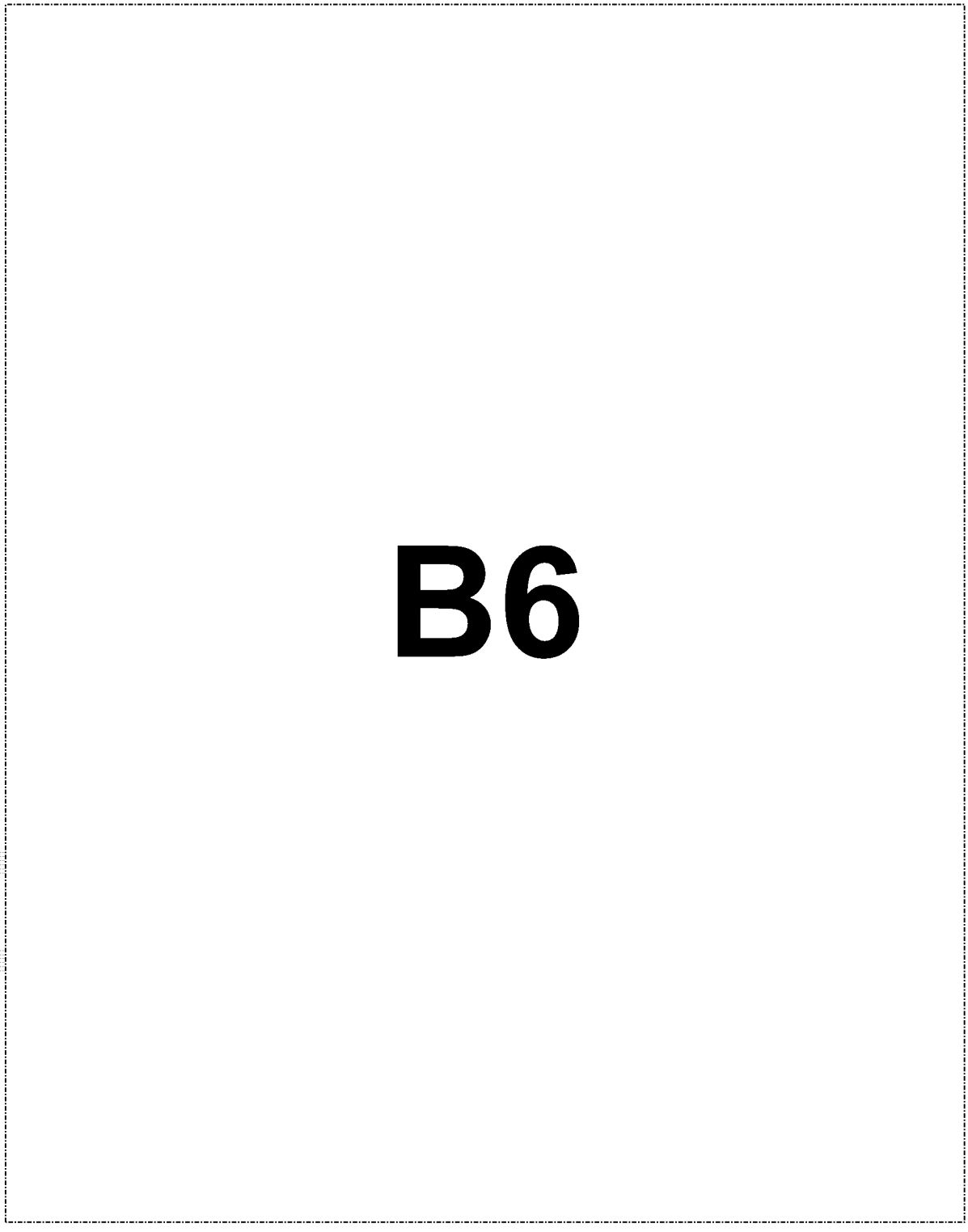
Accession ID:

Test	Results	Reference Range	Units

stringsoft

Printed Thursday, December 27, 2018

UCDavis Taurine Level



Lab Results IDEXX CARDIOPET proBNP 12/12/18

Client: B6
Patient:

Diet history 12/12/18

CARDIOLOGY DIET HISTORY FORM

Pet's name: B6

Client: **B6**
Patient:

Diet history 8/20/18

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: **B6** Owner's name: **B6** Today's date: 8/20/18

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)

   Example: Poor ________|______ Excellent

   Poor ____________________| Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
   ☐ Seems to prefer different foods than usual ☐ Other ____________

3. Over the last few weeks, has your pet (check one)
   ☐ Lost weight ☐ Gained weight ☒ Stayed about the same weight ☐ Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

   Food (include specific product and flavor) Form Amount How often? Fed since
   Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Autumn Grain Free Chicken, Lentil, & Sweet Potato Adult	dry	1 ½ cup	2x/day	Jan 2018
85% lean hamburger	microwaved	3 oz	1x/week	Jan 2018
Pupperoni original beef flavor	treat	½	1x/day	Aug 2018
Rawhide	treat	6 inch twist	1x/week	Dec 2015
[illegible] Free Run [illegible]		1.5 cups	2x/day	[illegible]
Blueberries, [illegible]		handful	[illegible] daily	
Apples, organic pumpkin		"	seasonal	
Bananas		½	[illegible] week	
organic peanut butter		[illegible]	[illegible]	
Boiled eggs		1	every other day	
Chicken		½ cup	1 day	[illegible]

*Any additional diet information can be listed on the back of this sheet

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☐ No		
Carnitine	☐ Yes ☐ No		
Antioxidants	☐ Yes ☐ No		
Multivitamin	☐ Yes ☐ No		
Fish oil	☐ Yes ☐ No		
Coenzyme Q10	☐ Yes ☐ No		
Other (please list):			
Example: Vitamin C		Nature's Bounty	500 mg tablets – 1 per day

6. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food
   ☐ I put them in a Pill Pocket or similar product
   ☒ I put them in foods (list foods): in peanutbutter / banana / canned food

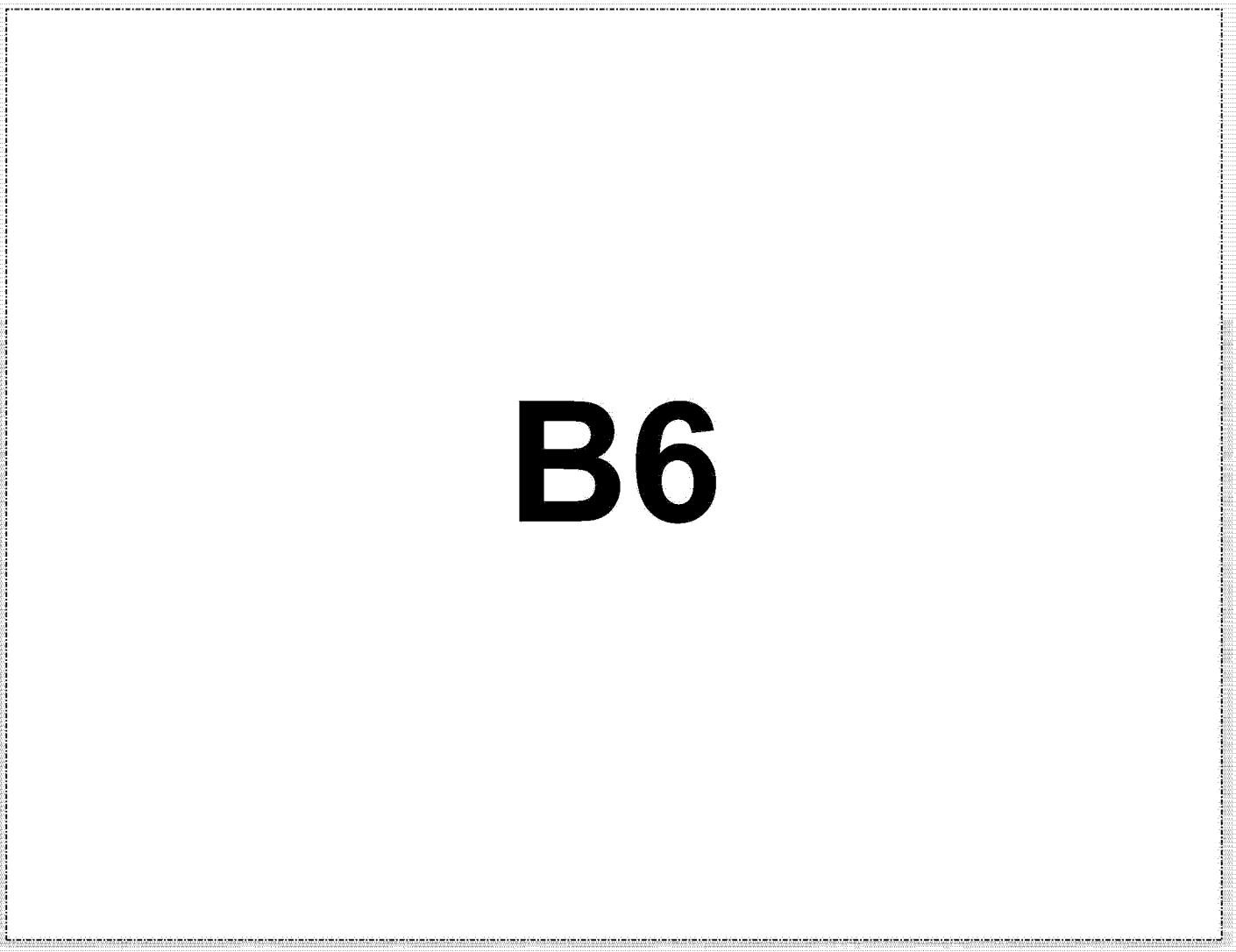
Client:
Patient: B6

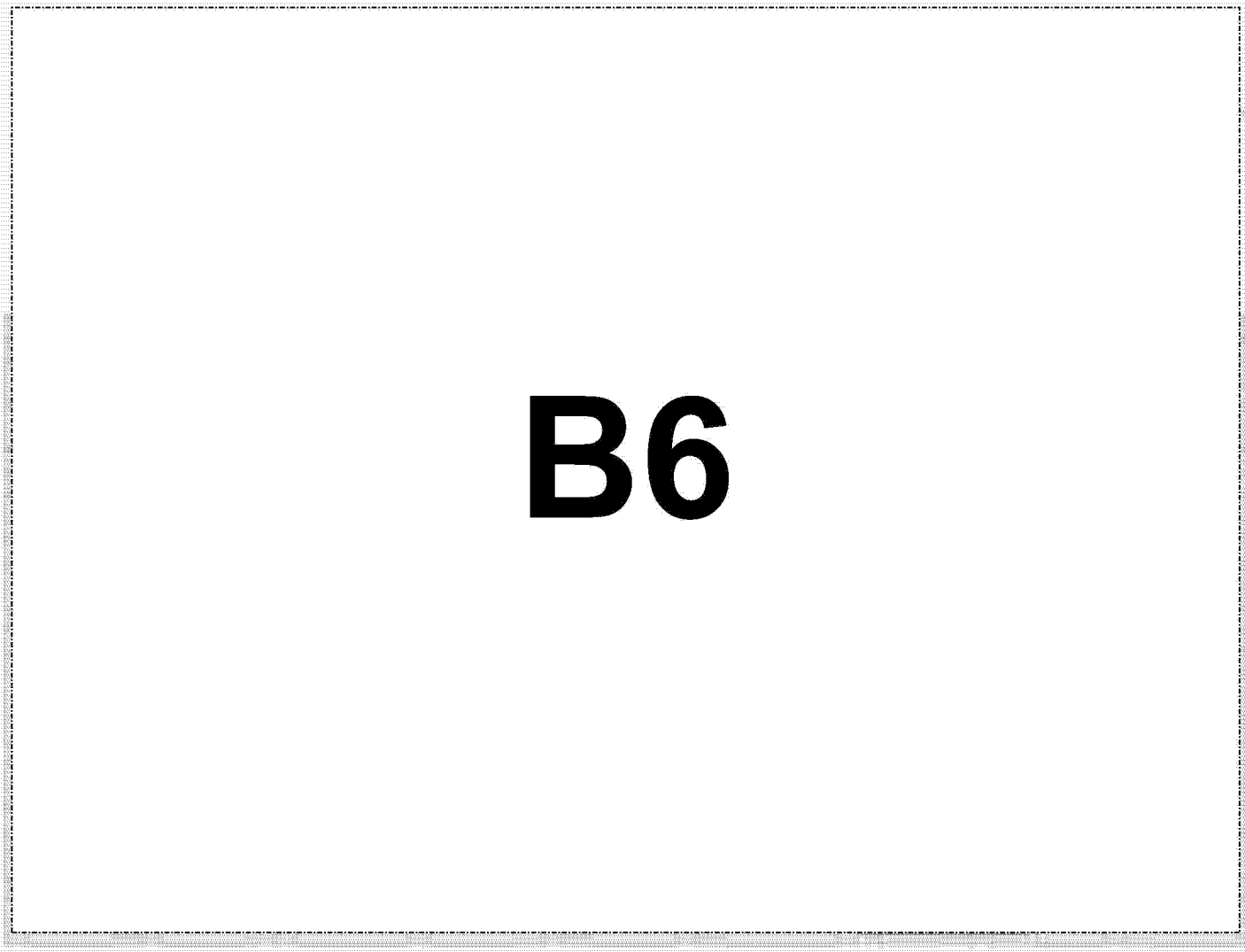
Vitals Results

8/20/2018 1:25:17 PM	Weight (kg)	38.1000

ECG from Cardio

ECG from Cardio

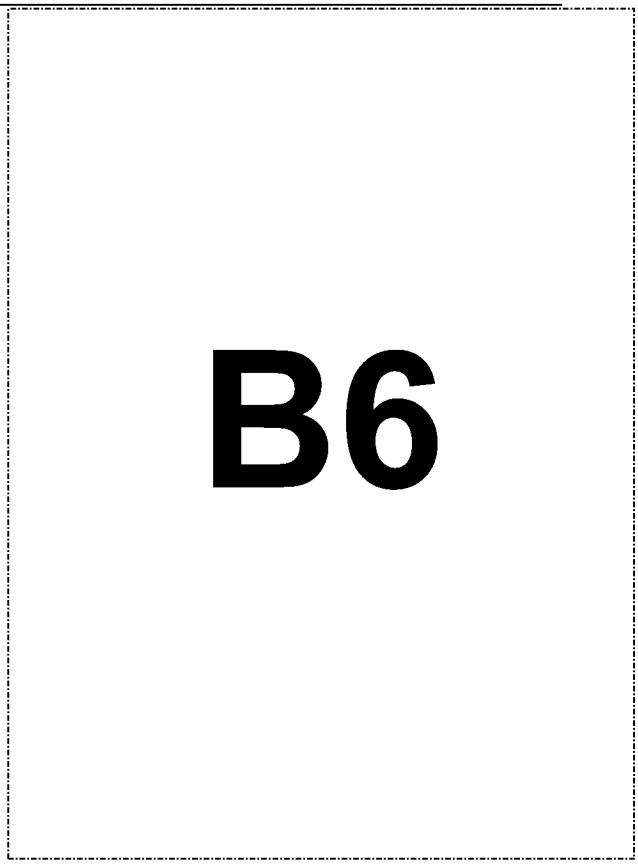




Client: B6
Patient:

Patient History

08/20/2018 12:48 PM	UserForm
08/20/2018 01:07 PM	Treatment
08/20/2018 01:20 PM	UserForm
08/20/2018 01:25 PM	Vitals
08/20/2018 01:26 PM	Purchase
08/20/2018 01:27 PM	Purchase
08/20/2018 01:27 PM	Purchase
10/17/2018 09:42 AM	Appointment
12/11/2018 07:22 PM	Appointment
12/12/2018 11:04 AM	UserForm
12/12/2018 11:07 AM	Treatment
12/12/2018 11:59 AM	Purchase
12/12/2018 11:59 AM	Purchase
12/12/2018 12:09 PM	UserForm
12/12/2018 12:24 PM	Purchase
12/12/2018 12:47 PM	Appointment



Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
56 Winward Street
North Grafton, MA 01536
Telephone: (508) 839-5395
Fax (508) 839-7956
http://vetmed.tufts.edu/

Discharge Instructions

Patient
Name: B6
Species: Canine
Breed/Sex: Female (Spayed) Doberman
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
B6

Cardiology Resident:
B6

Student: B6
Cardiology Technician:
B6

B6

B6

Cummings
Veterinary Medical Center
at Tufts University

B6

Patient ID: B6
B6 Center
B6 Canine Female Spayed Doberman Black/Tan

Cardiology Appointment Report

Date: 8/20/2018

Attending Cardiologist:

B6

Cardiology Resident:

B6

Cardiology Technician:

B6

Student: B6

B6

B6

B6

Assessment and recommendations:
Normal cardiac structure, although the contractile function is mildly decreased. This may be indicative of early cardiomyopathy. Taurine levels were submitted for analysis, and the patient will be switched off of the grain free diet. If contractile function is not improved at the 4 month rechecked despite change in diet, then we should submit a NT-proBNP to help us diagnose if the changes is indicated of primary DCM and not diet related.

Final Diagnosis:
Mild MMVD
R/O diet related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:
ISACHC Classification:
☑ IIa ☐ IIIa

☐ Ib ☐ IIb
☐ II

ACVIM Classification:
☐ A ☐ C
☒ B1 ☐ D
☐ B2

M-Mode

IVSd	cm
LVIDd	cm
LVPWd	cm
IVSs	cm
LVIDs	cm
LVPWs	cm
%FS	%
Ao Diam	cm
LA Diam	cm
LA/Ao	
Max LA	cm

M-Mode Normalized

IVSdN	(0.29 - 0.52)
LVIDdN	(1.35 - 1.73)
LVPWdN	(0.33 - 0.53)
IVSsN	(0.43 - 0.71) !
LVIDsN	(0.79 - 1.14) !
LVPWsN	(0.53 - 0.78) !
Ao Diam N	(0.68 - 0.89)
LA Diam N	(0.64 - 0.90)

2D

SA LA	cm
Ao Diam	cm
SA LA / Ao Diam	
LVId A4C	cm
LVEDV MOD A4C	ml
LVLs A4C	cm
LVESV MOD A4C	ml
LVEF MOD A4C	%
SV MOD A4C	ml

Doppler

MV E Vel	m/s
MV Dec T	ms
MV A Vel	m/s
MV E/A Ratio	
E'	m/s

B6

A'		m/s
E/E'		
PV Vmax		m/s
PV maxPG		mmHg
AV Vmax		m/s
AV maxPG		mmHg

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
56 Wilkins Street
North Grafton, MA 01536
Telephone: (508) 839-5395
Fax (508) 839-7956
http://vetmed.tufts.edu/

Discharge Instructions

Patient
Name: B6
Species: Canine
Breed/Sex: Female (Spayed) Doberman
B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
John E. Rush DVM, MS, DACVIM (Cardiology), DACVECC
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508.887.4676

B6

Patient ID: B6
B6 Gender
B6 Years Old Female (Spayed) Doberman Black/Tan

Cardiology Appointment Report

Date: 12/12/2018

Attending Cardiologist:
John E. Rush DVM, MS, DACVIM (Cardiology), DACVECC
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

B6

B6

B6

B6

Final Diagnosis:
– Very early DMVD
– Mild decreased contractile function r/o diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:
ISACHC Classifications:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classifications:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

M Mode	
IVSd	cm
LVIDd	cm
LVPWd	cm
IVSs	cm
LVIDs	cm
LVPWs	cm
LDV(Teich)	ml
LSV(Teich)	ml
EF(Teich)	%
%FS	%
SV(Teich)	ml
Ao Diam	cm
LA Diam	cm
LA/Ao	
Max LA	cm

2D	
SA LA	cm
Ao Diam	cm
SA LA / Ao Diam	
IVSd	cm
LVIDd	cm
LVPWd	cm
LDV(Teich)	ml
IVSs	cm
LVIDs	cm

B6

LVPWs		cm
LSV(Teich)		ml
LF(Teich)		%
%FS		%
SV(Teich)		ml
LVId A4C		cm
LVEDV MOD A4C		ml
LVIs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml
	B6	
Doppler		
MV E Vel		m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
30 Wilard Street
North Grafton, MA 01536
Telephone: (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6

B6

B6 Female (Spayed)
Canine Doberman Black/Tan

B6

9/24/2018

Dear D B6

Thank you for referring B6 with their p B6

If you have any questions, or concerns, please contact us at (508) 887-4088.

Thank you,

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
30 Wilard Street
North Grafton, MA 01536
Telephone: (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6

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B6

B6 female (Spayed)
Canine Doberman Black/Tan

12/19/2018

Dear Dr B6

Thank you for referring B6 with their pe B6

If you have any questions, or concerns, please contact us at (508) 887-4988.

Thank you,

B6